

Fitting genotype by environment models in sommer

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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 on 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, specifying heterogeneous variances, and obtaining other parameters such as BLUPs, BLUEs, residuals, fitted values, variances for fixed and random effects, etc.

The purpose of this vignette is to show how to fit different genotype by environment (GxE) models using the sommer package:

- 1) Single environment model
- 2) Multienvironment model: Main effect model
- 3) Multienvironment model: Diagonal model (DG)
- 4) Multienvironment model: Compound symmetry model (CS)
- 5) Multienvironment model: Unstructured model (US)
- 6) Multienvironment model: Random regression model (RR)
- 7) Multienvironment model: Other covariance structures for GxE
- 8) Finlay-Wilkinson regression
- 9) Two stage analysis

When the breeder decides to run a trial and apply selection in a single environment (whether because the amount of seed is a limitation or there's no availability for a location) the breeder takes the risk of selecting material for a target population of environments (TPEs) using an environment that is not representative of the larger TPE. Therefore, many breeding programs try to base their selection decision on multi-environment trial (MET) data. Models could be adjusted by adding additional information like spatial information, experimental design information, etc. In this tutorial we will focus mainly on the covariance structures for GxE and the incorporation of relationship matrices for the genotype effect.

1) Single environment model

A single-environment model is the one that is fitted when the breeding program can only afford one location, leaving out the possible information available from other environments. This will be used to further expand to GxE models.

```
library(sommer)
data(DT_example)
DT <- DT_example
A <- A_example

ansSingle <- mmer(Yield~1,
                  random= ~ vsr(Name, Gu=A),
                  rcov= ~ units,
```

```

      data=DT, verbose = FALSE)
summary(ansSingle)

## =====
##           Multivariate Linear Mixed Model fit by REML
## ***** sommer 4.1 *****
## =====
##           logLik      AIC      BIC Method Converge
## Value -78.80875 159.6175 162.8378      NR      TRUE
## =====
## Variance-Covariance components:
##           VarComp VarCompSE Zratio Constraint
## u:Name.Yield-Yield  6.529      2.202  2.965  Positive
## units.Yield-Yield  13.868      1.633  8.494  Positive
## =====
## Fixed effects:
##   Trait      Effect Estimate Std.Error t.value
## 1 Yield (Intercept)    11.74    0.4876   24.07
## =====
## Groups and observations:
##      Yield
## u:Name    41
## =====
## Use the '$' sign to access results and parameters
# or
Ai <- as(solve(A), Class="sparseMatrix")
ansSingle <- mmec(Yield~1,
  random= ~ vsc(isc(Name), Gu=Ai),
  rcov= ~ units,
  data=DT, verbose = FALSE)
summary(ansSingle)

## =====
##           Multivariate Linear Mixed Model fit by REML
## ***** sommer 4.1 *****
## =====
##           logLik      AIC      BIC Method Converge
## Value -359.0031 720.0062 723.2265      AI      TRUE
## =====
## Variance-Covariance components:
##           VarComp VarCompSE Zratio Constraint
## Name:Ai:isc:isc  6.497      1.479  4.392  Positive
## units:isc:isc   13.868      1.798  7.711  Positive
## =====
## Fixed effects:
##           Estimate Std.Error t.value
## (Intercept)    11.74    0.4862   24.14
## =====
## Use the '$' sign to access results and parameters

```

In this model, the only term to be estimated is the one for the germplasm (here called `Name`). For the sake of example we have added a relationship matrix among the levels of the random effect `Name`. This is just a diagonal matrix with as many rows and columns as levels present in the random effect `Name`, but any other non-diagonal relationship matrix could be used.

2) MET: main effect model

A multi-environment model is the one that is fitted when the breeding program can afford more than one location. The main effect model assumes that GxE doesn't exist and that the main genotype effect plus the fixed effect for environment is enough to predict the genotype effect in all locations of interest.

```
ansMain <- mmer(Yield~Env,
               random= ~ vsr(Name, Gu=A),
               rcov= ~ units,
               data=DT, verbose = FALSE)
summary(ansMain)
```

```
## =====
##           Multivariate Linear Mixed Model fit by REML
## ***** sommer 4.1 *****
## =====
##           logLik      AIC      BIC Method Converge
## Value -32.59421 71.18842 80.84949      NR      TRUE
## =====
## Variance-Covariance components:
##           VarComp VarCompSE Zratio Constraint
## u:Name.Yield-Yield  4.856    1.5233  3.188    Positive
## units.Yield-Yield   8.109    0.9615  8.434    Positive
## =====
## Fixed effects:
##   Trait      Effect Estimate Std.Error t.value
## 1 Yield (Intercept)   16.385    0.5849  28.012
## 2 Yield EnvCA.2012    -5.688    0.5741  -9.908
## 3 Yield EnvCA.2013    -6.218    0.6107 -10.182
## =====
## Groups and observations:
##           Yield
## u:Name      41
## =====
## Use the '$' sign to access results and parameters
# or
```

```
Ai <- as(solve(A), Class="sparseMatrix")
ansMain <- mmec(Yield~Env,
               random= ~ vsc(isc(Name), Gu=Ai),
               rcov= ~ units,
               data=DT, verbose = FALSE)
summary(ansMain)
```

```
## =====
##           Multivariate Linear Mixed Model fit by REML
## ***** sommer 4.1 *****
## =====
##           logLik      AIC      BIC Method Converge
## Value -313.3005 632.6011 642.2621      AI      TRUE
## =====
## Variance-Covariance components:
##           VarComp VarCompSE Zratio Constraint
## Name:Ai:isc:isc   4.852    1.449  3.349    Positive
```

```
## units:isc:isc      8.109      1.807  4.487   Positive
## =====
## Fixed effects:
##      Estimate Std.Error t.value
## Intercept    16.385    0.5847 28.021
## CA.2012      -5.688    0.5740 -9.909
## CA.2013      -6.219    0.6107 -10.183
## =====
## Use the '$' sign to access results and parameters
```

3) MET: diagonal model (DG)

A multi-environment model is the one that is fitted when the breeding program can afford more than one location. The diagonal model assumes that GxE exists and that the genotype variation is expressed differently at each location, therefore fitting a variance component for the genotype effect at each location. The main drawback is that this model assumes no covariance among locations, as if genotypes were independent (despite the fact that is the same genotypes). The fixed effect for environment plus the location-specific BLUP is used to predict the genotype effect in each locations of interest.

```
ansDG <- mmer(Yield~Env,
              random= ~ vsr(dsr(Env),Name, Gu=A),
              rcov= ~ units,
              data=DT, verbose = FALSE)
summary(ansDG)

## =====
##      Multivariate Linear Mixed Model fit by REML
## ***** sommer 4.1 *****
## =====
##      logLik      AIC      BIC Method Converge
## Value -21.04157 48.08315 57.74421      NR      TRUE
## =====
## Variance-Covariance components:
##      VarComp VarCompSE Zratio Constraint
## CA.2011:Name.Yield-Yield 17.493    6.1099 2.863   Positive
## CA.2012:Name.Yield-Yield  5.337    1.7662 3.022   Positive
## CA.2013:Name.Yield-Yield  7.884    2.5526 3.089   Positive
## units.Yield-Yield        4.381    0.6493 6.747   Positive
## =====
## Fixed effects:
##      Trait      Effect Estimate Std.Error t.value
## 1 Yield (Intercept)  16.621    0.948 17.532
## 2 Yield EnvCA.2012   -5.958    1.045 -5.699
## 3 Yield EnvCA.2013   -6.662    1.098 -6.067
## =====
## Groups and observations:
##      Yield
## CA.2011:Name 41
## CA.2012:Name 41
## CA.2013:Name 41
## =====
## Use the '$' sign to access results and parameters
```

```
# or
Ai <- as(solve(A), Class="sparseMatrix")
ansDG <- mmec(Yield~Env,
              random= ~ vsc(dsc(Env),isc(Name), Gu=Ai),
              rcov= ~ units,
              data=DT, verbose = FALSE)
summary(ansDG)

## =====
##           Multivariate Linear Mixed Model fit by REML
## ***** sommer 4.1 *****
## =====
##           logLik      AIC      BIC Method Converge
## Value -301.9224 609.8449 619.506      AI      TRUE
## =====
## Variance-Covariance components:
##           VarComp VarCompSE Zratio Constraint
## Env:Name:AI:CA.2011:CA.2011 15.792      3.405 4.638 Positive
## Env:Name:AI:CA.2012:CA.2012  5.192      2.846 1.825 Positive
## Env:Name:AI:CA.2013:CA.2013  7.717      2.947 2.618 Positive
## units:isc:isc              4.744      2.362 2.009 Positive
## =====
## Fixed effects:
##           Estimate Std.Error t.value
## Intercept    16.622     0.911 18.245
## CA.2012      -5.962     1.012 -5.888
## CA.2013      -6.664     1.067 -6.249
## =====
## Use the '$' sign to access results and parameters
```

4) MET: compound symmetry model (CS)

A multi-environment model is the one that is fitted when the breeding program can afford more than one location. The compound symmetry model assumes that GxE exists and that a main genotype variance-covariance component is expressed across all location. In addition, it assumes that a main genotype-by-environment variance is expressed across all locations. The main drawback is that the model assumes the same variance and covariance among locations. The fixed effect for environment plus the main effect for BLUP plus genotype-by-environment effect is used to predict the genotype effect in each location of interest.

```
E <- diag(length(unique(DT$Env)))
rownames(E) <- colnames(E) <- unique(DT$Env)
EA <- kronecker(E,A, make.dimnames = TRUE)
ansCS <- mmer(Yield~Env,
              random= ~ vsr(Name, Gu=A) + vsr(Env:Name, Gu=EA),
              rcov= ~ units,
              data=DT, verbose = FALSE)
summary(ansCS)

## =====
##           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
## u:Name.Yield-Yield      3.682      1.691  2.177   Positive
## u: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
## u:Name      41
## u:Env:Name  123
## =====
## Use the '$' sign to access results and parameters

## or
E <- diag(length(unique(DT$Env)));rownames(E) <- colnames(E) <- unique(DT$Env)
Ei <- solve(E)
Ai <- solve(A)
EAI <- kronecker(Ei,Ai, make.dimnames = TRUE)
Ei <- as(Ei, Class="sparseMatrix")
Ai <- as(Ai, Class="sparseMatrix")
EAI <- as(EAI, Class="sparseMatrix")
ansCS <- mmec(Yield~Env,
              random= ~ vsc(isc(Name), Gu=Ai) + vsc(isc(Env:Name), Gu=EAI),
              rcov= ~ units,
              data=DT, verbose = FALSE)
summary(ansCS)

## =====
##           Multivariate Linear Mixed Model fit by REML
## ***** sommer 4.1 *****
## =====
##           logLik      AIC      BIC Method Converge
## Value -300.8632 607.7264 617.3875      AI      TRUE
## =====
## Variance-Covariance components:
##           VarComp VarCompSE Zratio Constraint
## Name:AI:isc:isc      3.703      1.884  1.966   Positive
## Env:Name:EAI:isc:isc  5.132      2.428  2.114   Positive
## units:isc:isc        4.466      2.295  1.946   Positive
## =====
## Fixed effects:
##           Estimate Std.Error t.value
## Intercept  16.496      0.6863  24.035
## CA.2012    -5.777      0.7564  -7.637
## CA.2013    -6.380      0.7967  -8.008
## =====
## Use the '$' sign to access results and parameters
```

5) MET: unstructured model (US)

A multi-environment model is the one that is fitted when the breeding program can afford more than one location. The unstructured model is the most flexible model assuming that GxE exists and that an environment-specific variance exists in addition to as many covariances for each environment-to-environment combinations. The main drawback is that is difficult to make this models converge because of the large number of variance components, the fact that some of these variance or covariance components are zero, and the difficulty in choosing good starting values. The fixed effect for environment plus the environment specific BLUP (adjusted by covariances) is used to predict the genotype effect in each location of interest.

```
ansUS <- mmer(Yield~Env,
              random= ~ vsr(usr(Env),Name, Gu=A),
              rcov= ~ units,
              data=DT, verbose = FALSE)
summary(ansUS)
```

```
## =====
##           Multivariate Linear Mixed Model fit by REML
## ***** sommer 4.1 *****
## =====
##           logLik      AIC      BIC Method Converge
## Value -14.20951 34.41901 44.08008      NR      TRUE
## =====
## Variance-Covariance components:
##           VarComp VarCompSE Zratio Constraint
## CA.2011:Name.Yield-Yield      15.994      5.381  2.972  Positive
## CA.2012:CA.2011:Name.Yield-Yield  6.172      2.503  2.465  Unconstr
## CA.2012:Name.Yield-Yield      5.273      1.750  3.013  Positive
## CA.2013:CA.2011:Name.Yield-Yield  6.366      3.069  2.074  Unconstr
## CA.2013:CA.2012:Name.Yield-Yield  0.376      1.535  0.245  Unconstr
## CA.2013:Name.Yield-Yield      7.689      2.490  3.088  Positive
## units.Yield-Yield      4.386      0.650  6.748  Positive
## =====
## Fixed effects:
##   Trait      Effect Estimate Std.Error t.value
## 1 Yield (Intercept)  16.341      0.8141  20.072
## 2 Yield  EnvCA.2012   -5.696      0.7406  -7.692
## 3 Yield  EnvCA.2013   -6.286      0.8202  -7.664
## =====
## 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
```

```
# adjust variance BLUPs by adding covariances
# ansUS$U[1:6] <- unsBLUP(ansUS$U[1:6])

# or
Ai <- solve(A)
```

```

Ai <- as(Ai, Class="sparseMatrix")
ansUS <- mmec(Yield~Env,
              random= ~ vsc(usc(Env),isc(Name), Gu=Ai),
              rcov= ~ units,
              data=DT, verbose = FALSE)
summary(ansUS)

## =====
##           Multivariate Linear Mixed Model fit by REML
## ***** sommer 4.1 *****
## =====
##           logLik      AIC      BIC Method Converge
## Value -302.6944 611.3888 621.0499      AI      TRUE
## =====
## Variance-Covariance components:
##           VarComp VarCompSE Zratio Constraint
## Env:Name:AI:CA.2011:CA.2011  14.002      3.305 4.2366  Positive
## Env:Name:AI:CA.2011:CA.2012   4.951      1.785 2.7728  Unconstr
## Env:Name:AI:CA.2012:CA.2012   4.394      2.202 1.9956  Positive
## Env:Name:AI:CA.2011:CA.2013   6.145      2.427 2.5315  Unconstr
## Env:Name:AI:CA.2012:CA.2013   0.604      1.759 0.3433  Unconstr
## Env:Name:AI:CA.2013:CA.2013   7.946      2.774 2.8646  Positive
## units:isc:isc                2.663      1.770 1.5040  Positive
## =====
## Fixed effects:
##           Estimate Std.Error t.value
## Intercept    16.341    0.7432  21.987
## CA.2012      -5.685    0.6740  -8.435
## CA.2013      -6.265    0.7418  -8.446
## =====
## Use the '$' sign to access results and parameters

```

6) MET: random regression model

A multi-environment model is the one that is fitted when the breeding program can afford more than one location. The random regression model assumes that the environment can be seen as a continuous variable and therefore a variance component for the intercept and a variance component for the slope can be fitted. The number of variance components will depend on the order of the Legendre polynomial fitted.

```

library(orthopolynom)
DT$EnvN <- as.numeric(as.factor(DT$Env))
ansRR <- mmer(Yield~Env,
              random= ~ vsr(leg(EnvN,1),Name),
              rcov= ~ units,
              data=DT, verbose = FALSE)
summary(ansRR)

## =====
##           Multivariate Linear Mixed Model fit by REML
## ***** sommer 4.1 *****
## =====
##           logLik      AIC      BIC Method Converge
## Value -27.70318 61.40636 71.06743      NR      TRUE
## =====

```



```
## Variance-Covariance components:
##               VarComp VarCompSE Zratio Constraint
## leg0:Name.Yield-Yield 10.392    3.1473  3.302   Positive
## leg1:Name.Yield-Yield  2.079    0.9792  2.123   Positive
## units.Yield-Yield     6.297    0.8442  7.459   Positive
## =====
## Fixed effects:
##   Trait      Effect Estimate Std.Error t.value
## 1 Yield (Intercept) 16.541    0.6770  24.432
## 2 Yield  EnvCA.2012  -5.832    0.6425  -9.078
## 3 Yield  EnvCA.2013  -6.472    0.8239  -7.854
## =====
## Groups and observations:
##           Yield
## leg0:Name    41
## leg1:Name    41
## =====
## Use the '$' sign to access results and parameters
```

or

```
ansRR <- mmec(Yield~Env,
              random= ~ vsc(dsc(leg(EnvN,1)),isc(Name)),
              rcov= ~ units,
              data=DT, verbose = FALSE)
summary(ansRR)
```

```
## =====
##           Multivariate Linear Mixed Model fit by REML
## ***** sommer 4.1 *****
## =====
##           logLik      AIC      BIC Method Converge
## Value -308.4122 622.8243 632.4854      AI      TRUE
## =====
## Variance-Covariance components:
##               VarComp VarCompSE Zratio Constraint
## EnvN:Name:leg0:leg0 10.276    2.313  4.442   Positive
## EnvN:Name:leg1:leg1  2.086    1.756  1.188   Positive
## units:isc:isc       6.430    1.998  3.218   Positive
## =====
## Fixed effects:
##           Estimate Std.Error t.value
## Intercept 16.542    0.6745  24.523
## CA.2012   -5.833    0.6405  -9.107
## CA.2013   -6.473    0.8217  -7.877
## =====
## Use the '$' sign to access results and parameters
```

In addition, an unstructured, diagonal or other variance-covariance structure can be put on top of the polynomial model:

```
library(orthopolynom)
DT$EnvN <- as.numeric(as.factor(DT$Env))
ansRR <- mmer(Yield~Env,
              random= ~ vsr(usr(leg(EnvN,1)),Name),
              rcov= ~ units,
```

```

data=DT, verbose = FALSE)
summary(ansRR)

## =====
##           Multivariate Linear Mixed Model fit by REML
## ***** sommer 4.1 *****
## =====
##           logLik      AIC      BIC Method Converge
## Value -25.56967 57.13935 66.80042      NR      TRUE
## =====
## Variance-Covariance components:
##           VarComp VarCompSE Zratio Constraint
## leg0:Name.Yield-Yield      10.791      3.2745 3.295 Positive
## leg1:leg0:Name.Yield-Yield -2.428      1.3699 -1.772 Unconstr
## leg1:Name.Yield-Yield      2.286      1.0404 2.197 Positive
## units.Yield-Yield          6.260      0.8421 7.434 Positive
## =====
## Fixed effects:
##   Trait      Effect Estimate Std.Error t.value
## 1 Yield (Intercept) 16.501      0.7778 21.216
## 2 Yield EnvCA.2012 -5.791      0.6704 -8.638
## 3 Yield EnvCA.2013 -6.476      0.8554 -7.570
## =====
## Groups and observations:
##           Yield
## leg0:Name      41
## leg1:leg0:Name 82
## leg1:Name      41
## =====
## Use the '$' sign to access results and parameters

# or

ansRR <- mmec(Yield~Env,
              random= ~ vsc(usc(leg(EnvN,1)),isc(Name)),
              rcov= ~ units,
              data=DT, verbose = FALSE)
summary(ansRR)

## =====
##           Multivariate Linear Mixed Model fit by REML
## ***** sommer 4.1 *****
## =====
##           logLik      AIC      BIC Method Converge
## Value -309.2045 624.409 634.0701      AI      TRUE
## =====
## Variance-Covariance components:
##           VarComp VarCompSE Zratio Constraint
## EnvN:Name:leg0:leg0 10.5273      2.262 4.6532 Positive
## EnvN:Name:leg0:leg1 0.1493      1.468 0.1017 Unconstr
## EnvN:Name:leg1:leg1 2.0889      1.954 1.0691 Positive
## units:isc:isc      7.2282      2.126 3.4003 Positive
## =====
## Fixed effects:

```

```
##           Estimate Std.Error t.value
## Intercept    16.541     0.6916  23.916
## CA.2012      -5.836     0.6707  -8.703
## CA.2013      -6.471     0.8498  -7.614
## =====
## Use the '$' sign to access results and parameters
```

7) Other GxE covariance structures

Although not very commonly used in GxE models, the autoregressive of order 1 (AR1) and other covariance structures could be used in the GxE modeling. Here we show how to do it (not recommending it).

```
E <- AR1(DT$Env) # can be AR1() or CS(), etc.
rownames(E) <- colnames(E) <- unique(DT$Env)
EA <- kronecker(E,A, make.dimnames = TRUE)
ansCS <- mmer(Yield~Env,
              random= ~ vsr(Name, Gu=A) + vsr(Env:Name, Gu=EA),
              rcov= ~ units,
              data=DT, verbose = FALSE)
summary(ansCS)

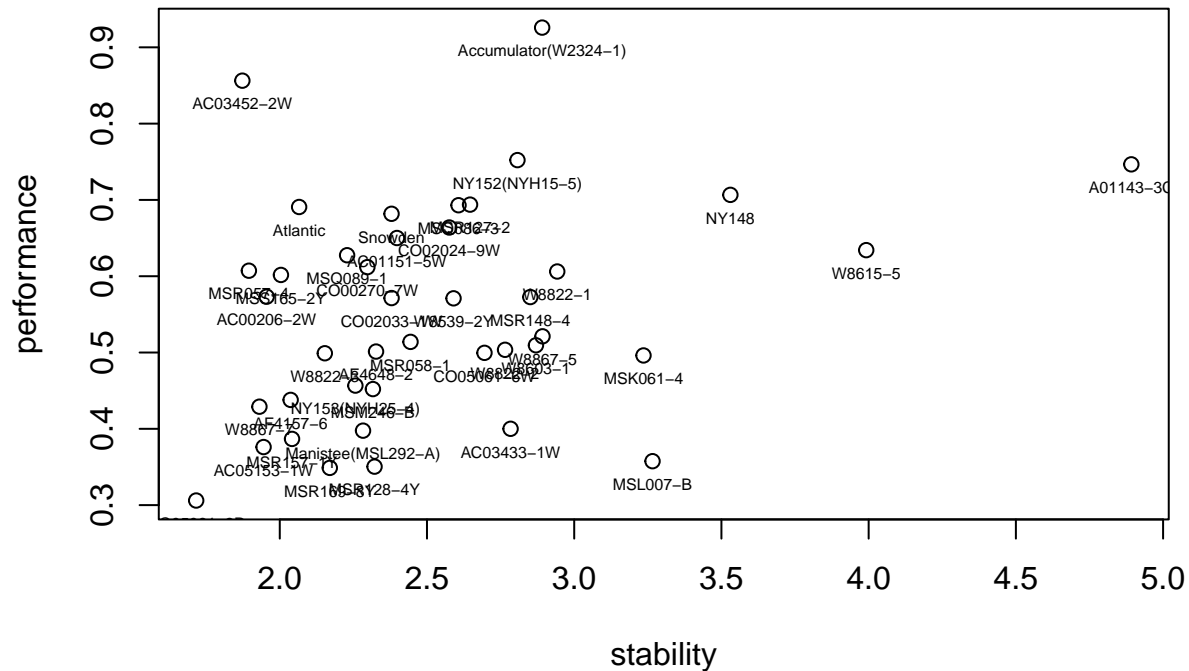
## =====
##           Multivariate Linear Mixed Model fit by REML
## ***** sommer 4.1 *****
## =====
##           logLik      AIC      BIC Method Converge
## Value -19.39067 44.78134 54.4424      NR      TRUE
## =====
## Variance-Covariance components:
##           VarComp VarCompSE Zratio Constraint
## u:Name.Yield-Yield      2.225      1.7536  1.269      Positive
## u:Env:Name.Yield-Yield    6.424      1.8293  3.512      Positive
## units.Yield-Yield        4.334      0.6418  6.752      Positive
## =====
## Fixed effects:
##   Trait      Effect Estimate Std.Error t.value
## 1 Yield (Intercept)    16.484     0.6735  24.474
## 2 Yield  EnvCA.2012    -5.780     0.7365  -7.848
## 3 Yield  EnvCA.2013    -6.372     0.7799  -8.170
## =====
## Groups and observations:
##           Yield
## u:Name         41
## u:Env:Name     123
## =====
## Use the '$' sign to access results and parameters
```

8) Finlay-Wilkinson regression

```
data(DT_h2)
DT <- DT_h2
```



```
pp <- predict(mix2,Dtable = Dt, D="Name")
preds <- pp$pvals
# preds[with(preds, order(-predicted.value)), ]
## performance vs stability (deviation from regression line)
plot(preds[,2]~e, ylab="performance", xlab="stability")
text(y=preds[,2],x=e, labels = rownames(mu), cex=0.5, pos = 1)
```



9) Two stage analysis

It is common then to fit a first model that accounts for the variation of random design elements, e.g., locations, years, blocks, and fixed genotype effects to obtain the estimated marginal means (EMMs) or best linear unbiased estimators (BLUES) as adjusted entry means. These adjusted entry means are then used as the phenotype or response variable in GWAS and genomic prediction studies.

```
#####
## stage 1
## use mmer for dense field trials
#####
data(DT_h2)
DT <- DT_h2
head(DT)
```

```
##           Name      Env Loc Year      Block y
## 1      W8822-3 FL.2012  FL 2012 FL.2012.1 2
## 2      W8867-7 FL.2012  FL 2012 FL.2012.2 2
## 3      MSL007-B MO.2011  MO 2011 MO.2011.1 3
## 4      CO00270-7W FL.2012  FL 2012 FL.2012.2 3
## 5 Manistee(MSL292-A) FL.2013  FL 2013 FL.2013.2 3
## 6      MSM246-B FL.2012  FL 2012 FL.2012.2 3
```

```
envs <- unique(DT$Env)
BLUEL <- list()
```

```

XtXL <- list()
for(i in 1:length(envs)){
  ans1 <- mmer(y~Name-1,
              random=~Block,
              verbose=FALSE,
              data=droplevels(DT[which(DT$Env == envs[i]),]
              )
  )
  ans1$Beta$Env <- envs[i]

  BLUEL[[i]] <- ans1$Beta
  XtXL[[i]] <- ans1$VarBeta
}

DT2 <- do.call(rbind, BLUEL)
OM <- do.call(adiag1,XtXL)

#####
## stage 2
## use mmec for sparse equation
#####
m <- matrix(1/var(DT2$Estimate, na.rm = TRUE))
ans2 <- mmec(Estimate~Env,
             random=~Effect + Env:Effect,
             rcov=~vsc(isc(units,thetaC = matrix(3), theta = m)),
             W=OM,
             verbose=FALSE,
             data=DT2
             )

## Using the weights matrix
summary(ans2)$varcomp

```

```

##
## Effect:isc:isc      2.463610 0.2275963 10.8244720 Positive
## Env:Effect:isc:isc  5.754576 0.6055289  9.5033881 Positive
## units:m:           1.000000 1.8910611  0.5288036 Fixed

```

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.