

Alencar Xavier

- Quantitative Geneticist, Corteva Agrisciences
- Adjunct Professor at Purdue University
- <https://alenxav.github.io/>

Outline

- Get data
- Build GRM
- Statistical model
- Matrices
- Henderson's equation
- Reduced animal model
- Variance of BLUEs
- Projection matrices
- BLUP solutions
- Variance of BLUPs
- Reliability
- Accuracy
- REML
- Expectation-Maximization
- Pseudo-Expectation
- MIVQUE
- Average-Information
- Gibbs sampling
- Marker effects
- Final remarks

Get some data

The code below fetches soybean data, a small subset from the SoyNAM project. We use two families (5,15) as training set, one (04) as prediction target. Phenotypes come from 10 incomplete blocks observed over 3 years.

```
tr = function(x) sum(diag(x)) # Trace function
data(met, package='NAM')
Obs$Sp = with(Obs, NAM::SPC(YLD, Block, Row, Col, 4, 4))
Obs$Block = factor(Obs$Block)
Gen2 = data.matrix(Gen[grep('-04', rownames(Gen)),])
Gen = data.matrix(Gen[grep('-05|-15', rownames(Gen)),])
Obs = droplevels(Obs[grep('-05|-15', Obs$ID),])
Obs = Obs[,c('Block', 'Sp', 'ID', 'YLD')]
Gen = Gen[,apply(Gen, 2, var)>0.1] # Observed individuals
Gen2 = Gen2[,colnames(Gen)] # Prediction target
```

Get some data

```
dim(Obs)
## [1] 1117      4
dim(Gen)
## [1] 280 3974
head(Obs)
##       Block      Sp        ID     YLD
## 16      9 56.56612 DS11-15004 52.16
## 28      7 55.90857 DS11-05089 68.25
## 36      8 57.66000 DS11-05042 58.94
## 76      3 66.27364 DS11-05156 75.38
## 83      9 56.98647 DS11-15133 66.93
## 113     8 53.03104 DS11-15119 72.64
```

Build GRM

From [Habier et al. 2007](#) and [VanRaden 2008](#), we have

$$A = \frac{(M - P)(M - P)'}{2\sum(1 + f_j)p_j(1 - p_j)}$$

Pre-center the markers ($\tilde{Z} = M - P$), then you get

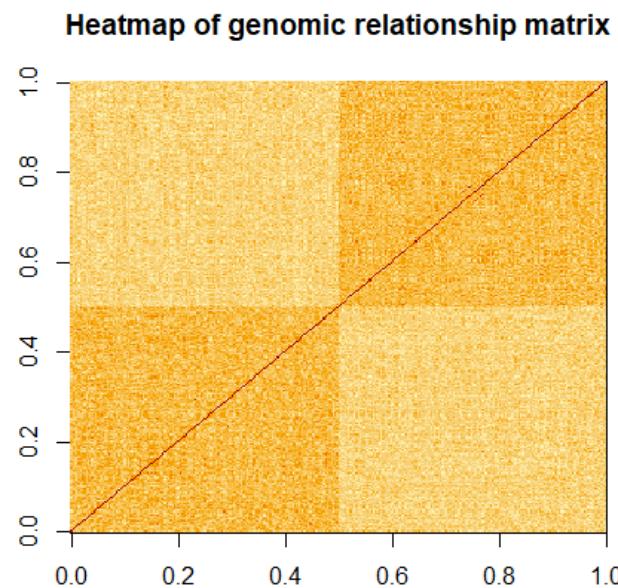
$$A = \alpha \tilde{Z} \tilde{Z}'$$

Where $\alpha^{-1} = n^{-1} \sum_{j=1}^p (\tilde{z}_j' \tilde{z}_j)$. Also, note that A stands here for additive relationship, **not as a pedigree matrix**.

Build GRM

```
z1 = apply(Gen, 2, function(x) x-mean(x)) # Observed  
individuals  
z2 = apply(Gen2, 2, function(x) x-mean(x)) # Prediction target  
A = tcrossprod(z1)  
alpha = 1/mean(diag(A))  
A = A*alpha  
diag(A) = diag(A)+0.01 # Stabilize GRM  
iA = solve(A) # Get inverse
```

Build GRM



Statistical model

- Linear model

$$\begin{aligned}y &= Xb + Zu + e \\y &\sim N(Xb, V)\end{aligned}$$

- Variances

$$\begin{aligned}Var(y) &= V = ZGZ' + R \\Var(u) &= G = A\sigma_a^2 \\Var(e) &= R = I\sigma_e^2\end{aligned}$$

Statistical model

The joint variance, including marker effects β , is defined as

$$Var \begin{bmatrix} y \\ u \\ \beta \\ e \end{bmatrix} = \begin{bmatrix} V & ZG & Z\tilde{Z}D & R \\ GZ' & G & \tilde{Z}D & 0 \\ D\tilde{Z}'Z' & D\tilde{Z}' & D & 0 \\ R & 0 & 0 & R \end{bmatrix}$$

where $u = \tilde{Z}\beta$, $\beta \sim N(0, D)$, $D = I_m\sigma_\beta^2$, and $G = A'\sigma_u^2 = \tilde{Z}D\tilde{Z}'$. The model could be described as:

$$y = Xb + Z(\tilde{Z}\beta) + e$$

Matrices - Design matrices

```
y = Obs$YLD
X = model.matrix(~Block+Block:Sp-1, Obs)
Z = model.matrix(~ID-1, Obs)

# Constants
n = length(y) # number of obs
q = ncol(Z) # levels of Z
rX = ncol(X) # rank of X

# If you are not sure X is full-rank, run
# rX = qr(X)$rank

# Check dimensions
print(c(n=n, q=q, rX=rX))
##      n      q      rX
## 1117   280     18
```

Matrices - Variance starting values

Let's assume a starting values of $h_0^2 \cong 0.25$. Now what?

If $\hat{\sigma}_{Y0}^2 = \frac{(y-Xb_{LS})'(y-Xb_{LS})}{n-r_X}$. Then,

$$\hat{\sigma}_e^2 = (1 - h_0^2)\hat{\sigma}_{Y0}^2 \text{ and } \hat{\sigma}_e^2 = h_0^2 \frac{\hat{\sigma}_{Y0}^2}{\sum_{j=1}^q \sigma_{z_j}^2}.$$

Starting values for variance components

```
b = qr.solve(X, y)
vy0 = c(crossprod(y-X%*%b) / (n-rX))
vu = 0.25*vy0/sum(apply(Z, 2, var))
ve = 0.75*vy0
vc = c(vu=vu, ve=ve)
print(vc)

##           vu             ve
## 15.42179 46.14134
```

Matrices - Variance-covariances

```
I = diag(n)
R = I^ve
G = A^vu
ZAZ = Z %*% A %*% t(Z)
V = Z %*% G %*% t(Z) + R
iG = solve(G)
iR = solve(I^ve)
iV = solve(V)
```

Henderson's equation

- Henderson's mixed model equation (HMME) for

$$y = Xb + Zu + e$$
$$\begin{bmatrix} X'R^{-1}X & Z'R^{-1}X \\ X'R^{-1}Z & Z'R^{-1}Z + G^{-1} \end{bmatrix} \begin{bmatrix} \hat{b} \\ \hat{u} \end{bmatrix} = \begin{bmatrix} X'R^{-1}y \\ Z'R^{-1}y \end{bmatrix}$$
$$\begin{bmatrix} C_{11} & C_{12} \\ C_{21} & C_{22} \end{bmatrix} \begin{bmatrix} \hat{g}_1 \\ \hat{g}_2 \end{bmatrix} = \begin{bmatrix} r_1 \\ r_2 \end{bmatrix}$$
$$C\hat{g} = r$$

where C is the *left-hand side*, r is the *right-hand side*.

Henderson's equation

$$y = Xb + Zu + e$$

Alternative notation

$$y = Wg + e$$

where $W = \{X, Z\}$, and $g = \{b, u\}$. Thus, MME

$$[W'R^{-1}W + \Sigma]\hat{g} = W'R^{-1}y$$

where

$$\Sigma = \begin{bmatrix} 0 & 0 \\ 0 & G^{-1} \end{bmatrix}$$

Henderson's equation

System of equations

```
Sigma = Matrix::bdiag(diag(0, rX), iG)  
W = cbind(X, Z)  
C = t(W) %*% iR %*% W + Sigma  
iC = solve(C)  
r = t(W) %*% iR %*% y
```

Compute coefficients

```
g = iC %*% r  
b = g[1:rX]  
u = g[-c(1:rX)]
```

Reduced animal model

The “reduced animal model” simplifies the mixed model equation

$$\begin{bmatrix} X'R^{-1}X & Z'R^{-1}X \\ X'R^{-1}Z & Z'R^{-1}Z + G^{-1} \end{bmatrix} \begin{bmatrix} \hat{b} \\ \hat{u} \end{bmatrix} = \begin{bmatrix} X'R^{-1}y \\ Z'R^{-1}y \end{bmatrix}$$

into

$$\begin{bmatrix} X'X & Z'X \\ X'Z & Z'Z + \lambda A^{-1} \end{bmatrix} \begin{bmatrix} \hat{b} \\ \hat{u} \end{bmatrix} = \begin{bmatrix} X'y \\ Z'y \end{bmatrix}$$

where $\lambda = \sigma_e^2 \sigma_u^{-2}$.

That is achieved by multiplying every thing by σ_e^2 .

Reduced animal model

From a data-augmentation standpoint, the reduced model is:

$$\begin{bmatrix} X'X & Z'X \\ X'Z & Z'Z \\ 0 & \lambda A^{-1} \end{bmatrix} \begin{bmatrix} \hat{b} \\ \hat{u} \end{bmatrix} = \begin{bmatrix} X'y \\ Z'y \\ 0 \end{bmatrix}$$

Variance of BLUEs

Let C^{-1} be described as

$$C^{-1} = \begin{bmatrix} C^{11} & C^{12} \\ C^{21} & C^{22} \end{bmatrix}$$

Useful because

$$\text{Var}(\hat{b}) = C^{11} = (X'V^{-1}X)^{-1}$$

Also, we'll need C^{22} to estimate variances later

```
C22 = as.matrix(iC[-c(1:rX), -c(1:rX)] )
```

Projection matrices

LS absorption

$$S = I - X(X'X)^{-1}X'$$

BLUE absorption

$$M = I - X(X'V^{-1}X)^{-1}X'V^{-1}$$

Random effect absorption

$$V^{-1} = R^{-1} - R^{-1}Z(Z'R^{-1}Z + G^{-1})^{-1}Z'R^{-1}$$

Mixed model absorption

$$P = V^{-1} - V^{-1}X(X'V^{-1}X)^{-1}X'V^{-1}$$

Projection matrices

$$H = WC^{-1}W'R^{-1}$$

$$Hy = \hat{y}$$

$$P = R^{-1}(I - H)$$

```
S = I - X %*% solve(t(X) %*% X) %*% t(X)
```

```
M = I - X %*% solve(t(X) %*% iV %*% X) %*% t(X) %*% iV
```

```
P = iV %*% M
```

```
H = W %*% iC %*% t(W) %*% iR
```

```
yHat = H %*% Y
```

```
e = Y - yHat
```

Projection matrices - Identities

$$SX = 0$$

$$PX = 0$$

$$SS = S$$

$$MX = 0$$

$$My = y - X\hat{b}$$

$$MM = M$$

$$MS = M$$

$$SM = S$$

$$PVP = P$$

$$P = V^{-1}M$$

$$P = (XX'\sigma_\infty^2 + V)^{-1}$$

$$ZAZ'Py = \frac{Z\hat{u}}{\hat{\sigma}_u^2}$$

$$Py = \frac{\hat{e}}{\hat{\sigma}_e^2}$$

BLUP solutions

$$\hat{u} = \hat{g}_2$$

$$\hat{u} = GZ'Py$$

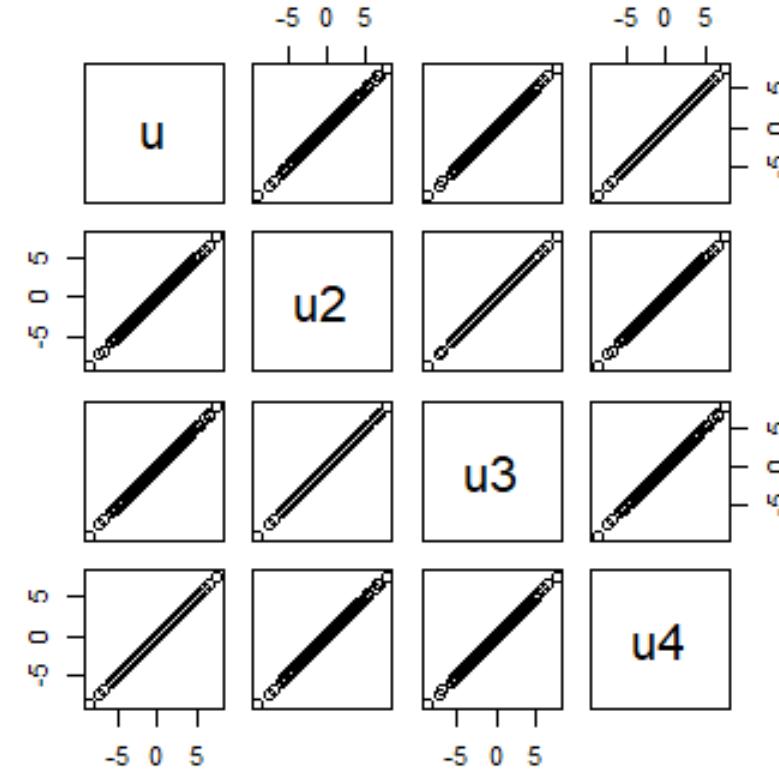
$$\hat{u} = (Z'R^{-1}Z + G^{-1})^{-1}Z'R^{-1}(y - X\hat{b})$$

$$\hat{u} = (Z'Z + \sigma_e^2 \sigma_u^{-2} A^{-1})^{-1} Z'(y - X\hat{b})$$

```

# Other ways to get BLUPs
u2 = G %*% t(Z) %*% P %*% y
u3 = solve( t(Z) %*% iR %*% Z + iC, t(Z) %*% iR %*% c(y-
X %*% b) )
u4 = solve( t(Z) %*% Z + iA*(ve/vu) , t(Z) %*% c(y-
X %*% b) )
plot(data.frame(u,u2,u3,u4))

```



Variance of BLUPs

The variance of u is

$$\text{Var}(u) = G$$

However, the variance of \hat{u}

$$\text{Var}(\hat{u}) = GZ'PZG$$

Or, in terms of C ,

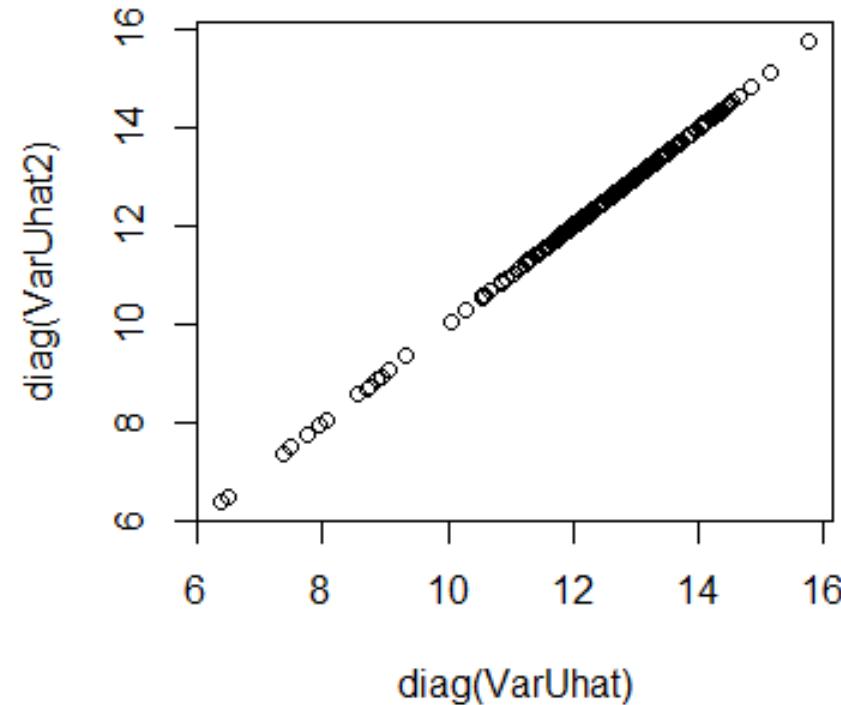
$$\text{Var}(\hat{u}) = G - C^{22}$$

```
# Variance of  $\hat{u}$ 
```

```
VarUhat = G %*% t(Z) %*% P %*% Z %*% G  
VarUhat2 = G - C22
```

Variance of BLUPs

```
plot(diag(VarUhat), diag(VarUhat2))
```



Reliability

Reliability is the observation-level heritability (r^2)

Under ML

$$r^2 = Z'V^{-1}ZG$$

Under REML

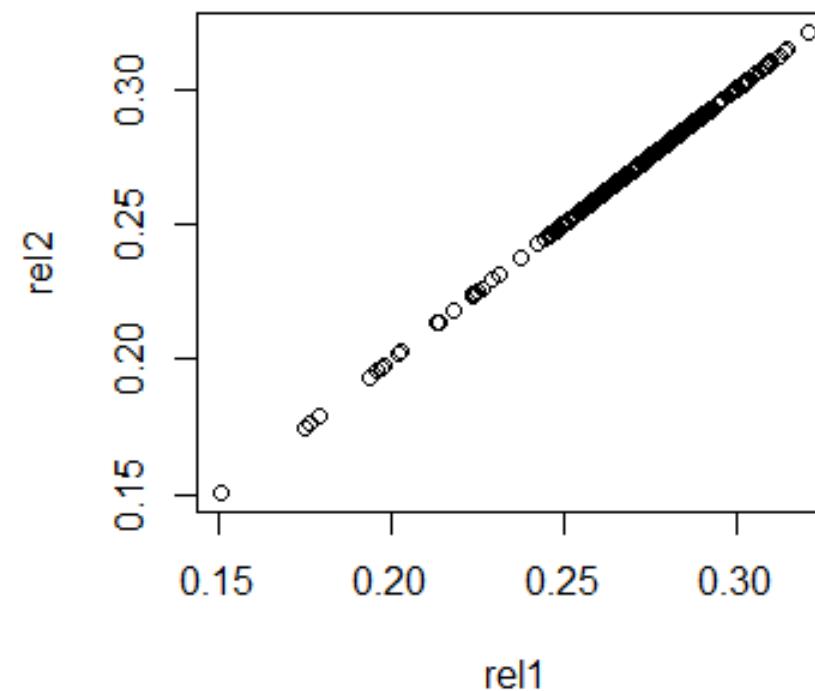
$$\begin{aligned} r^2 &= Z'P^{-1}ZG \\ r^2 &= I - C^{22}G^{-1} \end{aligned}$$

Alternatively

$$r^2 = \frac{Var(u)}{Var(\hat{u})}$$

```
rel1 = diag(diag(q)-C22 %*% iG)
rel2 = diag( t(Z) %*% P %*% Z %*% G )
plot(rel1,rel2)
```

Reliability



Accuracy

Accuracy is the square root of reliability ($a = \sqrt{r^2}$). Accuracy is generally defined as the correlation between estimated and true breeding values.

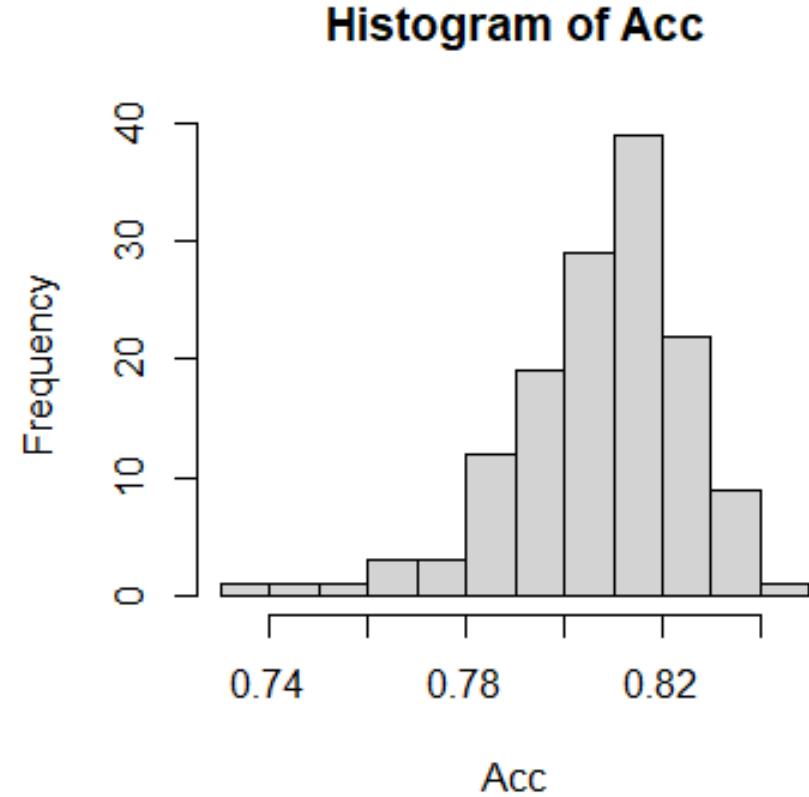
$$a = \text{cor}(u, \hat{u}) = \frac{\text{cov}(u, \hat{u})}{\text{sd}(u) \times \text{sd}(\hat{u})}$$

If the statistical model is the true model, $\sigma_i^2 = \hat{\sigma}_i^2$

$$a_i = \sqrt{\frac{\text{cov}(u, \hat{u})^2}{\text{var}(\hat{u})}} = \sqrt{\frac{G_{iy} Z' V^{-1} Z G_{yi}}{G_{ii}}}$$

When all individuals are observed, the denominator G_{ii} cancels out with the nominator G_{iy} , yielding $a = \sqrt{Z' V^{-1} Z G}$.

```
R2_by_ind = function(z){  
Cov12=(z%*%t(z1)*alpha)*vu  
Var22 = c(crossprod(z)*alpha)*vu  
Accuracy  
R2 = Cov12%*%t(Z)%*%iV%*%Z%*%t(Cov12)/Var22}  
Acc = sqrt(apply(Z2,1,R2_by_ind)); hist(Acc)
```



REML

Gaussian likelihood

$$L(X|\theta) = \frac{\exp((y - Xb)'V^{-1}(y - Xb))}{2\pi|V|}$$

Log-likelihood

$$-2LL(X|\theta) = \ln|V| + (y - Xb)'V^{-1}(y - Xb)$$

Restricted Log-likelihood (REML)

$$-2LL(X|\theta) = \ln|V| + \ln|X'V^{-1}X| + (y - Xb)'V^{-1}(y - Xb)$$

REML derived as pseudo-random

$$-2LL(X|\theta) = \ln|P| + y'Py$$

Expectation-Maximization

We EM simply by rearranging $\partial L / \partial \sigma_i^2$.

Genetic variance

$$\begin{aligned}\partial L / \partial \sigma_u^2 &= \text{tr}(PZAZ') - y'PZAZ'Py \\ \partial L / \partial \sigma_u^2 &= \frac{q}{\sigma_u^2} - \frac{u'A^{-1}u}{\sigma_u^4} - \frac{\text{tr}(A^{-1}C^{22})}{\sigma_u^4}\end{aligned}$$

Residual variance

$$\begin{aligned}\partial L / \partial \sigma_e^2 &= \text{tr}(PI) - y'PIP_y = \text{tr}(P) - y'P^2y \\ \partial L / \partial \sigma_e^2 &= \frac{n - r_X}{\sigma_e^2} - \frac{q}{\sigma_e^2} - \frac{\text{tr}(A^{-1}C^{22})}{\sigma_e^2 \sigma_u^2} - \frac{e'e}{\sigma_e^4}\end{aligned}$$

Expectation-Maximization

The final estimators turn out:

$$\hat{\sigma}_u^2 = \frac{\hat{u}' A^{-1} \hat{u} + \text{tr}(A^{-1} C^{22})}{q} = \frac{\hat{u}' A^{-1} \hat{u}}{q - \text{tr}(G^{-1} C^{22})}$$

$$\hat{\sigma}_e^2 = \frac{\hat{e}' \hat{e} + \text{tr}(W C^{-1} W') \hat{\sigma}_e^2}{n} = \frac{y' e}{n - r_X}$$

Expectation-Maximization

```
# Var e
Ve = c(crossprod(y,e)) / (n-rX)
# Var U
Vu = c(t(u) %*% iA %*% u + tr(iA%*%C22)) / q
# Var U (faster converging alternative)
Vu2 = c(t(u) %*% iA %*% u) / ( q - tr(iG%*%C22) )
# Check
print(c(Ve=Ve, Vu=Vu, Vu2=Vu2))
##           Ve            Vu            Vu2
## 52.18652 14.67906 12.66814
```

Pseudo-Expectation

Simplification of the likelihood. From

$$\partial L / \partial \sigma_i^2 = \text{tr}(PV_i) - y'PV_i'Py$$

To

$$\partial PL / \partial \sigma_i^2 = \text{tr}(SV_i) - y'SV_i'Py$$

Yielding ([Schaeffer 1986](#), [VanRaden 1988](#)):

$$\hat{\sigma}_u^2 = \frac{\tilde{u}'\hat{u}}{\text{tr}(AZ'SZ)} \text{ and } \hat{\sigma}_e^2 = \frac{y'S'\hat{e}}{n-r_X}$$

where $\tilde{u} = ySZ$.

Pseudo-Expectation

```
Sy = S %*% y
ZSy = t(Z) %*% Sy
trAZSZ = tr( S %*% ZAZ ) # In practice, only diagonals are
# computed
# Var U
c(u %*% ZSy) / trAZSZ
## [1] 9.506624
# Var E
c(t(e) %*% Sy) / (n-rX)
## [1] 52.18652
```

P.S.: Pseudo-Expectation works great for SNP-BLUP.

MIVQUE

Minimum Variance Quadratic Unbiased Estimator ([Rao 1971](#)):

- Unbiased variances: $E[\hat{\sigma}] = \sigma$
- Quadratic unbiasedness: $E[y'Qy] = E[\epsilon_i'Q\epsilon_i] = 0$
- Invariant: $QX = 0$
- $y'Qy = y'Q\epsilon_0 + y'Q\epsilon_1$ where $\epsilon_0 = e$ and $\epsilon_1 = Zu$.
- Iterations of MIVQUE yields REML, we use $Q = P$.
- General formulation:

$$\hat{\sigma} = S^{-1}q$$

Where S and q are defined next.

MIVQUE

$$\hat{\sigma} = S^{-1}q$$

Terms are defined as

$$S = \begin{bmatrix} P \frac{\partial V}{\partial \sigma_u^2} P \frac{\partial V}{\partial \sigma_u^2} & P \frac{\partial V}{\partial \sigma_u^2} P \frac{\partial V}{\partial \sigma_e^2} \\ P \frac{\partial V}{\partial \sigma_e^2} P \frac{\partial V}{\partial \sigma_u^2} & P \frac{\partial V}{\partial \sigma_e^2} P \frac{\partial V}{\partial \sigma_e^2} \end{bmatrix}$$
$$q = \begin{bmatrix} y' P \frac{\partial V}{\partial \sigma_u^2} P y \\ y' P \frac{\partial V}{\partial \sigma_e^2} P y \end{bmatrix}$$

where $\frac{\partial V}{\partial \sigma_u^2} = ZAZ'$ and $\frac{\partial V}{\partial \sigma_e^2} = I$

MIVQUE

```
PZAZ = P %*% ZAZ
S = matrix(c(
  tr( PZAZ %*% PZAZ ),      tr( PZAZ %*% P ),
  tr( P %*% I %*% PZAZ ),  tr( P %*% P ) ), 2, 2)
qs = c(Vu = c(t(y) %*% PZAZ %*% P %*% y),
        Ve = c(t(y) %*% P %*% P %*% y) )
solve(S, qs)
## [1] 8.495934 54.161688
```

Average-Information

Second-derivative methods (NR, FS, AI) work with:

$$\theta^{t+1} = \theta^t - \frac{f'}{f''}$$

Where f' and f'' are first and second derivatives, respectively. Where $f' = \Delta(\theta)$ is computed as

$$\Delta(\sigma_i^2) = \partial L / \partial \sigma_i^2 = \text{tr} \left(P \frac{\partial V}{\partial \sigma_i^2} \right) - y' P \frac{\partial V}{\partial \sigma_i^2} P y$$

And the ([average-information](#)) $f'' = AI(\theta)$ is computed as:

$$AI(\sigma_i^2, \sigma_j^2) = y' P \frac{\partial V}{\partial \sigma_i^2} P \frac{\partial V}{\partial \sigma_j^2} P y$$

Average-Information

```
SecDer1 = matrix(c(  
    t(y) * PZAZ * PZAZ * P * y, t(y) * PZAZ * P * P * y,  
    t(y) * P * PZAZ * P * y, t(y) * P * P * P * P * y ), 2, 2)  
FirDer1 = c( vu = tr(PZAZ) - t(y) * PZAZ * P * y ,  
           ve = tr(P * I) - t(y) * P * P * y )  
vc = solve(SecDer1,FirDer1)  
##          vu          ve  
##  5.614032 53.308581  
SecDer1 # AI matrix  
##          [,1]      [,2]  
## [1,] 0.12285971 0.04612028  
## [2,] 0.04612028 0.53927449
```

Average-Information

Building V and P is often **not feasible**. Let's check how to solve using the mixed model equations ([Meyer 1997](#)). We have seen solutions for first derivative, $\Delta(\theta)$, through C :

$$\begin{aligned}\partial L / \partial \sigma_u^2 &= \frac{q}{\sigma_u^2} - \frac{u' A^{-1} u}{\sigma_u^4} - \frac{\text{tr}(A^{-1} C^{22})}{\sigma_u^4} \\ \partial L / \partial \sigma_e^2 &= \frac{n - r_X}{\sigma_e^2} - \frac{q}{\sigma_e^2} - \frac{\text{tr}(A^{-1} C^{22})}{\sigma_e^2 \sigma_u^2} - \frac{e'e}{\sigma_e^4}\end{aligned}$$

Average-Information

The $AI(\theta)$ is obtained as follows.

$$M_B = \begin{bmatrix} C & W'R^{-1}B \\ B'R^{-1}W & B'R^{-1}B \end{bmatrix}$$
$$B = [ZAZ'Py \quad Py] = [Zu\sigma_u^{-2} \quad e\sigma_e^{-2}]$$

Take the Cholesky

$$M_B = LL'$$

Then we reconstruct the sub-matrix corresponding to $B'R^{-1}B$.

$$AI(\theta) = L_{22}'L_{22}$$

Average-Information

```
B = cbind( vu = Z %*% u / vu, ve = e / ve )
MB = chol(rbind(cbind(as.matrix(C), t(W) %*% iR %*% B),
                 cbind( t(B) %*% iR %*% W, t(B) %*% iR %*% B)))
LB = MB[ (ncol(MB)-1):ncol(MB), (ncol(MB)-1):ncol(MB) ]
SecDer2 =crossprod(LB)
FirDer2 =c(q/vu - (t(u) %*% iA %*% u) / (vu^2) - tr(iA %*% C22) / (vu^2),
           ((n-rX) / ve - (1/ve) * (q - tr(iA %*% C22) / (vu))) - crossprod(e) / (ve^2) )
vc = solve(SecDer2,FirDer2)
##          vu            ve
##  5.614032  53.308581
SecDer2 # AI matrix
##
##          0.12285971  0.04612028
##          0.04612028  0.53927449
```

Gibbs sampling

Simple Hierarchical Bayesian approach to estimate variance components, where the final estimates are the **average** of the samples *a posteriori*, $\pi(\theta|x)$, the distribution of parameters ($\theta = \{\sigma_u^2, \sigma_e^2, b, u\}$) given data ($x = \{y, X, Z, A\}$). The posterior is a function of the probability of the data, $p(x|\theta)$, and probability of priors, $\pi(\theta)$.

$$\begin{aligned}\pi(\theta|x) &\propto p(x|\theta)\pi(\theta) \\ p(x|\theta) &= N(Xb + Zu, R)N(u, G|\sigma_u^2)N(e, R|\sigma_e^2) \\ \pi(\theta) &= \chi^{-2}(\sigma_u^2|S_u, \nu_u)\chi^{-2}(\sigma_e^2|S_e, \nu_e)\end{aligned}$$

Gibbs sampling

We sample variance components from a scaled inverse-chi square distribution:

$$\sigma_u^2 | u, S_u, \nu_u \sim \frac{u' A^{-1} u + S_u \nu_u}{\chi^2(q + \nu_u)}$$

$$\sigma_e^2 | e, S_e, \nu_e \sim \frac{e'e + S_e \nu_e}{\chi^2(n + \nu_e)}$$

Using the mixed model equation ($Cg = r$) notation, we sample coefficients from:

$$g_j | x, g_{-j} \sim N \left(\frac{r_j - C_{-j,j} g_{-j}}{C_{j,j}}, \frac{1}{C_{j,j}} \right)$$

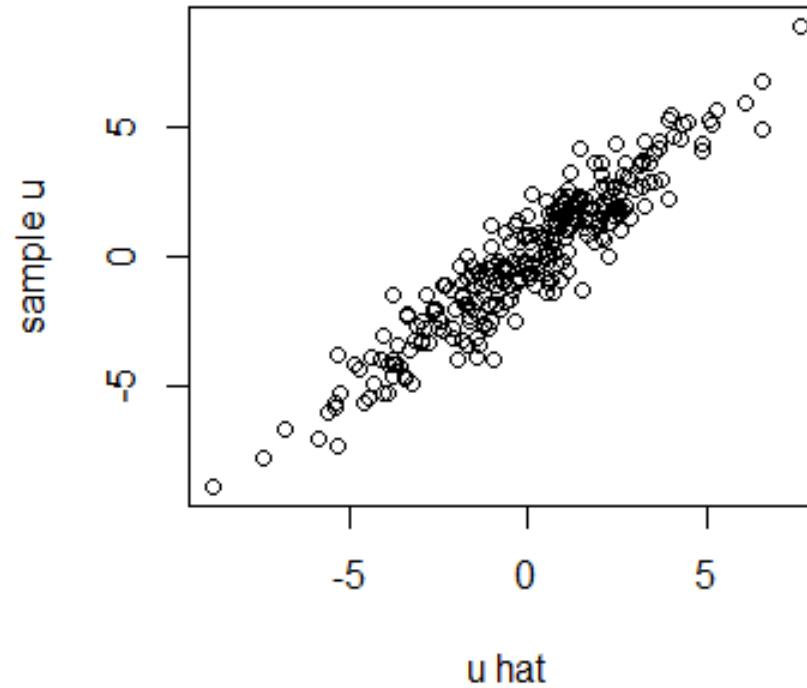
Gibbs sampling

```
# Priors
df0 = 5
Su = vu
Se = ve
# Sample genetic variance
c(t(u) %*% iA %*% u + Su^df0) / rchisq(1, q+df0)
## [1] 3.645489
# Sample residual variance
c(t(e) %*% e + Se^df0) / rchisq(1, n+df0)
## [1] 46.12222
```

```

g_samp = sapply(1:(rX+q), function(j) rnorm(n=1,
  mean=c(r[j]-C[j,-j]%^%g[-j])/C[j,j],
  sd=sqrt(1/C[j,j]))) Gibbs sampling
plot(g[-c(1:rX)],g_samp[-c(1:rX)],xlab='u
hat',ylab='sample u')

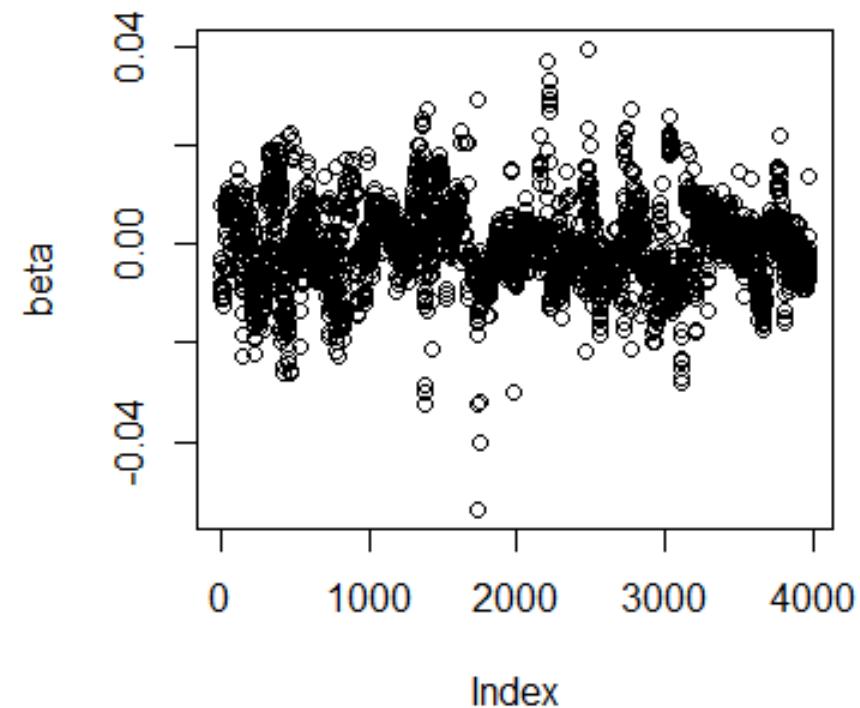
```



$$\hat{\beta}|\hat{u} = \hat{\sigma}_{\beta}^2 \tilde{Z}' G^{-1} \hat{u}$$

```
vb = vu * alpha  
beta = vb * c( t(z1) )  
plot(beta)
```

Marker effects



Final remarks

- Design matrices (Z, X) as sparse (*Matrix* pkg)
- Symmetric matrices (C, C^{-1}, A^{-1}) are stored in upper diagonals
- Implement with good linear algebra libraries (*RcppEigen*, *RcppArmadillo*)
- Same matrices are never computed (P, V, R, A)
- When only traces are needed, only diagonals are computed (e.g., $\text{tr}(Z'SZ)$)
- Absorption can be efficiently done one vector at a time (e.g., SZ)
- Factorization can help in specific situations (SVD, EVD, Cholesky)

THANK YOU