

SISG  
2014

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SISG Module 15:  
Mixed Models in  
Quantitative Genetics

19th Summer Institute in Statistical Genetics

**W** UNIVERSITY *of* WASHINGTON

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## SYLLABUS

### MIXED MODELS IN QUANTITATIVE GENETICS

#### INSTRUCTORS:

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LW = Lynch & Walsh: *Genetics and Analysis of Quantitative Traits* (book)

WL = Walsh & Lynch: *Evolution and Selection of Quantitative Traits* (website)  
[http://nitro.biosci.arizona.edu/zbook/NewVolume\\_2/newvol2.html](http://nitro.biosci.arizona.edu/zbook/NewVolume_2/newvol2.html)

#### LECTURE SCHEDULE

##### **Wednesday, 16 July**

- |              |   |
|--------------|---|
| 1:30 3:00 pm | 1. Introduction to matrix algebra and calculus (Walsh)<br>Background reading: LW, Chapter 8<br>Additional reading: LW Appendix 3; WL Appendix 5 |
| 3:00 3:30 pm | Break   |
| 3:30 5:00 pm | 2. The General Linear Model (Walsh)<br>Background reading: LW Chapter 8<br>Additional reading: LW Appendices 3, 4; WL Appendices 2, 3           |

##### **Thursday, 17 July**

- |                |  |
|----------------|--|
| 8:30 10:00 am  | 3. Overview and Derivation of the mixed model (Muir)<br>Additional reading: LW Chapters 26, 27 |
| 10:00 10:30 am | Break  |
| 10:30 12:00    | 4. Application: BLUP breeding values (Muir)<br>Additional reading: WL Chapter 19               |
| 12:00 1:30 pm  | Lunch  |
| 1:30 3:00 pm   | 5. Application: Genomic selection (Muir)   |
| 3:00 3:30 pm   | Break  |
| 3:30 5:00 pm   | 6. Application: QTL/association mapping (Walsh)<br>Additional reading: LW Chapters 14, 16      |

Evening                   Open session (review, R, etc)

**Friday, 18 July**

- |                  |   |
|------------------|---|
| 8:30 - 10:00 am  | 7. Application: BLUP maternal genetic (Walsh)                                   |
| 10:00 - 10:30 am | Break   |
| 10:30 - 12:00    | 8. Application: Associative effects (Muir)<br>Additional reading: WL Chapter 20 |
| 12:00 - 1:30 pm  | Lunch   |
| 1:30 - 3:00 pm   | 9. Application: $G \times E$ (Walsh)<br>Additional reading: WL Chapters 43, 44  |
| 3:00 - 3:30 pm   | Break   |
| 3:30 - 5:00 pm   | 10. Summary and wrap-up (Walsh and Muir)  |

# Lecture 1: Intro/refresher in Matrix Algebra

Bruce Walsh lecture notes  
SISG -Mixed Model Course  
Seattle, 16 - 18 July 2014

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## Matrix/linear algebra

- Compact way for **treating the algebra of systems of linear equations**
- Most common statistical methods can be written in matrix form
  - $\mathbf{y} = \mathbf{X}\beta + \mathbf{e}$  is the **general linear model**
    - OLS solution:  $\beta = (\mathbf{X}^T\mathbf{X})^{-1}\mathbf{X}^T\mathbf{y}$
  - $\mathbf{Y} = \mathbf{X}\beta + \mathbf{Z}\alpha + \mathbf{e}$  is the **general mixed model**

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# Topics

- Definitions, dimensionality, addition, subtraction
- Matrix multiplication
- Inverses, solving systems of equations
- Quadratic products and covariances
- The multivariate normal distribution
- Eigenstructure
- Basic matrix calculations in R

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## Matrices: An array of elements

**Vectors:** A matrix with either one row or one column.

Usually written in bold lowercase, e.g. **a**, **b**, **c**

$$\mathbf{a} = \begin{pmatrix} 12 \\ 13 \\ 47 \end{pmatrix} \quad \mathbf{b} = (2 \ 0 \ 5 \ 21)$$

Column vector      Row vector

( $3 \times 1$ )

( $1 \times 4$ )

Dimensionality of a matrix:  $r \times c$  (rows  $\times$  columns)  
think of Railroad Car

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## General Matrices

Usually written in bold uppercase, e.g.  $\mathbf{A}$ ,  $\mathbf{C}$ ,  $\mathbf{D}$

$$\mathbf{C} = \begin{pmatrix} 3 & 1 & 2 \\ 2 & 5 & 4 \\ 1 & 1 & 2 \end{pmatrix} \quad \mathbf{D} = \begin{pmatrix} 0 & 1 \\ 3 & 4 \\ 2 & 9 \end{pmatrix}$$

$(3 \times 3)$   $(3 \times 2)$

Square matrix

Dimensionality of a matrix:  $r \times c$  (rows  $\times$  columns)  
think of Railroad Car

A matrix is defined by a list of its elements.  
 $\mathbf{B}$  has  $ij$ -th element  $B_{ij}$  -- the element in row  $i$   
and column  $j$

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## Addition and Subtraction of Matrices

If two matrices have the same dimension (both are  $r \times c$ ),  
then matrix addition and subtraction simply follows by  
adding (or subtracting) on an element by element basis

Matrix addition:  $(\mathbf{A} + \mathbf{B})_{ij} = A_{ij} + B_{ij}$

Matrix subtraction:  $(\mathbf{A} - \mathbf{B})_{ij} = A_{ij} - B_{ij}$

Examples:

$$\mathbf{A} = \begin{pmatrix} 3 & 0 \\ 1 & 2 \end{pmatrix} \quad \text{and} \quad \mathbf{B} = \begin{pmatrix} 1 & 2 \\ 2 & 1 \end{pmatrix}$$

$$\mathbf{C} = \mathbf{A} + \mathbf{B} = \begin{pmatrix} 4 & 2 \\ 3 & 3 \end{pmatrix} \quad \text{and} \quad \mathbf{D} = \mathbf{A} - \mathbf{B} = \begin{pmatrix} 2 & -2 \\ -1 & 1 \end{pmatrix}$$

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# Partitioned Matrices

It will often prove useful to divide (or **partition**) the elements of a matrix into a matrix whose elements are itself matrices.

$$\mathbf{C} = \begin{pmatrix} 3 & 1 & 2 \\ 2 & 5 & 4 \\ 1 & 1 & 2 \end{pmatrix} = \begin{pmatrix} 3 & \vdots & 1 & 2 \\ \cdots & \cdots & \cdots & \cdots \\ 2 & \vdots & 5 & 4 \\ 1 & \vdots & 1 & 2 \end{pmatrix} = \begin{pmatrix} \mathbf{a} & \mathbf{b} \\ \mathbf{d} & \mathbf{B} \end{pmatrix}$$

$$\mathbf{a} = (3), \quad \mathbf{b} = (1 \ 2), \quad \mathbf{d} = \begin{pmatrix} 2 \\ 1 \end{pmatrix}, \quad \mathbf{B} = \begin{pmatrix} 5 & 4 \\ 1 & 2 \end{pmatrix}$$

One useful partition is to write the matrix as either a **row vector of column vectors** or a **column vector of row vectors**

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$$\mathbf{C} = \begin{pmatrix} 3 & 1 & 2 \\ 2 & 5 & 4 \\ 1 & 1 & 2 \end{pmatrix} = \begin{pmatrix} \mathbf{r}_1 \\ \mathbf{r}_2 \\ \mathbf{r}_3 \end{pmatrix} \quad \text{A column vector whose elements are row vectors}$$

$$\mathbf{r}_1 = (3 \ 1 \ 2)$$

$$\mathbf{r}_2 = (2 \ 5 \ 4)$$

$$\mathbf{r}_3 = (1 \ 1 \ 2)$$

$$\mathbf{C} = \begin{pmatrix} 3 & 1 & 2 \\ 2 & 5 & 4 \\ 1 & 1 & 2 \end{pmatrix} = (\mathbf{c}_1 \ \mathbf{c}_2 \ \mathbf{c}_3) \quad \text{A row vector whose elements are column vectors}$$

$$\mathbf{c}_1 = \begin{pmatrix} 3 \\ 2 \\ 1 \end{pmatrix}, \quad \mathbf{c}_2 = \begin{pmatrix} 1 \\ 5 \\ 1 \end{pmatrix}, \quad \mathbf{c}_3 = \begin{pmatrix} 2 \\ 4 \\ 2 \end{pmatrix}$$

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## Towards Matrix Multiplication: dot products

The **dot** (or **inner**) **product** of two vectors (both of length  $n$ ) is defined as follows:

$$\mathbf{a} \cdot \mathbf{b} = \sum_{i=1}^n a_i b_i$$

Example:

$$\mathbf{a} = \begin{pmatrix} 1 \\ 2 \\ 3 \\ 4 \end{pmatrix} \quad \text{and} \quad \mathbf{b} = (4 \ 5 \ 7 \ 9)$$

$$\mathbf{a} \cdot \mathbf{b} = 1*4 + 2*5 + 3*7 + 4*9 = 60$$

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Matrices are compact ways to write systems of equations

$$\begin{aligned} 5x_1 + 6x_2 + 4x_3 &= 6 \\ 7x_1 - 3x_2 + 5x_3 &= -9 \\ -x_1 - x_2 + 6x_3 &= 12 \end{aligned}$$

$$\begin{pmatrix} 5 & 6 & 4 \\ 7 & -3 & 5 \\ -1 & -1 & 6 \end{pmatrix} \begin{pmatrix} x_1 \\ x_2 \\ x_3 \end{pmatrix} = \begin{pmatrix} 6 \\ -9 \\ 12 \end{pmatrix}$$

$$\mathbf{Ax} = \mathbf{c}, \quad \text{or} \quad \mathbf{x} = \mathbf{A}^{-1}\mathbf{c}$$

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The least-squares solution for the linear model

$$y = \mu + \beta_1 z_1 + \cdots + \beta_n z_n$$

yields the following system of equations for the  $\beta_i$

$$\sigma(y, z_1) = \beta_1 \sigma^2(z_1) + \beta_2 \sigma(z_1, z_2) + \cdots + \beta_n \sigma(z_1, z_n)$$

$$\sigma(y, z_2) = \beta_1 \sigma(z_1, z_2) + \beta_2 \sigma^2(z_2) + \cdots + \beta_n \sigma(z_2, z_n)$$

$$\vdots \quad \vdots \quad \vdots \quad \ddots \quad \vdots$$

$$\sigma(y, z_n) = \beta_1 \sigma(z_1, z_n) + \beta_2 \sigma(z_2, z_n) + \cdots + \beta_n \sigma^2(z_n)$$

This can be more compactly written in matrix form as

$$\begin{pmatrix} \sigma^2(z_1) & \sigma(z_1, z_2) & \dots & \sigma(z_1, z_n) \\ \sigma(z_1, z_2) & \sigma^2(z_2) & \dots & \sigma(z_2, z_n) \\ \vdots & \vdots & \ddots & \vdots \\ \sigma(z_1, z_n) & \sigma(z_2, z_n) & \dots & \sigma^2(z_n) \end{pmatrix} \begin{pmatrix} \beta_1 \\ \beta_2 \\ \vdots \\ \beta_n \end{pmatrix} = \begin{pmatrix} \sigma(y, z_1) \\ \sigma(y, z_2) \\ \vdots \\ \sigma(y, z_n) \end{pmatrix}$$

$$X^T X$$

$$\beta$$

$$X^T y$$

T = transpose,  
discussed in slide 17-9

$$\text{or, } \beta = (X^T X)^{-1} X^T y$$

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## Matrix Multiplication:

The order in which matrices are multiplied affects the matrix product, e.g.  $AB \neq BA$

For the product of two matrices to exist, the matrices must **conform**. For  $AB$ , the number of columns of  $A$  must equal the number of rows of  $B$ .

The matrix  $C = AB$  has the same number of rows as  $A$  and the same number of columns as  $B$ .

$$C_{(r \times c)} = A_{(r \times k)} B_{(k \times c)}$$

ij-th element of C is given by

$$C_{ij} = \sum_{l=1}^k A_{il} B_{lj}$$

Elements in the jth column of B

Elements in the ith row of matrix A

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Outer indices give dimensions of resulting matrix, with r rows (A) and c columns (B)

$$C_{(r \times c)} = A_{(r \times k)} B_{(k \times c)}$$

Inner indices must match columns of A = rows of B

Example: Is the product ABCD defined? If so, what is its dimensionality? Suppose

$$A_{3 \times 5} B_{5 \times 9} C_{9 \times 6} D_{6 \times 23}$$

Yes, defined, as **inner indices match**. Result is a  $3 \times 23$  matrix (3 rows, 23 columns)

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More formally, consider the product  $L = MN$

Express the matrix M as a column vector of row vectors

$$M = \begin{pmatrix} m_1 \\ m_2 \\ \vdots \\ m_r \end{pmatrix} \quad \text{where} \quad m_i = (M_{i1} \quad M_{i2} \quad \cdots \quad M_{ic})$$

Likewise express N as a row vector of column vectors

$$N = (n_1 \quad n_2 \quad \cdots \quad n_b) \quad \text{where} \quad n_j = \begin{pmatrix} N_{1j} \\ N_{2j} \\ \vdots \\ N_{cj} \end{pmatrix}$$

The ij-th element of L is the inner product of M's row i with N's column j

$$L = \begin{pmatrix} m_1 \cdot n_1 & m_1 \cdot n_2 & \cdots & m_1 \cdot n_b \\ m_2 \cdot n_1 & m_2 \cdot n_2 & \cdots & m_2 \cdot n_b \\ \vdots & \vdots & \ddots & \vdots \\ m_r \cdot n_1 & m_r \cdot n_2 & \cdots & m_r \cdot n_b \end{pmatrix}$$

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# Example

$$\mathbf{AB} = \begin{pmatrix} a & b \\ c & d \end{pmatrix} \begin{pmatrix} e & f \\ g & h \end{pmatrix} = \begin{pmatrix} ae + bg & af + bh \\ ce + dg & cf + dh \end{pmatrix}$$

Likewise

$$\mathbf{BA} = \begin{pmatrix} ae + cf & eb + df \\ ga + ch & gd + dh \end{pmatrix}$$

**ORDER of multiplication matters!** Indeed, consider  $C_{3 \times 5} D_{5 \times 5}$  which gives a  $3 \times 5$  matrix, versus  $D_{5 \times 5} C_{3 \times 5}$ , which is not defined.

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## Matrix multiplication in R

```
> A<-matrix(c(1,2,3,4),nrow=2)
> B<-matrix(c(4,5,6,7),nrow=2)
> A
[,1] [,2]
[1,]    1    3
[2,]    2    4
> B
[,1] [,2]
[1,]    4    6
[2,]    5    7
> A %*% B
[,1] [,2]
[1,]   19   27
[2,]   28   40
```

R fills in the matrix from the list c by filling in as columns, here with 2 rows (nrow=2)

Entering A or B displays what was entered (always a good thing to check)

The command `%*%` is the R code for the multiplication of two matrices

On your own: What is the matrix resulting from BA?  
What is A if nrow=1 or nrow=4 is used?

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# The Transpose of a Matrix

The transpose of a matrix exchanges the rows and columns,  $A^T_{ij} = A_{ji}$

Useful identities

$$(AB)^T = B^T A^T \quad a = \begin{pmatrix} a_1 \\ \vdots \\ a_n \end{pmatrix} \quad b = \begin{pmatrix} b_1 \\ \vdots \\ b_n \end{pmatrix}$$

Inner product =  $a^T b = a^T_{(1 \times n)} b_{(n \times 1)}$

Indices match, matrices conform

Dimension of resulting product is  $1 \times 1$  (i.e. a scalar)

$$(a_1 \ \dots \ a_n) \begin{pmatrix} b_1 \\ \vdots \\ b_n \end{pmatrix} = a^T b = \sum_{i=1}^n a_i b_i \quad \text{Note that } b^T a = (b^T a)^T = a^T b$$

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Outer product =  $ab^T = a_{(n \times 1)} b^T_{(1 \times n)}$

Resulting product is an  $n \times n$  matrix

$$\begin{aligned} & \begin{pmatrix} a_1 \\ a_2 \\ \vdots \\ a_n \end{pmatrix} (b_1 \ b_2 \ \dots \ b_n) \\ &= \begin{pmatrix} a_1 b_1 & a_1 b_2 & \dots & a_1 b_n \\ a_2 b_1 & a_2 b_2 & \dots & a_2 b_n \\ \vdots & \vdots & \ddots & \vdots \\ a_n b_1 & a_n b_2 & \dots & a_n b_n \end{pmatrix} \end{aligned}$$

# R code for transposition

```
> t(A)          t(A) = transpose of A
[1,] [,1] [,2]
[1,]     1    2
[2,]     3    4
[3,]

> a<-matrix(c(1,2,3),nrow=3) Enter the column vector a
> a
[1,] [,1]
[1,]     1
[2,]     2
[3,]     3
> t(a) %*% a      Compute inner product  $a^T a$ 
[1,] [,1]
[1,]    14
> a %*% t(a)      Compute outer product  $aa^T$ 
[1,] [,1] [,2] [,3]
[1,]     1    2    3
[2,]     2    4    6
[3,]
```

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# Solving equations

- The **identity matrix  $I$** 
  - Serves the same role as 1 in scalar algebra, e.g.,  $a*1=1*a=a$ , with  $AI=IA=A$
- The **inverse matrix  $A^{-1}$  (IF it exists)**
  - Defined by  $A A^{-1} = I$ ,  $A^{-1}A = I$
  - Serves the same role as scalar division
    - To solve  $ax = c$ , multiply both sides by  $(1/a)$  to give:
    - $(1/a)*ax = (1/a)c$  or  $(1/a)*a*x = 1*x = x$ ,
    - Hence  $x = (1/a)c$
  - To solve  $Ax = c$ ,  $A^{-1}Ax = A^{-1}c$
  - Or  $A^{-1}Ax = Ix = x = A^{-1}c$

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# The Identity Matrix, I

The identity matrix serves the role of the number 1 in matrix multiplication:  $AI = A, IA = A$

I is a square diagonal matrix, with all diagonal elements being one, all off-diagonal elements zero.

$$I_{ij} = \begin{cases} 1 & \text{for } i = j \\ 0 & \text{otherwise} \end{cases}$$

$$I_{3 \times 3} = \begin{pmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{pmatrix}$$

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# The Identity Matrix in R

`diag(k)`, where k is an integer, return the  $k \times k$  I matix

```
> I<-diag(4)
> I
      [,1] [,2] [,3] [,4]
[1,]    1    0    0    0
[2,]    0    1    0    0
[3,]    0    0    1    0
[4,]    0    0    0    1
> I2 <-diag(2)
> I2
      [,1] [,2]
[1,]    1    0
[2,]    0    1
```

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# The Inverse Matrix, $A^{-1}$

For a square matrix  $A$ , define its **Inverse  $A^{-1}$** , as the matrix satisfying

$$A^{-1}A = AA^{-1} = I$$

For  $A = \begin{pmatrix} a & b \\ c & d \end{pmatrix}$   $A^{-1} = \frac{1}{ad - bc} \begin{pmatrix} d & -b \\ -c & a \end{pmatrix}$



If this quantity (the **determinant**) is zero, the inverse does not exist.

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If  $\det(A)$  is not zero,  $A^{-1}$  exists and  $A$  is said to be **non-singular**. If  $\det(A) = 0$ ,  $A$  is **singular**, and no **unique** inverse exists (**generalized inverses** do)

**Generalized inverses**, and their uses in solving systems of equations, are discussed in Appendix 3 of Lynch & Walsh

$A^-$  is the typical notation to denote the  $G$ -inverse of a matrix

When a  $G$ -inverse is used, provided the system is **consistent**, then some of the variables have a family of solutions (e.g.,  $x_1 = 2$ , but  $x_2 + x_3 = 6$ )

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# Inversion in R

`solve(A)` computes  $A^{-1}$

`det(A)` computes determinant of  $A$

```
> A          Using A entered earlier
      [,1] [,2]
[1,]    1    3
[2,]    2    4
> solve(A)   Compute A-1
      [,1] [,2]
[1,]   -2   1.5
[2,]    1  -0.5
> solve(A) %*% A   Showing that A-1 A = I
      [,1]      [,2]
[1,]    1 -8.881784e-16
[2,]    0  1.000000e+00
> det(A)     Computing determinant of A
[1] -2
```

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# Homework

Put the following system of equations in matrix form, and solve using R

$$\begin{aligned}3x_1 + 4x_2 + 4x_3 + 6x_4 &= -10 \\9x_1 + 2x_2 - x_3 - 6x_4 &= 20 \\x_1 + x_2 + x_3 - 10x_4 &= 2 \\2x_1 + 9x_2 + 2x_3 - x_4 &= -10\end{aligned}$$

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Example: solve the OLS for  $\beta = (\beta_1, \beta_2)^\top$   
in  $y = \alpha + \beta_1 z_1 + \beta_2 z_2 + e$

$$\beta = V^{-1} c \quad c = \begin{pmatrix} \sigma(y, z_1) \\ \sigma(y, z_2) \end{pmatrix} \quad V = \begin{pmatrix} \sigma^2(z_1) & \sigma(z_1, z_2) \\ \sigma(z_1, z_2) & \sigma^2(z_2) \end{pmatrix}$$

It is more compact to use  $\sigma(z_1, z_2) = \rho_{12} \sigma(z_1) \sigma(z_2)$

$$V^{-1} = \frac{1}{\sigma^2(z_1)\sigma^2(z_2)(1-\rho_{12}^2)} \begin{pmatrix} \sigma^2(z_2) & -\sigma(z_1, z_2) \\ -\sigma(z_1, z_2) & \sigma^2(z_1) \end{pmatrix}$$

$$\begin{pmatrix} \beta_1 \\ \beta_2 \end{pmatrix} = \frac{1}{\sigma^2(z_1)\sigma^2(z_2)(1-\rho_{12}^2)} \begin{pmatrix} \sigma^2(z_2) & -\sigma(z_1, z_2) \\ -\sigma(z_1, z_2) & \sigma^2(z_1) \end{pmatrix} \begin{pmatrix} \sigma(y, z_1) \\ \sigma(y, z_2) \end{pmatrix}$$

$$\beta_1 = \frac{1}{1-\rho_{12}^2} \left[ \frac{\sigma(y, z_1)}{\sigma^2(z_1)} - \rho_{12} \frac{\sigma(y, z_2)}{\sigma(z_1)\sigma(z_2)} \right]$$

$$\beta_2 = \frac{1}{1-\rho_{12}^2} \left[ \frac{\sigma(y, z_2)}{\sigma^2(z_2)} - \rho_{12} \frac{\sigma(y, z_1)}{\sigma(z_1)\sigma(z_2)} \right]$$

If  $\rho_{12} = 0$ , these reduce to the two univariate slopes,

$$\beta_1 = \frac{\sigma(y, z_1)}{\sigma^2(z_1)} \quad \text{and} \quad \beta_2 = \frac{\sigma(y, z_2)}{\sigma^2(z_2)}$$

Likewise, if  $\rho_{12} = 1$ , this reduces to a univariate regression,

## Useful identities

$$(A^T)^{-1} = (A^{-1})^T$$

$$(AB)^{-1} = B^{-1} A^{-1}$$

For a diagonal matrix  $D$ , then  $\det(D)$ , which is also denoted by  $|D|$ , = product of the diagonal elements

Also, the determinant of any square matrix  $A$ ,  $\det(A)$ , is simply the product of the **eigenvalues**  $\lambda$  of  $A$ , which satisfy

$$Ae = \lambda e$$

If  $A$  is  $n \times n$ , solutions to  $\lambda$  are an  $n$ -degree polynomial.  $e$  is the **eigenvector** associated with  $\lambda$ . If any of the roots to the equation are zero,  $A^{-1}$  is not defined. In this case, for some linear combination  $b$ , we have  $Ab = 0$ .

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## Variance-Covariance matrix

- A very important square matrix is the **variance-covariance matrix**  $V$  associated with a vector  $x$  of random variables.
- $V_{ij} = \text{Cov}(x_i, x_j)$ , so that the  $i$ -th diagonal element of  $V$  is the variance of  $x_i$ , and off-diagonal elements are covariances
- $V$  is a symmetric, square matrix

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# The trace

The trace,  $\text{tr}(A)$  or  $\text{trace}(A)$ , of a square matrix  $A$  is simply the sum of its diagonal elements

The importance of the trace is that it equals the sum of the eigenvalues of  $A$ ,  $\text{tr}(A) = \sum \lambda_i$

For a covariance matrix  $V$ ,  $\text{tr}(V)$  measures the total amount of variation in the variables

$\lambda_i / \text{tr}(V)$  is the fraction of the total variation in  $x$  contained in the linear combination  $e_i^T x$ , where  $e_i$ , the  $i$ -th principal component of  $V$  is also the  $i$ -th eigenvector of  $V$  ( $V e_i = \lambda_i e_i$ )

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# Eigenstructure in R

`eigen(A)` returns the eigenvalues and vectors of  $A$

```
> V<-matrix(c(10,-5,10,-5,20,0,10,0,30),nrow=3)
> V
 [,1] [,2] [,3]
[1,] 10   -5   10
[2,] -5    20   0
[3,] 10    0    30
> eigen(V)
$values
[1] 34.410103 21.117310  4.472587
$vectors
[,1]      [,2]      [,3]
[1,] 0.3996151 0.2117936 0.8918807
[2,] -0.1386580 -0.9477830 0.2871955
[3,] 0.9061356 -0.2384340 -0.3493816
```

Trace = 60

PC 1 accounts for  $34.4/60 = 57\%$  of all the variation

PC 1

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# Quadratic and Bilinear Forms

**Quadratic product:** for  $A_{n \times n}$  and  $x_{n \times 1}$

$$\mathbf{x}^T \mathbf{A} \mathbf{x} = \sum_{i=1}^n \sum_{j=1}^n a_{ij} x_i x_j \quad \text{Scalar } (1 \times 1)$$

**Bilinear Form** (generalization of quadratic product)  
for  $A_{m \times n}$ ,  $a_{n \times 1}$ ,  $b_{m \times 1}$  their bilinear form is  $b^T A a$

$$\mathbf{b}^T \mathbf{A} \mathbf{a} = \sum_{i=1}^m \sum_{j=1}^n A_{ij} b_i a_j$$

Note that  $b^T A a = a^T A^T b$

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## Covariance Matrices for Transformed Variables

What is the variance of the linear combination,  
 $c_1 x_1 + c_2 x_2 + \dots + c_n x_n$ ? (note this is a scalar)

$$\begin{aligned} \sigma^2(c^T \mathbf{x}) &= \sigma^2 \left( \sum_{i=1}^n c_i x_i \right) = \sigma \left( \sum_{i=1}^n c_i x_i, \sum_{j=1}^n c_j x_j \right) \\ &= \sum_{i=1}^n \sum_{j=1}^n \sigma(c_i x_i, c_j x_j) = \sum_{i=1}^n \sum_{j=1}^n c_i c_j \sigma(x_i, x_j) \\ &= \mathbf{c}^T \mathbf{V} \mathbf{c} \end{aligned}$$

Likewise, the covariance between two linear combinations can be expressed as a bilinear form,

$$\sigma(\mathbf{a}^T \mathbf{x}, \mathbf{b}^T \mathbf{x}) = \mathbf{a}^T \mathbf{V} \mathbf{b}$$

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Example: Suppose the variances of  $x_1$ ,  $x_2$ , and  $x_3$  are 10, 20, and 30.  $x_1$  and  $x_2$  have a covariance of -5,  $x_1$  and  $x_3$  of 10, while  $x_2$  and  $x_3$  are uncorrelated.

What are the variances of the new variables  
 $y_1 = x_1 - 2x_2 + 5x_3$  and  $y_2 = 6x_2 - 4x_3$ ?

$$\mathbf{V} = \begin{pmatrix} 10 & -5 & 10 \\ -5 & 20 & 0 \\ 10 & 0 & 30 \end{pmatrix}, \quad \mathbf{c}_1 = \begin{pmatrix} 1 \\ -2 \\ 5 \end{pmatrix}, \quad \mathbf{c}_2 = \begin{pmatrix} 0 \\ 6 \\ -4 \end{pmatrix}$$

$$\text{Var}(y_1) = \text{Var}(\mathbf{c}_1^\top \mathbf{x}) = \mathbf{c}_1^\top \text{Var}(\mathbf{x}) \mathbf{c}_1 = 960$$

$$\text{Var}(y_2) = \text{Var}(\mathbf{c}_2^\top \mathbf{x}) = \mathbf{c}_2^\top \text{Var}(\mathbf{x}) \mathbf{c}_2 = 1200$$

$$\text{Cov}(y_1, y_2) = \text{Cov}(\mathbf{c}_1^\top \mathbf{x}, \mathbf{c}_2^\top \mathbf{x}) = \mathbf{c}_1^\top \text{Var}(\mathbf{x}) \mathbf{c}_2 = -910$$

Homework: use R to compute the above values

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Now suppose we transform one vector of random variables into another vector of random variables

Transform  $\mathbf{x}$  into

- (i)  $\mathbf{y}_{k \times 1} = \mathbf{A}_{k \times n} \mathbf{x}_{n \times 1}$
- (ii)  $\mathbf{z}_{m \times 1} = \mathbf{B}_{m \times n} \mathbf{x}_{n \times 1}$

The covariance between the elements of these two transformed vectors is an  $k \times m$  covariance matrix =  $\mathbf{AVB}^\top$

For example, the covariance between  $y_i$  and  $y_j$  is given by the  $ij$ -th element of  $\mathbf{AVB}^\top$

Likewise, the covariance between  $y_i$  and  $z_j$  is given by the  $ij$ -th element of  $\mathbf{AVB}^\top$

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# Positive-definite matrix

- A matrix  $V$  is **positive-definite** if for all vectors  $c$  containing at least one non-zero member,  $c^T V c > 0$ .
- A **non-negative definite matrix** satisfies  $c^T V c \geq 0$ .
- Any covariance-matrix is (at least) non-negative definite, as  $\text{Var}(c^T x) = c^T V c \geq 0$ .
- Any nonsingular covariance matrix is positive-definite
  - Nonsingular means  $\det(V) > 0$
  - Equivalently, **all eigenvalues of  $V$  are positive**,  $\lambda_i > 0$ .

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# The Multivariate Normal Distribution (MVN)

Consider the pdf for  $n$  independent normal random variables, the  $i$ th of which has mean  $\mu_i$  and variance  $\sigma_i^2$ ,

$$\begin{aligned} p(\mathbf{x}) &= \prod_{i=1}^n (2\pi)^{-1/2} \sigma_i^{-1} \exp\left(-\frac{(x_i - \mu_i)^2}{2\sigma_i^2}\right) \\ &= (2\pi)^{-n/2} \left(\prod_{i=1}^n \sigma_i\right)^{-1} \exp\left(-\sum_{i=1}^n \frac{(x_i - \mu_i)^2}{2\sigma_i^2}\right) \end{aligned}$$

This can be expressed more compactly in matrix form

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Define the **covariance matrix**  $\mathbf{V}$  for the vector  $\mathbf{x}$  of the  $n$  normal random variable by

$$\mathbf{V} = \begin{pmatrix} \sigma_1^2 & 0 & \cdots & 0 \\ 0 & \sigma_2^2 & \cdots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & \cdots & \cdots & \sigma_n^2 \end{pmatrix} \quad |\mathbf{V}| = \prod_{i=1}^n \sigma_i^2$$

Define the mean vector  $\mu$  as  $\mu = \begin{pmatrix} \mu_1 \\ \mu_2 \\ \vdots \\ \mu_n \end{pmatrix}$  gives

$$\sum_{i=1}^n \frac{(x_i - \mu_i)^2}{\sigma_i^2} = (\mathbf{x} - \boldsymbol{\mu})^T \mathbf{V}^{-1} (\mathbf{x} - \boldsymbol{\mu})$$

Hence in matrix form the MVN pdf becomes

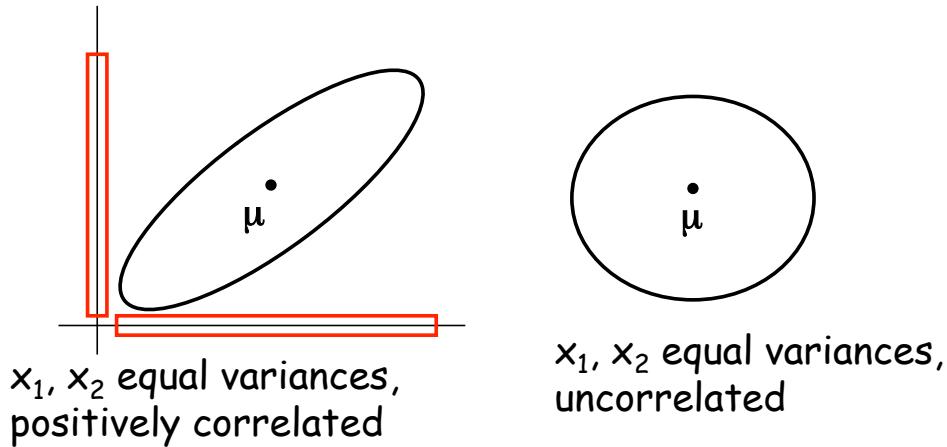
$$p(\mathbf{x}) = (2\pi)^{-n/2} |\mathbf{V}|^{-1/2} \exp \left[ -\frac{1}{2} (\mathbf{x} - \boldsymbol{\mu})^T \mathbf{V}^{-1} (\mathbf{x} - \boldsymbol{\mu}) \right]$$

Notice this holds for any vector  $\mu$  and symmetric positive-definite matrix  $\mathbf{V}$ , as  $|\mathbf{V}| > 0$ . 39

## The multivariate normal

- Just as a univariate normal is defined by its mean and spread (variance), a multivariate normal is defined by its mean vector  $\mu$  (also called the centroid) and variance-covariance matrix  $\mathbf{V}$  (the distribution, or spread, of values around the centroid).

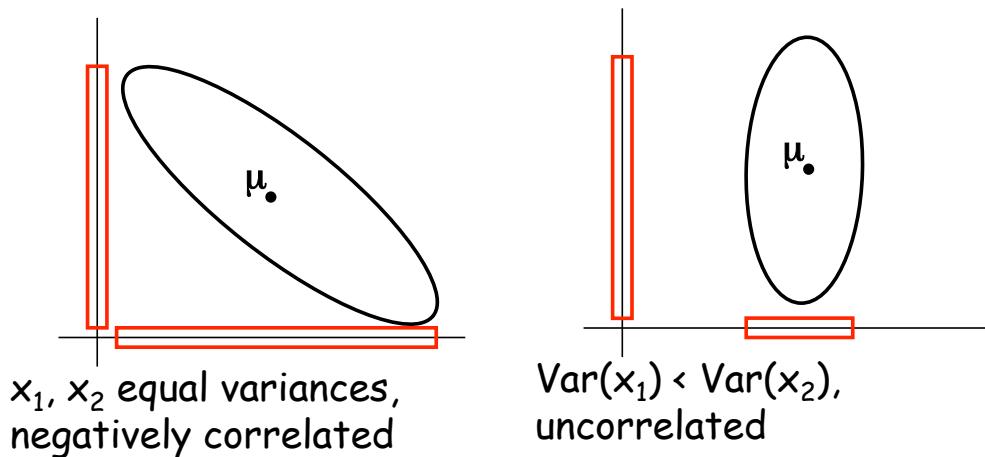
Vector of means  $\mu$  determines location  
 Spread (geometry) about  $\mu$  determined by  $V$



**Eigenstructure** (the eigenvectors and their corresponding eigenvalues) determines the geometry of  $V$ .

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Vector of means  $\mu$  determines location  
 Spread (geometry) about  $\mu$  determined by  $V$

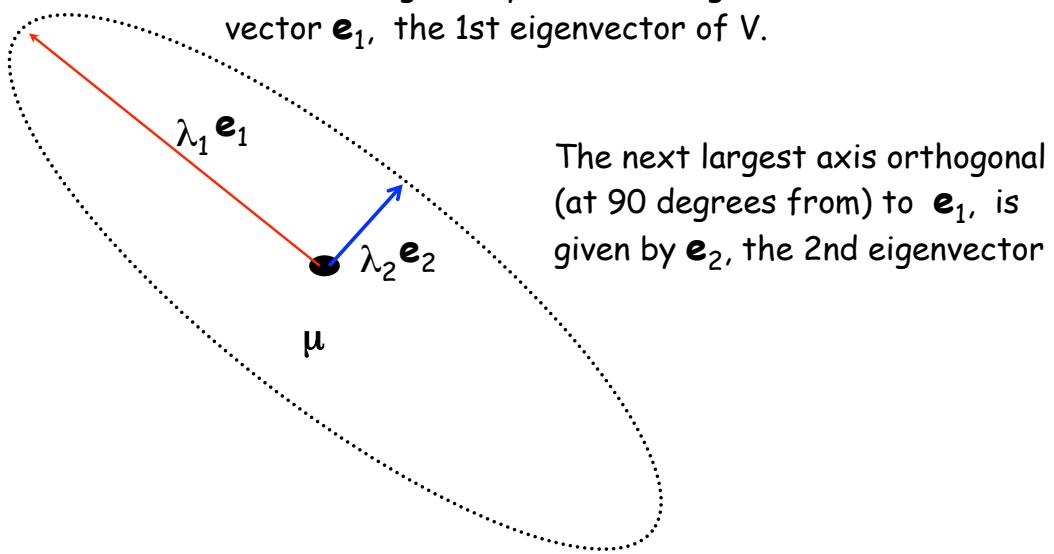


Positive tilt = positive correlations  
 Negative tilt = negative correlation  
 No tilt = uncorrelated

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# Eigenstructure of V

The direction of the largest axis of variation is given by the unit-length vector  $\mathbf{e}_1$ , the 1st eigenvector of  $V$ .



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## Properties of the MVN - I

1) If  $\mathbf{x}$  is MVN, any subset of the variables in  $\mathbf{x}$  is also MVN

2) If  $\mathbf{x}$  is MVN, any linear combination of the elements of  $\mathbf{x}$  is also MVN. If  $\mathbf{x} \sim \text{MVN}(\mu, V)$

for  $\mathbf{y} = \mathbf{x} + \mathbf{a}$ ,  $\mathbf{y}$  is  $\text{MVN}_n(\mu + \mathbf{a}, V)$

for  $y = \mathbf{a}^T \mathbf{x} = \sum_{k=1}^n a_i x_i$ ,  $y$  is  $N(\mathbf{a}^T \mu, \mathbf{a}^T V \mathbf{a})$

for  $\mathbf{y} = \mathbf{Ax}$ ,  $\mathbf{y}$  is  $\text{MVN}_m (\mathbf{A}\mu, \mathbf{A}^T V \mathbf{A})$

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# Principal components

- The principal components (or PCs) of a covariance matrix define the axes of variation.
  - PC1 is the direction (linear combination  $\mathbf{c}^T \mathbf{x}$ ) that explains the most variation.
  - PC2 is the next largest direction (at 90degree from PC1), and so on
- $\mathbf{P}\mathbf{C}_i$  = ith eigenvector of  $\mathbf{V}$
- Fraction of variation accounted for by  $\mathbf{P}\mathbf{C}_i = \lambda_i / \text{trace}(\mathbf{V})$
- If  $\mathbf{V}$  has a few large eigenvalues, most of the variation is distributed along a few linear combinations (axis of variation)

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## Properties of the MVN - II

3) Conditional distributions are also MVN. Partition  $\mathbf{x}$  into two components,  $\mathbf{x}_1$  (m dimensional column vector) and  $\mathbf{x}_2$  (n-m dimensional column vector)

$$\mathbf{x} = \begin{pmatrix} \mathbf{x}_1 \\ \mathbf{x}_2 \end{pmatrix} \quad \mu = \begin{pmatrix} \mu_1 \\ \mu_2 \end{pmatrix} \quad \text{and} \quad \mathbf{V} = \begin{pmatrix} \mathbf{V}_{\mathbf{x}_1 \mathbf{x}_1} & \mathbf{V}_{\mathbf{x}_1 \mathbf{x}_2} \\ \mathbf{V}_{\mathbf{x}_1 \mathbf{x}_2}^T & \mathbf{V}_{\mathbf{x}_2 \mathbf{x}_2} \end{pmatrix}$$

$\mathbf{x}_1 | \mathbf{x}_2$  is MVN with m-dimensional mean vector

$$\mu_{\mathbf{x}_1 | \mathbf{x}_2} = \mu_1 + \mathbf{V}_{\mathbf{x}_1 \mathbf{x}_2} \mathbf{V}_{\mathbf{x}_2 \mathbf{x}_2}^{-1} (\mathbf{x}_2 - \mu_2)$$

and m x m covariance matrix

$$\mathbf{V}_{\mathbf{x}_1 | \mathbf{x}_2} = \mathbf{V}_{\mathbf{x}_1 \mathbf{x}_1} - \mathbf{V}_{\mathbf{x}_1 \mathbf{x}_2} \mathbf{V}_{\mathbf{x}_2 \mathbf{x}_2}^{-1} \mathbf{V}_{\mathbf{x}_1 \mathbf{x}_2}^T$$

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## Properties of the MVN - III

- 4) If  $x$  is MVN, the regression of any subset of  $x$  on another subset is linear and homoscedastic

$$\begin{aligned} \mathbf{x}_1 &= \boldsymbol{\mu}_{\mathbf{x}_1|\mathbf{x}_2} + \mathbf{e} \\ &= \boldsymbol{\mu}_1 + \mathbf{V}_{\mathbf{x}_1\mathbf{x}_2}\mathbf{V}_{\mathbf{x}_2\mathbf{x}_2}^{-1}(\mathbf{x}_2 - \boldsymbol{\mu}_2) + \mathbf{e} \end{aligned}$$

Where  $e$  is MVN with mean vector  $\mathbf{0}$  and variance-covariance matrix  $\mathbf{V}_{\mathbf{x}_1|\mathbf{x}_2}$

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$$\boldsymbol{\mu}_1 + \mathbf{V}_{\mathbf{x}_1\mathbf{x}_2}\mathbf{V}_{\mathbf{x}_2\mathbf{x}_2}^{-1}(\mathbf{x}_2 - \boldsymbol{\mu}_2) + \mathbf{e}$$



The regression is linear because it is a linear function of  $x_2$

The regression is homoscedastic because the variance-covariance matrix for  $e$  does not depend on the value of the  $x$ 's

$$\mathbf{V}_{\mathbf{x}_1|\mathbf{x}_2} = \mathbf{V}_{\mathbf{x}_1\mathbf{x}_1} - \mathbf{V}_{\mathbf{x}_1\mathbf{x}_2}\mathbf{V}_{\mathbf{x}_2\mathbf{x}_2}^{-1}\mathbf{V}_{\mathbf{x}_1\mathbf{x}_2}^T$$

All these matrices are constant, and hence the same for any value of  $x$

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Example: Regression of Offspring value on Parental values

Assume the vector of offspring value and the values of both its parents is MVN. Then from the correlations among (outbred) relatives,

$$\begin{pmatrix} z_o \\ z_s \\ z_d \end{pmatrix} \sim \text{MVN} \left[ \begin{pmatrix} \mu_o \\ \mu_s \\ \mu_d \end{pmatrix}, \sigma_z^2 \begin{pmatrix} 1 & h^2/2 & h^2/2 \\ h^2/2 & 1 & 0 \\ h^2/2 & 0 & 1 \end{pmatrix} \right]$$

Let  $\mathbf{x}_1 = (z_o), \quad \mathbf{x}_2 = \begin{pmatrix} z_s \\ z_d \end{pmatrix}$

$$\mathbf{V}_{\mathbf{x}_1, \mathbf{x}_1} = \sigma_z^2, \quad \mathbf{V}_{\mathbf{x}_1, \mathbf{x}_2} = \frac{h^2 \sigma_z^2}{2} \begin{pmatrix} 1 & 1 \end{pmatrix}, \quad \mathbf{V}_{\mathbf{x}_2, \mathbf{x}_2} = \sigma_z^2 \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix}$$

$$= \boldsymbol{\mu}_1 + \mathbf{V}_{\mathbf{x}_1 \mathbf{x}_2} \mathbf{V}_{\mathbf{x}_2 \mathbf{x}_2}^{-1} (\mathbf{x}_2 - \boldsymbol{\mu}_2) + \mathbf{e}$$

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Regression of Offspring value on Parental values (cont.)

$$= \boldsymbol{\mu}_1 + \mathbf{V}_{\mathbf{x}_1 \mathbf{x}_2} \mathbf{V}_{\mathbf{x}_2 \mathbf{x}_2}^{-1} (\mathbf{x}_2 - \boldsymbol{\mu}_2) + \mathbf{e}$$

$$\mathbf{V}_{\mathbf{x}_1, \mathbf{x}_1} = \sigma_z^2, \quad \mathbf{V}_{\mathbf{x}_1, \mathbf{x}_2} = \frac{h^2 \sigma_z^2}{2} \begin{pmatrix} 1 & 1 \end{pmatrix}, \quad \mathbf{V}_{\mathbf{x}_2, \mathbf{x}_2} = \sigma_z^2 \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix}$$

Hence,

$$\begin{aligned} z_o &= \mu_o + \frac{h^2 \sigma_z^2}{2} (1 \ 1) \sigma_z^{-2} \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} \begin{pmatrix} z_s - \mu_s \\ z_d - \mu_d \end{pmatrix} + e \\ &= \mu_o + \frac{h^2}{2} (z_s - \mu_s) + \frac{h^2}{2} (z_d - \mu_d) + e \end{aligned}$$

where  $e$  is normal with mean zero and variance

$$\mathbf{V}_{\mathbf{x}_1 | \mathbf{x}_2} = \mathbf{V}_{\mathbf{x}_1 \mathbf{x}_1} - \mathbf{V}_{\mathbf{x}_1 \mathbf{x}_2} \mathbf{V}_{\mathbf{x}_2 \mathbf{x}_2}^{-1} \mathbf{V}_{\mathbf{x}_1 \mathbf{x}_2}^T$$

$$\begin{aligned} \sigma_e^2 &= \sigma_z^2 - \frac{h^2 \sigma_z^2}{2} (1 \ 1) \sigma_z^{-2} \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} \frac{h^2 \sigma_z^2}{2} \begin{pmatrix} 1 \\ 1 \end{pmatrix} \\ &= \sigma_z^2 \left( 1 - \frac{h^4}{2} \right) \end{aligned}$$

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Hence, the regression of offspring trait value given the trait values of its parents is

$$z_o = \mu_o + h^2/2(z_s - \mu_s) + h^2/2(z_d - \mu_d) + e$$

where the residual  $e$  is normal with mean zero and  $\text{Var}(e) = \sigma_z^2(1-h^4/2)$

Similar logic gives the regression of offspring breeding value on parental breeding value as

$$\begin{aligned} A_o &= \mu_o + (A_s - \mu_s)/2 + (A_d - \mu_d)/2 + e \\ &= A_s/2 + A_d/2 + e \end{aligned}$$

where the residual  $e$  is normal with mean zero and  $\text{Var}(e) = \sigma_A^2/2$

## Ordinary least squares

For the general linear model

$$\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{e}$$

The predicted values given  $\boldsymbol{\beta}$  and the resulting residuals are given by

$$\hat{\mathbf{y}} = \mathbf{X}\boldsymbol{\beta}, \quad \mathbf{e} = \mathbf{y} - \mathbf{X}\boldsymbol{\beta}$$

Ordinary least squares (OLS) finds the value  $\boldsymbol{\beta}$  that minimizes the sum of squared residuals

$$\sum e_i^2 = \mathbf{e}^T \mathbf{e}$$

or

$$(\mathbf{y} - \mathbf{X}\boldsymbol{\beta})^T (\mathbf{y} - \mathbf{X}\boldsymbol{\beta})$$

The solution is given by setting the derivative of this function with respect to  $\boldsymbol{\beta}$  equal to zero and solving.

**Hence, we need to discuss vector/matrix derivatives**

## The gradient, the derivative of a vector-valued function

$$\nabla_{\mathbf{x}}[f] = \frac{\partial f}{\partial \mathbf{x}} = \begin{pmatrix} \frac{\partial f}{\partial x_1} \\ \frac{\partial f}{\partial x_2} \\ \vdots \\ \frac{\partial f}{\partial x_n} \end{pmatrix}$$

Compute the gradient for

$$f(\mathbf{x}) = \sum_{i=1}^n x_i^2 = \mathbf{x}^T \mathbf{x}$$

Since  $\partial f / \partial x_i = 2x_i$ , the gradient vector is just  $\nabla_{\mathbf{x}}[f(\mathbf{x})] = 2\mathbf{x}$ .

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## Some common derivatives

$$\begin{aligned}\nabla_{\mathbf{x}} [\mathbf{a}^T \mathbf{x}] &= \nabla_{\mathbf{x}} [\mathbf{x}^T \mathbf{a}] = \mathbf{a} \\ \nabla_{\mathbf{x}} [\mathbf{A}\mathbf{x}] &= \mathbf{A}^T\end{aligned}$$

Turning to quadratic forms, if  $\mathbf{A}$  is symmetric, then

$$\begin{aligned}\nabla_{\mathbf{x}} [\mathbf{x}^T \mathbf{A}\mathbf{x}] &= 2 \cdot \mathbf{A}\mathbf{x} \\ \nabla_{\mathbf{x}} [(\mathbf{x} - \mathbf{a})^T \mathbf{A}(\mathbf{x} - \mathbf{a})] &= 2 \cdot \mathbf{A}(\mathbf{x} - \mathbf{a}) \\ \nabla_{\mathbf{x}} [(\mathbf{a} - \mathbf{x})^T \mathbf{A}(\mathbf{a} - \mathbf{x})] &= -2 \cdot \mathbf{A}(\mathbf{a} - \mathbf{x})\end{aligned}$$

Taking  $\mathbf{A} = \mathbf{I}$ ,

$$\nabla_{\mathbf{x}} [\mathbf{x}^T \mathbf{x}] = \nabla_{\mathbf{x}} [\mathbf{x}^T \mathbf{I}\mathbf{x}] = 2 \cdot \mathbf{I}\mathbf{x} = 2 \cdot \mathbf{x}$$

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$$\begin{aligned}
\sum_{i=1}^n e_i^2 &= \mathbf{e}^T \mathbf{e} = (\mathbf{y} - \mathbf{X}\boldsymbol{\beta})^T (\mathbf{y} - \mathbf{X}\boldsymbol{\beta}) \\
&= \mathbf{y}^T \mathbf{y} - \boldsymbol{\beta}^T \mathbf{X}^T \mathbf{y} - \mathbf{y}^T \mathbf{X}\boldsymbol{\beta} + \boldsymbol{\beta}^T \mathbf{X}^T \mathbf{X}\boldsymbol{\beta} \\
&= \mathbf{y}^T \mathbf{y} - 2\boldsymbol{\beta}^T \mathbf{X}^T \mathbf{y} + \boldsymbol{\beta}^T \mathbf{X}^T \mathbf{X}\boldsymbol{\beta}
\end{aligned}$$

where the last step follows since the matrix product  $\boldsymbol{\beta}^T \mathbf{X}^T \mathbf{y}$  yields a scalar, and hence it equals its transpose,

$$\boldsymbol{\beta}^T \mathbf{X}^T \mathbf{y} = (\boldsymbol{\beta}^T \mathbf{X}^T \mathbf{y})^T = \mathbf{y}^T \mathbf{X}\boldsymbol{\beta}$$

To find the vector  $\boldsymbol{\beta}$  that minimizes  $\mathbf{e}^T \mathbf{e}$ , taking the derivative with respect to  $\boldsymbol{\beta}$  and using Equations A5.1a/c gives

$$\frac{\partial \mathbf{e}^T \mathbf{e}}{\partial \boldsymbol{\beta}} = -2\mathbf{X}^T \mathbf{y} + 2\mathbf{X}^T \mathbf{X}\boldsymbol{\beta}$$

Setting this equal to zero gives  $\mathbf{X}^T \mathbf{X}\boldsymbol{\beta} = \mathbf{X}^T \mathbf{y}$  giving

$$\boldsymbol{\beta} = (\mathbf{X}^T \mathbf{X})^{-1} \mathbf{X}^T \mathbf{y}$$

## Additional R matrix commands

Operator or Function	Description
<code>A * B</code>	Element-wise multiplication
<code>A %*% B</code>	Matrix multiplication
<code>A %o% B</code>	Outer product. $\mathbf{A}\mathbf{B}'$
<code>crossprod(A,B)</code> <code>crossprod(A)</code>	$\mathbf{A}'\mathbf{B}$ and $\mathbf{A}'\mathbf{A}$ respectively.
<code>t(A)</code>	Transpose
<code>diag(x)</code>	Creates diagonal matrix with elements of $x$ in the principal diagonal
<code>diag(A)</code>	Returns a vector containing the elements of the principal diagonal
<code>diag(k)</code>	If $k$ is a scalar, this creates a $k \times k$ identity matrix. Go figure.
<code>solve(A, b)</code>	Returns vector $x$ in the equation $b = Ax$ (i.e., $A^{-1}b$ )
<code>solve(A)</code>	Inverse of $A$ where $A$ is a square matrix.
<code>ginv(A)</code>	Moore-Penrose Generalized Inverse of $A$ . <code>ginv(A)</code> requires loading the <code>MASS</code> package.
<code>y&lt;-eigen(A)</code>	$y\$val$ are the eigenvalues of $A$ $y\$vec$ are the eigenvectors of $A$
<code>y&lt;-svd(A)</code>	Single value decomposition of $A$ . $y\$d$ = vector containing the singular values of $A$ $y\$u$ = matrix with columns contain the left singular vectors of $A$ $y\$v$ = matrix with columns contain the right singular vectors of $A$

## Additional R matrix commands (cont)

<code>R &lt;- chol(A)</code>	Choleski factorization of A. Returns the upper triangular factor, such that $R'R = A$ .
<code>y &lt;- qr(A)</code>	QR decomposition of A. <code>y\$qr</code> has an upper triangle that contains the decomposition and a lower triangle that contains information on the Q decomposition. <code>y\$rank</code> is the rank of A. <code>y\$qraux</code> a vector which contains additional information on Q. <code>y\$pivot</code> contains information on the pivoting strategy used.
<code>cbind(A,B,...)</code>	Combine matrices(vectors) horizontally. Returns a matrix.
<code>rbind(A,B,...)</code>	Combine matrices(vectors) vertically. Returns a matrix.
<code>rowMeans(A)</code>	Returns vector of row means.
<code>rowSums(A)</code>	Returns vector of row sums.
<code>colMeans(A)</code>	Returns vector of column means.
<code>colSums(A)</code>	Returns vector of column means.

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## Additional references

- Lynch & Walsh Chapter 8 (intro to matrices)
- Online notes (Walsh & Lynch):
  - Appendix 4 (Matrix geometry)
  - Appendix 5 (Matrix derivatives)

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# Lecture 2: Linear and Mixed Models

Bruce Walsh lecture notes  
SISG -Mixed Model Course  
Seattle, 16 - 18 July 2014

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## Quick Review of the Major Points

The general linear model can be written as

$$\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{e}$$

- $\mathbf{y}$  = vector of observed **response** values
- $\mathbf{X}$  = Design matrix: observations of the **explanatory** variables in the assumed linear model
- $\boldsymbol{\beta}$  = vector of unknown parameters to estimate
- $\mathbf{e}$  = vector of residuals (deviation from model fit),  
$$\mathbf{e} = \mathbf{y} - \mathbf{X} \boldsymbol{\beta}$$

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$$\mathbf{y} = \mathbf{X}\beta + \mathbf{e}$$

Solution to  $\beta$  depends on the **covariance structure**  
 (= covariance matrix) of the vector  $\mathbf{e}$  of residuals

### Ordinary least squares (OLS)

- OLS:  $\mathbf{e} \sim MVN(\mathbf{0}, \sigma^2 \mathbf{I})$
- Residuals are **homoscedastic** and uncorrelated,  
 so that we can write the cov matrix of  $\mathbf{e}$  as  $Cov(\mathbf{e}) = \sigma^2 \mathbf{I}$
- the OLS estimate,  $OLS(\beta) = \mathbf{b} = (\mathbf{X}^\top \mathbf{X})^{-1} \mathbf{X}^\top \mathbf{y}$

### Generalized least squares (GLS)

- GLS:  $\mathbf{e} \sim MVN(\mathbf{0}, \mathbf{V})$
- Residuals are **heteroscedastic** and/or dependent,
- $GLS(\beta) = (\mathbf{X}^\top \mathbf{V}^{-1} \mathbf{X})^{-1} \mathbf{X}^\top \mathbf{V}^{-1} \mathbf{y}$

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## BLUE

- Both the OLS and GLS solutions are also called the **Best Linear Unbiased Estimator** (or **BLUE** for short)
- Whether the OLS or GLS form is used depends on the assumed covariance structure for the residuals
  - Special case of  $Var(\mathbf{e}) = \sigma_e^2 \mathbf{I}$  -- OLS
  - All others, i.e.,  $Var(\mathbf{e}) = \mathbf{R}$  -- GLS

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# Linear Models

One tries to explain a response (or **dependent**) variable  $y$  as a linear function of a number of explanatory (or **predictor**) variables.

A **multiple regression** is a typical linear model,

$$y = \mu + \beta_1 x_1 + \beta_2 x_2 + \cdots + \beta_n x_n + e$$

Here  $e$  is the **residual**, or deviation between the true value observed and the value predicted by the linear model.

The (**partial**) **regression coefficients** are interpreted as follows: a unit change in  $x_i$  while holding all other variables constant is associated with a change of  $\beta_i$  in  $y$

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# Linear Models

As with a univariate regression ( $y = a + bx + e$ ), the model parameters are typically chosen by **least squares**, wherein they are chosen to **minimize the sum of squared residuals**,  $\sum e_i^2$

This unweighted sum of squared residuals assumes an OLS error structure, so all residuals are equally weighted (homoscedastic) and uncorrelated

If the residuals differ in variances and/or some are correlated (GLS conditions), then we need to minimize the weighted sum  $\mathbf{e}^T \mathbf{V}^{-1} \mathbf{e}$ , which removes correlations and gives all residuals equal variance.

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# Predictor and Indicator Variables

Suppose we measure the offspring of  $p$  sires. One linear model would be

$$y_{ij} = \mu + s_i + e_{ij}$$

$y_{ij}$  = trait value of offspring  $j$  from sire  $i$

$\mu$  = overall mean. This term is included to give the  $s_i$  terms a mean value of zero, i.e., they are expressed as **deviations from the mean**

$s_i$  = The effect for sire  $i$  (the mean of its offspring). Recall that variance in the  $s_i$  estimates  $\text{Cov}(\text{half sibs}) = V_A/4$

$e_{ij}$  = The deviation of the  $j$ th offspring from the family mean of sire  $i$ . The variance of the  $e$ 's estimates the within-family variance.

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# Predictor and Indicator Variables

In a regression, the predictor variables are typically continuous, although they need not be.

$$y_{ij} = \mu + s_i + e_{ij}$$

Note that the predictor variables here are the  $s_i$ , (the value associated with sire  $i$ ) something that we are trying to estimate

We can write this in linear model form,  $y_{ij} = \mu + \sum_k x_{ik}s_i + e_{ij}$ , by using **indicator variables**

$$x_{ik} = \begin{cases} 1 & \text{if sire } k = i \\ 0 & \text{otherwise} \end{cases}$$

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Models consisting entirely of indicator variables are typically called **ANOVA**, or **analysis of variance models**

Models that contain no indicator variables (other than for the mean), but rather consist of observed values of continuous or discrete values are typically called **regression models**

Both are special cases of the **General Linear Model** (or **GLM**)

$$Y_{ijk} = \mu + s_i + d_{ij} + \beta x_{ijk} + e_{ijk}$$

Example: Nested half sib/full sib design with an age correction  $\beta$  on the trait

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Example: Nested half sib/full sib design with an age correction  $\beta$  on the trait

ANOVA model

$$Y_{ijk} = \mu + s_i + d_{ij} + \beta x_{ijk} + e_{ijk}$$



Regression model

$s_i$  = effect of sire i

$d_{ij}$  = effect of dam j crossed to sire i

$x_{ijk}$  = age of the kth offspring from i x j cross

# Linear Models in Matrix Form

Suppose we have 3 variables in a multiple regression, with four  $(y, x)$  vectors of observations.

$$y_i = \mu + \beta_1 x_{i1} + \beta_2 x_{i2} + \beta_3 x_{i3} + e_i$$

In matrix form,  $\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{e}$

$$\mathbf{y} = \begin{pmatrix} y_1 \\ y_2 \\ y_3 \\ y_4 \end{pmatrix} \quad \boldsymbol{\beta} = \begin{pmatrix} \mu \\ \beta_1 \\ \beta_2 \\ \beta_3 \end{pmatrix} \quad \mathbf{X} = \begin{pmatrix} 1 & x_{11} & x_{12} & x_{13} \\ 1 & x_{21} & x_{22} & x_{23} \\ 1 & x_{31} & x_{32} & x_{33} \\ 1 & x_{41} & x_{42} & x_{43} \end{pmatrix} \quad \mathbf{e} = \begin{pmatrix} e_1 \\ e_2 \\ e_3 \\ e_4 \end{pmatrix}$$

The **design (or incidence) matrix**  $\mathbf{X}$ . Details of both the experimental design and the observed values of the predictor variables **all reside solely in  $\mathbf{X}$**

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## In-class Exercise

Suppose you measure height and sprint speed for five individuals, with heights ( $x$ ) of 9, 10, 11, 12, 13 and associated sprint speeds ( $y$ ) of 60, 138, 131, 170, 221

1) Write in matrix form (i.e., the design matrix  $\mathbf{X}$  and vector  $\boldsymbol{\beta}$  of unknowns) the following models

- $y = bx$
- $y = a + bx$
- $y = bx^2$
- $y = a + bx + cx^2$

2) Using the  $\mathbf{X}$  and  $\mathbf{y}$  associated with these models, compute the OLS BLUE,  $\mathbf{b} = (\mathbf{X}^T \mathbf{X})^{-1} \mathbf{X}^T \mathbf{y}$  for each

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# Rank of the design matrix

- With  $n$  observations and  $p$  unknowns,  $X$  is an  $n \times p$  matrix, so that  $X^T X$  is  $p \times p$
- Thus, at most  $X$  can provide unique estimates for up to  $p < n$  parameters
- The rank of  $X$  is the number of independent rows of  $X$ . If  $X$  is of **full rank**, then rank =  $p$
- A parameter is said to be **estimable** if we can **provide a unique estimate of it**. If the rank of  $X$  is  $k < p$ , then exactly  $k$  parameters are estimable (some as linear combinations, e.g.  $\beta_1 - 3\beta_3 = 4$ )
- if  $\det(X^T X) = 0$ , then  $X$  is not of full rank
- Number of nonzero eigenvalues of  $X^T X$  gives the rank of  $X$ .**

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# Experimental design and $X$

- The structure of  $X$  determines not only which parameters are estimable, but **also the expected sample variances**, as  $\text{Var}(\hat{\beta}) = \text{var}(e)^* (X^T X)^{-1}$
- Experimental design determines the structure of  $X$  before an experiment** (of course, missing data almost always means the final  $X$  is different from the proposed  $X$ )
- Different criteria used for an optimal design. Let  $V = (X^T X)^{-1}$ . The idea is to choose a design for  $X$  given the constraints of the experiment that:
  - **A-optimality**: minimizes  $\text{tr}(V)$
  - **D-optimality**: minimizes  $\det(V)$
  - **E-optimality**: minimizes leading eigenvalue of  $V$

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# Ordinary Least Squares (OLS)

When the covariance structure of the residuals has a certain form, we solve for the vector  $\beta$  using OLS

If residuals follow a MVN distribution, OLS = ML solution

If the residuals are homoscedastic and uncorrelated,  $\sigma^2(e_i) = \sigma_e^2$ ,  $\sigma(e_i, e_j) = 0$ . Hence, each residual is equally weighted,

Sum of squared residuals can be written as

$$\sum_{i=1}^n \hat{e}_i^2 = \hat{\mathbf{e}}^T \hat{\mathbf{e}} = (\mathbf{y} - \mathbf{X}\beta)^T (\mathbf{y} - \mathbf{X}\beta)$$

Predicted value of the y's

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# Ordinary Least Squares (OLS)

$$\sum_{i=1}^n \hat{e}_i^2 = \hat{\mathbf{e}}^T \hat{\mathbf{e}} = (\mathbf{y} - \mathbf{X}\beta)^T (\mathbf{y} - \mathbf{X}\beta)$$

Taking (matrix) derivatives shows this is minimized by

$$\beta = (\mathbf{X}^T \mathbf{X})^{-1} \mathbf{X}^T \mathbf{y}$$

This is the OLS estimate of the vector  $\beta$

The variance-covariance estimate for the sample estimates is

$$\mathbf{V}_\beta = (\mathbf{X}^T \mathbf{X})^{-1} \sigma_e^2$$

The ij-th element gives the covariance between the estimates of  $\beta_i$  and  $\beta_j$ .

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# Sample Variances/Covariances

The residual variance can be estimated as

$$\widehat{\sigma}_e^2 = \frac{1}{n - \text{rank}(X)} \sum_{i=1}^n \widehat{e}_i^2$$

The estimated residual variance can be substituted into

$$\mathbf{V}_\beta = (\mathbf{X}^T \mathbf{X})^{-1} \sigma_e^2$$

To give an approximation for the sampling variance and covariances of our estimates.

Confidence intervals follow since the vector of estimates  
 $\sim \text{MVN}(\beta, \mathbf{V}_\beta)$

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## Example: Regression Through the Origin

$$y_i = \beta x_i + e_i$$

Here  $\mathbf{X} = \begin{pmatrix} x_1 \\ x_2 \\ \vdots \\ x_n \end{pmatrix}$   $\mathbf{y} = \begin{pmatrix} y_1 \\ y_2 \\ \vdots \\ y_n \end{pmatrix}$   $\beta = (\beta)$

$$\mathbf{X}^T \mathbf{X} = \sum_{i=1}^n x_i^2 \quad \mathbf{X}^T \mathbf{y} = \sum_{i=1}^n x_i y_i$$

$\beta = (\mathbf{X}^T \mathbf{X})^{-1} \mathbf{X}^T \mathbf{y} = \frac{\sum x_i y_i}{\sum x_i^2}$	$\sigma^2(\beta) = \frac{1}{n-1} \frac{\sum (y_i - \beta x_i)^2}{\sum x_i^2}$	$\sigma^2(\beta) = (\mathbf{X}^T \mathbf{X})^{-1} \sigma_e^2 = \frac{\sigma_e^2}{\sum x_i^2}$
--	---	---

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# Polynomial Regressions

GLM can easily handle any function of the observed predictor variables, provided the parameters to estimate are still linear, e.g.  $y = \alpha + \beta_1 f(x) + \beta_2 g(x) + \dots + e$

Quadratic regression:

$$y_i = \alpha + \beta_1 x_i + \beta_2 x_i^2 + e_i$$

$$\boldsymbol{\beta} = \begin{pmatrix} \alpha \\ \beta_1 \\ \beta_2 \end{pmatrix} \quad \mathbf{X} = \begin{pmatrix} 1 & x_1 & x_1^2 \\ 1 & x_2 & x_2^2 \\ \vdots & \vdots & \vdots \\ 1 & x_n & x_n^2 \end{pmatrix}$$

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# Interaction Effects

Interaction terms (e.g. sex  $\times$  age) are handled similarly

$$y_i = \alpha + \beta_1 x_{i1} + \beta_2 x_{i2} + \beta_3 x_{i1}x_{i2} + e_i$$

$$\boldsymbol{\beta} = \begin{pmatrix} \alpha \\ \beta_1 \\ \beta_2 \\ \beta_3 \end{pmatrix} \quad \mathbf{X} = \begin{pmatrix} 1 & x_{11} & x_{12} & x_{11}x_{12} \\ 1 & x_{21} & x_{22} & x_{21}x_{22} \\ \vdots & \vdots & \vdots & \vdots \\ 1 & x_{n1} & x_{n2} & x_{n1}x_{n2} \end{pmatrix}$$

With  $x_1$  held constant, a unit change in  $x_2$  changes  $y$  by  $\beta_2 + \beta_3 x_1$  (i.e., the slope in  $x_2$  depends on the current value of  $x_1$ )

Likewise, a unit change in  $x_1$  changes  $y$  by  $\beta_1 + \beta_3 x_2$

# The GLM lets you build your own model!

- Suppose you want a quadratic regression forced through the origin where the slope of the quadratic term can vary over the sexes (pollen vs. seed parents)
- $Y_i = \beta_1 x_i + \beta_2 x_i^2 + \beta_3 s_i x_i^2$
- $s_i$  is an indicator (0/1) variable for the sex (0 = male, 1 = female).
  - Male slope =  $\beta_2$ ,
  - Female slope =  $\beta_2 + \beta_3$

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## Generalized Least Squares (GLS)

Suppose the residuals no longer have the same variance (i.e., display heteroscedasticity). Clearly we do not wish to minimize the unweighted sum of squared residuals, because those residuals with smaller variance should receive more weight.

Likewise in the event the residuals are correlated, we also wish to take this into account (i.e., perform a suitable transformation to remove the correlations) before minimizing the sum of squares.

Either of the above settings leads to a GLS solution in place of an OLS solution.

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In the GLS setting, the covariance matrix for the vector  $e$  of residuals is written as  $R$  where

$$R_{ij} = \sigma(e_i, e_j)$$

The linear model becomes  $y = X\beta + e$ ,  $\text{cov}(e) = R$

The GLS solution for  $\beta$  is

$$\hat{\beta} = (X^T R^{-1} X)^{-1} X^T R^{-1} y$$

The variance-covariance of the estimated model parameters is given by

$$V_{\hat{\beta}} = (X^T R^{-1} X)^{-1} \sigma_e^2$$

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## Model diagnostics

- **It's all about the residuals**
- Plot the residuals
  - Quick and easy screen for outliers
- Test for normality among estimated residuals
  - Q-Q plot
  - Shapiro-Wilk test
  - If non-normal, try transformations, such as log

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## OLS, GLS summary

	OLS	GLS
Assumed distribution of residuals	$\mathbf{e} \sim (\mathbf{0}, \sigma_e^2 \mathbf{I})$	$\mathbf{e} \sim (\mathbf{0}, \mathbf{V})$
Least-squares estimator of $\beta$	$\hat{\beta} = (\mathbf{X}^T \mathbf{X})^{-1} \mathbf{X}^T \mathbf{y}$	$\hat{\beta} = (\mathbf{X}^T \mathbf{V}^{-1} \mathbf{X})^{-1} \mathbf{X}^T \mathbf{V}^{-1} \mathbf{y}$
$\text{Var}(\hat{\beta})$	$(\mathbf{X}^T \mathbf{X})^{-1} \sigma_e^2$	$(\mathbf{X}^T \mathbf{V}^{-1} \mathbf{X})^{-1}$
Predicted values, $\hat{\mathbf{y}} = \mathbf{X}\hat{\beta}$	$\mathbf{X}(\mathbf{X}^T \mathbf{X})^{-1} \mathbf{X}^T \mathbf{y}$	$\mathbf{X}(\mathbf{X}^T \mathbf{V}^{-1} \mathbf{X})^{-1} \mathbf{X}^T \mathbf{V}^{-1} \mathbf{y}$
$\text{Var}(\hat{\mathbf{y}})$	$\mathbf{X}(\mathbf{X}^T \mathbf{X})^{-1} \mathbf{X}^T \sigma_e^2$	$\mathbf{X}(\mathbf{X}^T \mathbf{V}^{-1} \mathbf{X})^{-1} \mathbf{X}^T$

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## Fixed vs. Random Effects

In linear models we are trying to accomplish two goals: estimation the values of model parameters and estimate any appropriate variances.

For example, in the simplest regression model,  $y = \alpha + \beta x + e$ , we estimate the values for  $\alpha$  and  $\beta$  and also the variance of  $e$ . We, of course, can also estimate the  $e_i = y_i - (\alpha + \beta x_i)$

Note that  $\alpha/\beta$  are **fixed constants** we trying to estimate (**fixed factors** or **fixed effects**), while the  $e_i$  values are drawn from some probability distribution (typically Normal with mean 0, variance  $\sigma_e^2$ ). The  $e_i$  are **random effects**.

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This distinction between fixed and random effects is extremely important in terms of how we analyze a model.

If a parameter is a fixed constant we wish to estimate, it is a fixed effect. If a parameter is drawn from some probability distribution and we are trying to make inferences on either the distribution and/or specific realizations from this distribution, it is a random effect.

We generally speak of estimating fixed factors (BLUE) and predicting random effects (BLUP -- best linear unbiased Predictor)

"Mixed" models (MM) contain both fixed and random factors

$$y = Xb + Zu + e, \quad u \sim MVN(0, R), \quad e \sim MVN(0, \sigma^2_e I)$$

Key: need to specify covariance structures for MM

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## Example: Sire model

$$Y_{ij} = \mu + s_i + e_{ij}$$

Here  $\mu$  is a fixed effect, and  $e$  is a random effect

Is the sire effect  $s$  fixed or random ?

It depends. If we have (say) 10 sires, if we are ONLY interested in the values of these particular 10 sires and don't care to make any other inferences about the population from which the sires are drawn, then we can treat them as fixed effects. In the case, the model is fully specified by the covariance structure for the residuals. Thus, we need to estimate  $\mu, s_1$  to  $s_{10}$  and  $\sigma^2_e$ , and we write the model as  $y_{ij} = \mu + s_i + e_{ij}, \sigma^2(e) = \sigma^2_e I$

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# Random effects models

- It is often useful to treat certain effects as random, as opposed to fixed
  - Suppose we have  $k$  effects. If we treat these as fixed, we **spend  $k$  degrees of freedom**
  - If we assume each of the  $k$  realizations are drawn from a normal with mean zero and unknown variance, only **one degree of freedom lost** --- that for estimating the variance
    - We can then predict the values of the  $k$  realizations

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# Environmental effects

- Consider yield data measured over several years in a series of plots.
- Standard to treat year-to-year variation at a specific site as being random effects
- Often the plot effects (mean value over years) are also treated as random.
- For example, consider plants group in **growing region  $i$ , location  $k$  within that region, and year (season)  $j$**  for that location-region effect
  - $E = R_i + L_{ik} + e_{ijk}$
  - Typically  $R$  can be a fixed effect, while  $L$  and  $e$  are random effects,  $L_{ik} \sim N(0, \sigma^2_L)$  and  $e_{ijk} \sim N(0, \sigma^2_e)$

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# Random models

- With a random model, one is assuming that all "levels" of a factor are not observed. Rather, some subset of values are drawn from some underlying distribution
  - For example, year to year variation in rainfall at a location. Each year is a random sample from the long-term distribution of rainfall values
  - Typically, assume a functional form for this underlying distribution (e.g., normal with mean 0) and then use observations to estimate the distribution parameters (here, the variance)

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## Random models (cont)

- Key feature:
  - Only one degree of freedom used (estimate of the variance)
  - Using the fixed effects and the estimated underlying distribution parameters, one then predicts the actual realizations of the individual values (i.e., the year effects)
  - Assumption: the covariance structure among the individual realizations of the realized effects. If only a variance is assumed, this implies each realization is independent. If realizations are assumed to be correlated, this structure must be estimated.

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# Random models

- Let's go back to treating yearly effects as random
- If assume these are uncorrelated, only use one degree of freedom, but makes assumptions about covariance structure
  - Standard: Uncorrelated
  - Option: some sort of autocorrelation process, say with a yearly decay of  $r$  (must also be estimated)
- Conversely, could all be treated as fixed, but would use  $k$  degrees of freedom for  $k$  years, but no assumptions on their relationships (covariance structure)

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$$y_{ij} = \mu + s_i + e_{ij}$$

Conversely, if we are not only interested in these 10 particular sires but also wish to make some inference about the population from which they were drawn (such as the additive variance, since  $\sigma^2_A = 4\sigma^2_{s_i}$ ), then the  $s_i$  are **random effects**. In this case we wish to estimate  $\mu$  and the variances  $\sigma^2_s$  and  $\sigma^2_e$ . Since  $2s_i$  also estimates (or predicts) the breeding value for sire  $i$ , we also wish to estimate (predict) these as well. Under a random-effects interpretation, we write the model as

$y_{ij} = \mu + s_i + e_{ij}, \sigma^2(e) = \sigma^2_e I, \sigma^2(s) = \sigma^2_A A$

The **relationship matrix**  $A$  of know constants is given by the pedigree and is discussed later

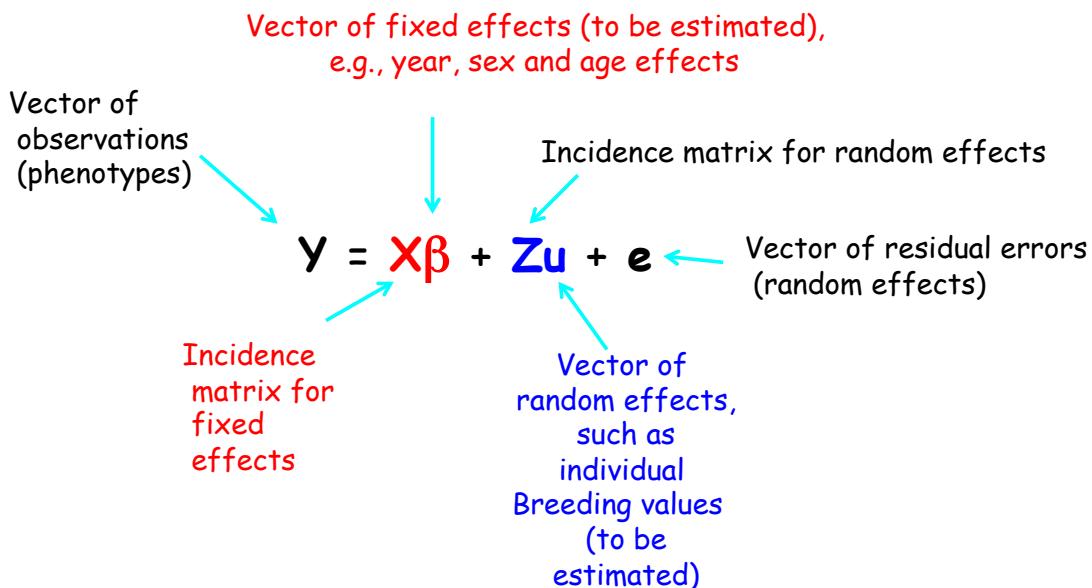
34

# Identifiability

- Recall that a fixed effect is said to be **estimable** if we can obtain a unique estimate for it (either because  $X$  is of full rank or when using a generalized inverse it returns a unique estimate)
  - Lack of estimable arises because the experiment design confounds effects
- The analogous term for random models is **identifiability**
  - The variance components have unique estimates

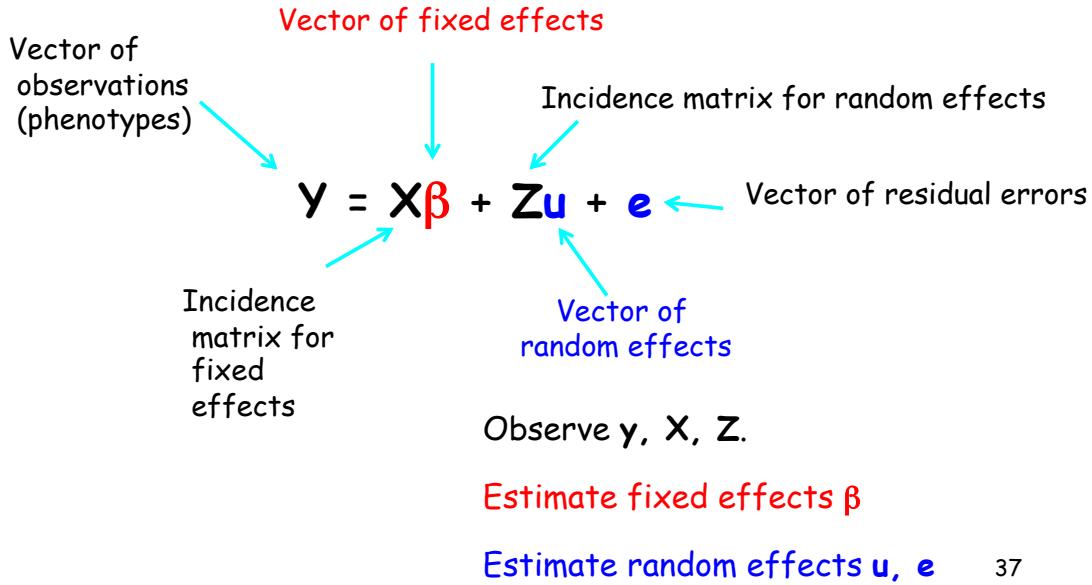
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## The general linear mixed model



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# The general mixed model



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Means & Variances for  $\mathbf{y} = \mathbf{X}\beta + \mathbf{Z}\mathbf{u} + \mathbf{e}$

Means:  $E(\mathbf{u}) = E(\mathbf{e}) = 0, E(\mathbf{y}) = \mathbf{X}\beta$

Variances:

Let  $\mathbf{R}$  be the covariance matrix for the residuals. We typically assume  $\mathbf{R} = \sigma_e^2 * \mathbf{I}$

Let  $\mathbf{G}$  be the covariance matrix for the vector  $\mathbf{u}$  of random effects

The covariance matrix for  $\mathbf{y}$  becomes

$$\mathbf{V} = \mathbf{Z}\mathbf{G}\mathbf{Z}^T + \mathbf{R}$$

Hence,  $\mathbf{y} \sim MVN(\mathbf{X}\beta, \mathbf{V})$

Mean  $\mathbf{X}\beta$  due to fixed effects

Variance  $\mathbf{V}$  due to random effects

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## Chi-square and F distributions

Let  $U_i \sim N(0,1)$ , i.e., a unit normal

The sum  $U_1^2 + U_2^2 + \dots + U_k^2$  is a chi-square random variable with  $k$  degrees of freedom

Under appropriate normality assumptions, the sums of squares that appear in linear models are also chi-square distributed. In particular,

$$\sum_{i=1}^n (x_i - \bar{x})^2 \sim \chi_{n-1}^2$$

The ratio of two chi-squares is an F distribution

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In particular, an F distribution with  $k$  numerator degrees of freedom, and  $n$  denominator degrees of freedom is given by

$$\frac{\chi_k^2/k}{\chi_n^2/n} \sim F_{k,n}$$

The expected value of a chi-square with  $k$  degrees of freedom is  $k$ , hence numerator and denominator both have expected value one

F distributions frequently arise in tests of linear models, as these usually involve ratios of sums of squares.

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## Sums of Squares in linear models

The total sums of squares ( $SST$ ) of a linear model can be written as the sum of the error (or residual) sum of squares and the model (or regression) sum of squares

$$SS_T = SS_M + SS_E$$

$$\sum(y_i - \bar{y})^2 \quad \sum(\hat{y}_i - \bar{y})^2 \quad \sum(y_i - \hat{y}_i)^2$$

$r^2$ , the coefficient of determination, is the fraction of variation accounted for by the model

$$r^2 = \frac{SS_M}{SS_T} = 1 - \frac{SS_E}{SS_T}$$
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Sums of Squares are quadratic products

$$SS_T = \sum_{i=1}^n (y_i - \bar{y})^2 = \sum_{i=1}^n y_i^2 - \bar{y}^2 = \sum_{i=1}^n y_i^2 - \frac{1}{n^2} \left( \sum_{i=1}^n y_i \right)^2$$

We can write this as a quadratic product as

$$SS_T = \mathbf{y}^T \mathbf{y} - \frac{1}{n} \mathbf{y}^T \mathbf{J} \mathbf{y} = \mathbf{y}^T \left( \mathbf{I} - \frac{1}{n} \mathbf{J} \right) \mathbf{y}$$

Where  $\mathbf{J}$  is a matrix all of whose elements are 1's

$$SS_E = \sum_{i=1}^n (y_i - \hat{y}_i)^2 = \sum_{i=1}^n \hat{e}_i^2$$

$$SS_E = \mathbf{y}^T \left( \mathbf{I} - \mathbf{X} \left( \mathbf{X}^T \mathbf{X} \right)^{-1} \mathbf{X}^T \right) \mathbf{y}$$

$$SS_M = SS_T - SS_E = \mathbf{y}^T \left( \mathbf{X} \left( \mathbf{X}^T \mathbf{X} \right)^{-1} \mathbf{X}^T - \frac{1}{n} \mathbf{J} \right) \mathbf{y}$$
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# Expected value of sums of squares

- In ANOVA tables, the  $E(MS)$ , or expected value of the Mean Squares (scaled SS or Sum of Squares), often appears
- This directly follows from the quadratic product. If  $E(\mathbf{x}) = \boldsymbol{\mu}$ ,  $\text{Var}(\mathbf{x}) = \mathbf{V}$ , then
  - $E(\mathbf{x}^T \mathbf{A} \mathbf{x}) = \text{tr}(\mathbf{AV}) + \boldsymbol{\mu}^T \mathbf{A} \boldsymbol{\mu}$

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## Hypothesis testing

Provided the residual errors in the model are MVN, then for a model with  $n$  observations and  $p$  estimated parameters,

$$\frac{SS_E}{\sigma_e^2} \sim \chi_{n-p}^2$$

Consider the comparison of a full ( $p$  parameters) and reduced ( $q < p$ ) models, where  $SSE_r$  = error SS for reduced model,  $SSE_f$  = error SS for full model

$$\left( \frac{SSE_r - SSE_f}{p - q} \right) / \left( \frac{SSE_f}{n - p} \right) = \left( \frac{n - p}{p - q} \right) \left( \frac{SSE_r}{SSE_f} - 1 \right)$$

The difference in the error sum of squares for the full and reduced model provided a test for whether the model fit is the same

This ratio follows an  $F_{p-q, n-p}$  distribution

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Does our model account for a significant fraction of the variation?

Here the reduced model is just  $y_i = u + e_i$

In this case, the error sum of squares for the reduced model is just the total sum of squares, and the F test ratio becomes

$$\left( \frac{n-p}{p-1} \right) \left( \frac{SS_T}{SS_{E_f}} - 1 \right) = \left( \frac{n-p}{p-1} \right) \left( \frac{r^2}{1-r^2} \right)$$

This ratio follows an  $F_{p-1, n-p}$  distribution

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## Different statistical models

- **GLM = general linear model**
  - OLS ordinary least squares:  $e \sim MVN(0, cI)$
  - GLS generalized least squares:  $e \sim MVN(0, R)$
- **Non-linear models**
  - Parametric growth curves
- **Mixed models**
  - Both fixed and random effects (beyond the residual)
- **Mixture models**
  - A weighted mixture of distributions
- **Generalized linear models**
  - Nonlinear functions, non-normality

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# Mixture models

- Under a mixture model, an observation potentially comes from **one of several different distributions**, so that the density function is  $\pi_1\phi_1 + \pi_2\phi_2 + \pi_3\phi_3$ 
  - The mixture proportions  $\pi_i$  sum to one
  - The  $\phi_i$  represent different distribution, e.g., normal with mean  $\mu_i$  and variance  $\sigma^2$
- Mixture models come up in QTL mapping -- an individual could have QTL genotype QQ, Qq, or qq
  - See Lynch & Walsh Chapter 13
- They also come up in codon models of evolution, where a site may be neutral, deleterious, or advantageous, each with a different distribution of selection coefficients
  - See Walsh & Lynch (volume 2A website), Chapters 10,11

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# Generalized linear models

The Generalized Linear Model (note the ized ending) takes this a step further by assuming for some monotonic function  $g$ , that

$$E[y_i] = g\left(\mu + \sum_{k=1}^n \beta_k x_{ik}\right) \quad (2)$$

In particular, taking the inverse  $g^{-1}$  of the function  $g$  returns a linear model, with

$$g^{-1}(E[y_i]) = \mu + \sum_{k=1}^n \beta_k x_{ik} \quad (3)$$

The function  $f$  with the property that expresses the expected value of the response variable as a linear function of the predictor variables, i.e.,

$$f(E[y_i]) = \mu + \sum_{k=1}^n \beta_k x_{ik}$$

is called the link function of the particular generalized linear model.

Typically assume non-normal distribution for residuals, e.g., Poisson, binomial, gamma, etc

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# Likelihoods for GLMs

Under assumption of MVN,  $x \sim MVN(\beta, V)$ , the likelihood function becomes

$$L(\beta, V | x) = (2\pi)^{-n/2} |V|^{-1/2} \exp \left[ -\frac{1}{2}(x - \beta)^T V^{-1} (x - \beta) \right]$$

Variance components (e.g.,  $\sigma^2_A$ ,  $\sigma^2_e$ , etc.) are included in  $V$

**REML = restricted maximum likelihood.** Method of choice for variance components, as it maximizes that part of the likelihood function that is independent of the fixed effects,  $\beta$ .

# Overview And Introduction to Mixed Models

- References
  - Searle, S.R. 1971 Linear Models, Wiley
  - Schaefer, L.R., Linear Models and Computer Strategies in Animal Breeding
  - Lynch and Walsh Chapter 8

1

## Linear vs non-linear

Linear  
2<sup>nd</sup> order Polynomial

$$Y_i = b_0 + b_1 X_{1i} + b_2 X_{1i}^2 + b_3 X_{3i} + b_4 X_{4i}^2 + b_5 (X_{1i} X_{2i}) + \varepsilon_i$$

Non-linear

$$Y_i = b_0 e^{-b_1 X_i} \varepsilon_i$$

log-linear

$$\ln(Y_i) = \ln(b_0) - b_1 X_i + \ln(\varepsilon_i)$$

2

# Why Linear: Life is Non-Linear

Taylor Expansion

$$Y = f(X)$$

$$Y \approx f(a) + \frac{f'(a)(x-a)}{1!} + \frac{f''(a)(x-a)^2}{2!} + \dots + \frac{f^n(a)(x-a)^n}{n!}$$

$$Y = e^{-X} \quad Y' = -e^{-X} \quad Y'' = e^{-X}$$

At  $a=0$       
$$Y \approx 1 - x + \frac{x^2}{2!} - \frac{x^3}{3!} + \frac{x^4}{4!} + \dots$$

3

## Lower Order Terms Are more Important than higher

Works for other values of 'a' but not as exact, example  $a=.1$

$$Y = e^{-X} \quad Y \approx 1 - x + \frac{x^2}{2!} - \frac{x^3}{3!} + \frac{x^4}{4!} + \dots$$

$X=.1$

$Y \approx 1$

$$Y = e^{-1} = .904837 \quad Y \approx 1 - x = 1 - .1 = .9$$

$$Y \approx 1 - x + \frac{x^2}{2!} = 1 - .1 + \frac{.1^2}{2!} = .905$$

$$Y \approx 1 - x + \frac{x^2}{2!} - \frac{x^3}{3!} = 1 - .1 + \frac{.1^2}{2!} - \frac{.1^3}{3!} = .904833$$

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## Generality

- Any underlying unknown function can be approximated by a polynomial equation (linear Model)
  - Lower order terms are more important than higher order
  - Model does not have any basis in biological function
  - Even highly non-linear systems can be approximated by a linear model with only lower order terms
  - Purely Descriptive
  - Allows tests of hypothesis related to treatment effects
  - Allows limited prediction (expansion is around a point)

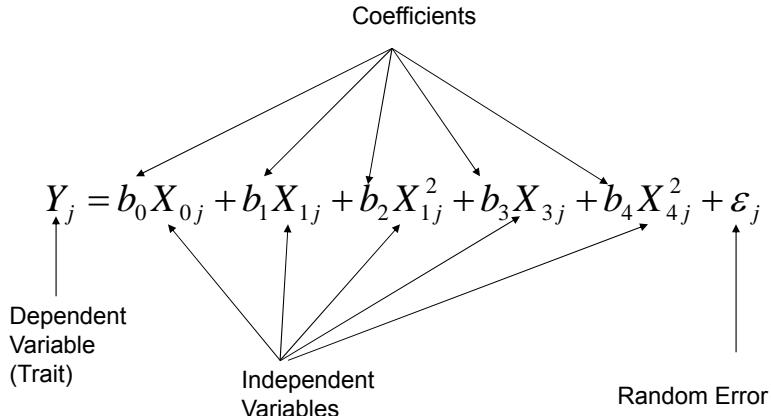
5

## Linear Model

- Can be used to approximate highly non-additive genetic systems, including dominance and epistasis
- Predictive ability is fairly good, even if underlying mode of gene action is non-additive
- Linear Models Extensively Used in Animal Breeding

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## One Random effect Linear Model



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## Matrix Notation

$$Y_1 = b_0 X_{01} + b_1 X_{11} + b_2 X_{11}^2 + b_3 X_{31} + b_4 X_{41}^2 + \varepsilon_1$$

$$Y_2 = b_0 X_{02} + b_1 X_{12} + b_2 X_{12}^2 + b_3 X_{32} + b_4 X_{42}^2 + \varepsilon_2$$

⋮

$$Y_n = b_0 X_{0n} + b_1 X_{1n} + b_2 X_{1n}^2 + b_3 X_{3n} + b_4 X_{4n}^2 + \varepsilon_n$$

$$\begin{bmatrix} Y_1 \\ Y_2 \\ \vdots \\ Y_n \end{bmatrix} = \begin{bmatrix} X_{01} & X_{11} & X_{11}^2 & X_{21} & X_{21}^2 \\ X_{02} & X_{12} & X_{12}^2 & X_{22} & X_{22}^2 \\ \vdots & \vdots & \vdots & \vdots & \vdots \\ X_{0n} & X_{1n} & X_{1n}^2 & X_{2n} & X_{2n}^2 \end{bmatrix} \begin{bmatrix} b_0 \\ b_1 \\ b_2 \\ b_3 \\ b_4 \end{bmatrix} + \begin{bmatrix} \varepsilon_1 \\ \varepsilon_2 \\ \vdots \\ \varepsilon_n \end{bmatrix}$$

$\mathbf{Y} = \mathbf{X}\mathbf{B} + \boldsymbol{\varepsilon}$

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## Estimation

$$\mathbf{Y} = \mathbf{XB} + \boldsymbol{\varepsilon}$$

### Ordinary Least Squares

- Independent variables ( $\mathbf{X}$ )
  - fixed
  - measured without error
- Residuals
  - Random
  - Independently and Identically Distributed (IID) with Mean 0 and variance  $\sigma^2$

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Independently and Identically Distributed  
with Mean 0 and variance  $\sigma^2$

$$V(\boldsymbol{\varepsilon}) = E[\boldsymbol{\varepsilon} - E(\boldsymbol{\varepsilon})]^2$$
$$V(\boldsymbol{\varepsilon}) = \begin{bmatrix} \sigma_e^2 & 0 & 0 & 0 \\ 0 & \sigma_e^2 & 0 & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & 0 & \sigma_e^2 \end{bmatrix}$$

The error distribution from which each observation is sampled is the same

No Environmental Correlations

When would these assumptions be violated?

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## Ordinary Least Squares Estimator

Find Solutions such that the sum of the residuals squared is minimum

$$\varepsilon_j = Y_j - E(Y_j)$$

$$E(Y_j) = \sum_{i=0}^k b_i X_{ij}$$

$$\sum_{j=1}^n \varepsilon_j^2 = \boldsymbol{\varepsilon}' \boldsymbol{\varepsilon} = \begin{bmatrix} \varepsilon_1 & \varepsilon_2 & \cdots & \varepsilon_n \end{bmatrix} \begin{bmatrix} \varepsilon_1 \\ \varepsilon_2 \\ \vdots \\ \varepsilon_n \end{bmatrix}$$

$$\varepsilon_j = Y_j - \sum_{i=0}^k b_i X_{ij}$$

$$\boldsymbol{\varepsilon}' \boldsymbol{\varepsilon} = \sum_{j=1}^n \varepsilon_j^2 = \sum_{j=1}^n \left( Y_j - \sum_{i=0}^k b_i X_{ij} \right)^2$$

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## Least Square Estimators

$$\boldsymbol{\varepsilon}' \boldsymbol{\varepsilon} = \sum_{j=1}^n \varepsilon_j^2 = \sum_{j=1}^n \left( Y_j - \sum_{i=0}^m b_i X_{ij} \right)^2$$

Find all  $b_i$  such that sum of residuals squared is minimum

$$\frac{\partial(\boldsymbol{\varepsilon}' \boldsymbol{\varepsilon})}{\partial b_i} = 2 \sum_{j=1}^n \left( Y_j - \sum_{i=0}^m b_i X_{ij} \right) \left[ -X_{ij} \right]$$

Set=0 for each  $i$  and solve system

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## Normal Equations

$$\begin{bmatrix} \sum x_{0j}^2 & \sum x_{0j}x_{1j} & \cdots & \sum x_{0j}x_{kj} \\ \sum x_{0j}x_{1j} & \sum x_{1j}^2 & \cdots & \sum x_{1j}x_{kj} \\ \vdots & \vdots & & \vdots \\ \sum x_{0j}x_{kj} & \sum x_{1j}x_{kj} & \cdots & \sum x_{kj}^2 \end{bmatrix} \begin{bmatrix} b_0 \\ b_1 \\ \vdots \\ b_k \end{bmatrix} = \begin{bmatrix} \sum x_{0j}y_j \\ \sum x_{1j}y_j \\ \vdots \\ \sum x_{kj}y_j \end{bmatrix}$$

$$\mathbf{X}'\mathbf{X}\hat{\mathbf{B}} = \mathbf{X}'\mathbf{Y}$$

$$\hat{\mathbf{B}} = (\mathbf{X}'\mathbf{X})^{-1}(\mathbf{X}'\mathbf{Y})$$

$$V(\hat{\mathbf{B}}) = \sigma_e^2 (\mathbf{X}'\mathbf{X})^{-1}$$

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## Prediction

$$\hat{\mathbf{Y}} = \mathbf{X}\hat{\mathbf{B}}$$

$$\hat{\mathbf{B}} = (\mathbf{X}'\mathbf{X})^{-1}(\mathbf{X}'\mathbf{Y})$$

$$V(\hat{\mathbf{Y}}) = V(\mathbf{X}\hat{\mathbf{B}})$$

$$V(\hat{\mathbf{B}}) = \sigma_e^2 (\mathbf{X}'\mathbf{X})^{-1}$$

$$V(\hat{\mathbf{Y}}) = \mathbf{X}V(\hat{\mathbf{B}})\mathbf{X}'$$

$$V(\hat{\mathbf{Y}}) = \mathbf{X}(\mathbf{X}'\mathbf{X})^{-1}\mathbf{X}'\sigma_e^2$$

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## Example Factor Affecting Fatty Acid From Gill, J. Design and Analysis of experiments

Fatty Acid	Amount over Weight (Kg)	Age
10	6	28
20	12	40
17	10	32
12	8	36
11	9	34

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### R Code Example 1

```
Y = matrix( c(10,  
           20,  
           17,  
           12,  
           11 ), 5,1)  
  
> B  
[.1] 2.3333333  
[2.] 2.0833333  
[3.] -0.2083333  
  
X = matrix(c( 1, 6, 28,  
           1, 12, 40,  
           1, 10, 32,  
           1, 8, 36,  
           1, 9, 34 ),5,3, byrow = TRUE)  
LHS =(t(X) %*% X )  
RHS =(t(X) %*% Y)  
C = solve(LHS)  
B = C %*% RHS  
B
```

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## OLS by IML

```
• *data from Gill, Design and  
Analysis of experiments;  
• *Demonstrates OLS  
estimation via matrix methods;  
  
proc iml;  
start main;  
y={ 10,  
    20,  
    17,  
    12,  
    11 };  
x={ 1 6 28,  
    1 12 40,  
    1 10 32,  
    1 8 36,  
    1 9 34 };  
  
b=inv(x*x)*x*y;  
Yhat=x*b;  
e=y-x*b;  
sse=e`*e;  
df=1/2;  
rms=sse#df;  
vb=inv(x*x)#rms;  
Vyhat=x*inv(x*x)*x`#rms;  
print b vb y yhat e sse rms vyhat;  
finish main;  
run;quit;
```

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## BY GLM

- **data** one;
- **input** fatty\_acid over\_wt age;
- cards;
- 10 6 28
- 20 12 40
- 17 10 32
- 12 8 36
- 11 9 34
- ;
- **proc** glm;
- **model** fatty\_acid=over\_wt age / solution;
- **run**;
- **quit**;
- Compare results from IML to GLM

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## Generalized Least Squares (GLS)

- Ordinary Least Squares
    - Independent variables
      - fixed
      - measured without error
    - Residuals
      - Random
      - Independently and Identically Distributed (IID) with Mean 0 and variance  $\sigma^2$
  - Generalized Least Squares
    - Independent variables
      - fixed
      - measured without error
    - Residuals
      - Random
- $$V(\varepsilon) = \mathbf{V}$$

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## GLS

Minimize  
weighted SS

$$(\mathbf{y} - \mathbf{X}\mathbf{b})' \mathbf{V}^{-1} (\mathbf{y} - \mathbf{X}\mathbf{b})$$

Weighting by the inverse of the variance

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

If

$$\mathbf{V} = \mathbf{I} \sigma_e^2$$

$$\hat{\mathbf{b}} = (\mathbf{X}' \mathbf{X})^{-1} (\mathbf{X}' \mathbf{y})$$

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## Maximum Likelihood (ML) Solution to Same Problem

- Generalized Least Squares
    - Independent variables
      - fixed
      - measured without error
    - Residuals
      - Random
  - Maximum Likelihood
    - Independent variables
      - fixed
      - measured without error
    - Residuals
      - Random
- $$V(\varepsilon) = \mathbf{V}$$
- $$\varepsilon \approx N(\mathbf{0}, \mathbf{V})$$

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## ML

$$L = \frac{1}{(2\pi)^{\frac{N}{2}} |\mathbf{V}|^{\frac{1}{2}}} e^{-\frac{1}{2} (\mathbf{y} - \mathbf{X}\mathbf{b})' \mathbf{V}^{-1} (\mathbf{y} - \mathbf{X}\mathbf{b})}$$

$$\text{Maximize w.r.t } \mathbf{b} \quad \frac{\partial(\ln L)}{\partial \mathbf{b}} = 0$$

$$\ln L = \ln(C) - \frac{1}{2} (\mathbf{y} - \mathbf{X}\mathbf{b})' \mathbf{V}^{-1} (\mathbf{y} - \mathbf{X}\mathbf{b})$$

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$$\frac{\partial(\ln L)}{\partial \mathbf{b}} = -\frac{1}{2}(\mathbf{y} - \mathbf{X}\mathbf{b})' \mathbf{V}^{-1}(-\mathbf{X}) - \frac{1}{2}(-\mathbf{X})' \mathbf{V}^{-1}(\mathbf{y} - \mathbf{X}\mathbf{b})$$

$$\frac{\partial(\ln L)}{\partial \mathbf{b}} = (\mathbf{y} - \mathbf{X}\mathbf{b})' \mathbf{V}^{-1} \mathbf{X}$$

$$(\mathbf{y} - \mathbf{X}\mathbf{b})' \mathbf{V}^{-1} \mathbf{X} = 0$$

$$(\mathbf{y}' - (\mathbf{X}\mathbf{b})') \mathbf{V}^{-1} \mathbf{X} = 0$$

$$(\mathbf{y}' - \mathbf{b}' \mathbf{X}') \mathbf{V}^{-1} \mathbf{X} = 0$$

$$\mathbf{b}' \mathbf{X}' \mathbf{V}^{-1} \mathbf{X} = \mathbf{y}' \mathbf{V}^{-1} \mathbf{X} \quad \text{Same as GLS}$$

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

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

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## Variance of b

$$V(\mathbf{b}) = (\mathbf{X}' \mathbf{V}^{-1} \mathbf{X})^{-1}$$

Note if  $\mathbf{V} = \mathbf{I} \sigma_e^2$

$$V(\mathbf{b}) = \sigma_e^2 (\mathbf{X}' \mathbf{X})^{-1}$$

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# BLUP Best Linear Unbiased Prediction-Estimation

- References
- Searle, S.R. 1971 Linear Models, Wiley
- Schaefer, L.R., Linear Models and Computer Strategies in Animal Breeding
- Lynch and Walsh Chapter 26

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OLS Independently and Identically Distributed Errors with Mean 0 and variance  $\sigma^2$

$$V(\varepsilon) = E[\varepsilon - E(\varepsilon)]^2$$
$$V(\varepsilon) = \begin{bmatrix} \sigma_e^2 & 0 & 0 & 0 \\ 0 & \sigma_e^2 & 0 & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & 0 & \sigma_e^2 \end{bmatrix}$$
$$V(\varepsilon) = \mathbf{I}\sigma_e^2$$

The residual distribution from which each observation is sampled is the same

For Some Traits Mean and Variance Correlated

Individuals Reared in Same Pen or Cage Cause these to be nonzero

Residuals independent

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## Solutions

- GLS
  - Fixes problem with changing variances and correlations in the data
- What about fixed effects?
  - How does one correct for
    - Environmental trend without a control
    - Herd effects
    - Year effects
    - Hatch effects
    - Confounding

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## Confounding of data

- Herd effects
  - Balanced design no problem
  - Require sample of every family in every herd
  - Old solution was within herd deviations
  - What if better herds have better genetics
- Fixed effects must be adjusted for genetic differences
- Random effects must be adjusted for fixed effects

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## Mixed Model

Simultaneous Adjustment of Fixed and Random effects

- Separates

Independent variable  
into those that are

- Fixed
- Random

$$\begin{matrix} \mathbf{Xb} \\ \mathbf{Zu} \end{matrix}$$

X=value of each fixed effect  
b=linear regression coefficients  
Z=incidence matrix of random  
effect, usually a 1 corresponding to  
each animal  
u=estimate of random effects  
(breeding value)

$$\mathbf{Y} = \mathbf{Xb} + \mathbf{Zu} + \mathbf{e}$$

More importantly model's the variance structure

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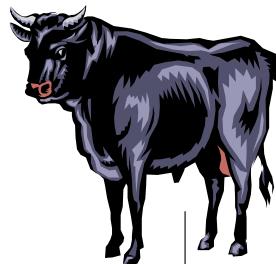
## Fixed and Random Effects

- Fixed Effect
  - Inference Space only to those levels
  - Age, Hatch, Location, Parity, and Sex effects
- Random Effect

- Effect Sampled From a Distribution of Effects
- Inference Space To The Population From Which The Random Effect Was Sampled
- If a new sample of observations were made (a new experiment), and the levels were completely different between the two samples, then the factors is usually random

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## Random Effect



Gametes

Each sample from  
the bull is different,  
no two gametes  
are the same

Sample

Bad

Good

Inference is to the genetic worth of the bull (breeding value)

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## Variances In Mixed Models

$$\begin{aligned}
 \mathbf{Y} &= \mathbf{X}\mathbf{b} + \mathbf{Z}\mathbf{u} + \mathbf{e} & V(\mathbf{b}) &= \mathbf{0} \\
 V(\mathbf{u}) &= E(\mathbf{u}\mathbf{u}') = \mathbf{G} \\
 V(\mathbf{e}) &= E(\mathbf{e}\mathbf{e}') = \mathbf{R} \\
 V(\mathbf{Y}) &= V(\mathbf{X}\mathbf{b} + \mathbf{Z}\mathbf{u} + \mathbf{e}) = \mathbf{ZGZ}' + \mathbf{R}
 \end{aligned}$$

Estimate the breeding values “ $\mathbf{u}$ ” and fixed effects simultaneously

Old concept was to first adjust for the fixed effects, output the residuals and estimate the random effects

Resulted in Biased Estimates of Both Fixed and Random Effects

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## ML Derivation of Solutions

$$\text{Joint density of } \mathbf{y} \text{ and } \mathbf{u} \quad f(\mathbf{y}, \mathbf{u}) = g(\mathbf{y}/\mathbf{u})h(\mathbf{u})$$

$$g(\mathbf{y}/\mathbf{u}) = g(\mathbf{e})$$

$$g(\mathbf{e}) = \frac{1}{(2\pi)^{\frac{1}{2}N} V(e)^{\frac{1}{2}}} e^{-\frac{1}{2}\mathbf{e}'V(\mathbf{e})^{-1}\mathbf{e}} \quad h(\mathbf{u}) = \frac{1}{(2\pi)^{\frac{1}{2}N} V(\mathbf{u})^{\frac{1}{2}}} e^{-\frac{1}{2}\mathbf{u}'V(\mathbf{u})^{-1}\mathbf{u}}$$

$$f(\mathbf{y}, \mathbf{u}) = \frac{1}{(2\pi)^{\frac{1}{2}N} v(e)^{\frac{1}{2}}} e^{-\frac{1}{2}\mathbf{e}'\mathbf{R}^{-1}\mathbf{e}} - \frac{1}{(2\pi)^{\frac{1}{2}N} v(u)^{\frac{1}{2}}} e^{-\frac{1}{2}\mathbf{u}'\mathbf{G}^{-1}\mathbf{u}}$$

$$f(\mathbf{y}, \mathbf{u}) = c_1 e^{-\frac{1}{2}\mathbf{e}'\mathbf{R}^{-1}\mathbf{e}} c_2 e^{-\frac{1}{2}\mathbf{u}'\mathbf{G}^{-1}\mathbf{u}}$$

$$f(\mathbf{y}, \mathbf{u}) = ce^{-\frac{1}{2}\mathbf{e}'\mathbf{R}^{-1}\mathbf{e}} e^{-\frac{1}{2}\mathbf{u}'\mathbf{G}^{-1}\mathbf{u}}$$

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$$f(\mathbf{y}, \mathbf{u}) = L = ce^{-\frac{1}{2}\mathbf{e}'\mathbf{R}^{-1}\mathbf{e}} e^{-\frac{1}{2}\mathbf{u}'\mathbf{G}^{-1}\mathbf{u}}$$

Maximize w.r.t  $\mathbf{b}$  and  $\mathbf{u}$

$$\ln(L) = \ln(c) - \frac{1}{2}\mathbf{e}'\mathbf{R}^{-1}\mathbf{e} - \frac{1}{2}\mathbf{u}'\mathbf{G}^{-1}\mathbf{u}$$

$$\mathbf{e} = \mathbf{Y} - \mathbf{X}\mathbf{b} - \mathbf{Z}\mathbf{u}$$

$$\begin{aligned} \ln(L) &= \ln(c) - \frac{1}{2}(\mathbf{Y} - \mathbf{X}\mathbf{b} - \mathbf{Z}\mathbf{u})' \mathbf{R}^{-1} (\mathbf{Y} - \mathbf{X}\mathbf{b} - \mathbf{Z}\mathbf{u}) \\ &\quad - \frac{1}{2}\mathbf{u}'\mathbf{G}^{-1}\mathbf{u} \end{aligned}$$

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SIMPLIFY FIRST THEN TAKE DERIVATIVES

$$\begin{aligned}
 & (\mathbf{Y} - \mathbf{X}\mathbf{b} - \mathbf{Z}\mathbf{u})' \mathbf{R}^{-1} (\mathbf{Y} - \mathbf{X}\mathbf{b} - \mathbf{Z}\mathbf{u}) + \mathbf{u}' \mathbf{G}^{-1} \mathbf{u} \\
 &= [\mathbf{Y}' - (\mathbf{X}\mathbf{b})' - (\mathbf{Z}\mathbf{u})'] \mathbf{R}^{-1} (\mathbf{Y} - \mathbf{X}\mathbf{b} - \mathbf{Z}\mathbf{u}) + \mathbf{u}' \mathbf{G}^{-1} \mathbf{u} \\
 &= \mathbf{Y}' \mathbf{R}^{-1} \mathbf{Y} - \mathbf{Y}' \mathbf{R}^{-1} \mathbf{X}\mathbf{b} - \mathbf{Y}' \mathbf{R}^{-1} \mathbf{Z}\mathbf{u} \\
 &\quad - (\mathbf{X}\mathbf{b})' \mathbf{R}^{-1} \mathbf{Y} + (\mathbf{X}\mathbf{b})' \mathbf{R}^{-1} \mathbf{X}\mathbf{b} + (\mathbf{X}\mathbf{b})' \mathbf{R}^{-1} \mathbf{Z}\mathbf{u} \\
 &\quad - (\mathbf{Z}\mathbf{u})' \mathbf{R}^{-1} \mathbf{Y} + (\mathbf{Z}\mathbf{u})' \mathbf{R}^{-1} \mathbf{X}\mathbf{b} + (\mathbf{Z}\mathbf{u})' \mathbf{R}^{-1} \mathbf{Z}\mathbf{u} + \mathbf{u}' \mathbf{G}^{-1} \mathbf{u} \\
 \hline
 \frac{\partial(\ln L)}{\partial \mathbf{b}} = 0 & \quad -\mathbf{Y}' \mathbf{R}^{-1} \mathbf{X} - \mathbf{X}' \mathbf{R}^{-1} \mathbf{Y} + (\mathbf{X}\mathbf{b})' \mathbf{R}^{-1} \mathbf{X} + \\
 & \quad \mathbf{X}' \mathbf{R}^{-1} \mathbf{X}\mathbf{b} + \mathbf{X}' \mathbf{R}^{-1} \mathbf{Z}\mathbf{u} + (\mathbf{Z}\mathbf{u})' \mathbf{R}^{-1} \mathbf{X} = 0 \\
 \\ 
 & -2\mathbf{X}' \mathbf{R}^{-1} \mathbf{Y} + 2\mathbf{X}' \mathbf{R}^{-1} \mathbf{X}\mathbf{b} + 2\mathbf{X}' \mathbf{R}^{-1} \mathbf{Z}\mathbf{u} = 0 \\
 & \mathbf{X}' \mathbf{R}^{-1} \mathbf{X}\mathbf{b} + \mathbf{X}' \mathbf{R}^{-1} \mathbf{Z}\mathbf{u} = \mathbf{X}' \mathbf{R}^{-1} \mathbf{Y}
 \end{aligned}$$

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Take Derivative w.r.t  $\mathbf{u}$

$$\begin{aligned}
 & (\mathbf{Y} - \mathbf{X}\mathbf{b} - \mathbf{Z}\mathbf{u})' \mathbf{R}^{-1} (\mathbf{Y} - \mathbf{X}\mathbf{b} - \mathbf{Z}\mathbf{u}) + \mathbf{u}' \mathbf{G}^{-1} \mathbf{u} \\
 &= \mathbf{Y}' \mathbf{R}^{-1} \mathbf{Y} - \mathbf{Y}' \mathbf{R}^{-1} \mathbf{X}\mathbf{b} - \mathbf{Y}' \mathbf{R}^{-1} \mathbf{Z}\mathbf{u} \\
 &\quad - (\mathbf{X}\mathbf{b})' \mathbf{R}^{-1} \mathbf{Y} + (\mathbf{X}\mathbf{b})' \mathbf{R}^{-1} \mathbf{X}\mathbf{b} + (\mathbf{X}\mathbf{b})' \mathbf{R}^{-1} \mathbf{Z}\mathbf{u} \\
 &\quad - (\mathbf{Z}\mathbf{u})' \mathbf{R}^{-1} \mathbf{Y} + (\mathbf{Z}\mathbf{u})' \mathbf{R}^{-1} \mathbf{X}\mathbf{b} + (\mathbf{Z}\mathbf{u})' \mathbf{R}^{-1} \mathbf{Z}\mathbf{u} + \mathbf{u}' \mathbf{G}^{-1} \mathbf{u} \\
 \hline
 \frac{\partial(\ln L)}{\partial \mathbf{u}} = 0 & \quad -\mathbf{Y}' \mathbf{R}^{-1} \mathbf{Z} + (\mathbf{X}\mathbf{b})' \mathbf{R}^{-1} \mathbf{Z} - (\mathbf{Z})' \mathbf{R}^{-1} \mathbf{Y} + (\mathbf{Z})' \mathbf{R}^{-1} \mathbf{X}\mathbf{b} \\
 & \quad + (\mathbf{Z})' \mathbf{R}^{-1} \mathbf{Z}\mathbf{u} + (\mathbf{Z}\mathbf{u})' \mathbf{R}^{-1} \mathbf{Z} + 2\mathbf{G}^{-1} \mathbf{u} = 0 \\
 \\ 
 & -2\mathbf{Y}' \mathbf{R}^{-1} \mathbf{Z} + 2\mathbf{Z}' \mathbf{R}^{-1} \mathbf{X}\mathbf{b} + 2\mathbf{Z}' \mathbf{R}^{-1} \mathbf{Z}\mathbf{u} + 2\mathbf{G}^{-1} \mathbf{u} = 0 \\
 & \mathbf{Z}' \mathbf{R}^{-1} \mathbf{X}\mathbf{b} + \mathbf{Z}' \mathbf{R}^{-1} \mathbf{Z}\mathbf{u} + \mathbf{G}^{-1} \mathbf{u} = \mathbf{Z}' \mathbf{R}^{-1} \mathbf{Y}
 \end{aligned}$$

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## Mixed Model Equations

$$\mathbf{X}'\mathbf{R}^{-1}\mathbf{X}\mathbf{b} + \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z}\mathbf{u} = \mathbf{X}'\mathbf{R}^{-1}\mathbf{Y}$$

$$\mathbf{Z}'\mathbf{R}^{-1}\mathbf{X}\mathbf{b} + \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z}\mathbf{u} + \mathbf{G}^{-1}\mathbf{u} = \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Y}$$

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

Simplifications If  $\mathbf{R} = \mathbf{I}\sigma_e^2$

$$\begin{bmatrix} \mathbf{X}'\mathbf{X} & \mathbf{X}'\mathbf{Z} \\ \mathbf{Z}'\mathbf{X} & \mathbf{Z}'\mathbf{Z} + \sigma_e^2\mathbf{G}^{-1} \end{bmatrix} \begin{bmatrix} \mathbf{b} \\ \mathbf{u} \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{Y} \\ \mathbf{Z}'\mathbf{Y} \end{bmatrix}$$

Alternative derivations are possible that do not require Normal Dist'n Assumptions,  
resulting in these same solutions and are therefore also Best Linear Unbiased  
Predictors (BLUP)

## BLUP Breeding Values

$$\begin{bmatrix} \mathbf{X}'\mathbf{X} & \mathbf{X}'\mathbf{Z} \\ \mathbf{Z}'\mathbf{X} & \mathbf{Z}'\mathbf{Z} + \sigma_e^2 \mathbf{G}^{-1} \end{bmatrix} \begin{bmatrix} \mathbf{b} \\ \mathbf{u} \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{Y} \\ \mathbf{Z}'\mathbf{Y} \end{bmatrix}$$

With Diploid Organisms and  
Assuming Additivity

$$\mathbf{G} = \mathbf{A}\sigma_a^2 \quad \mathbf{G}^{-1} = \frac{1}{\sigma_a^2} \mathbf{A}^{-1}$$

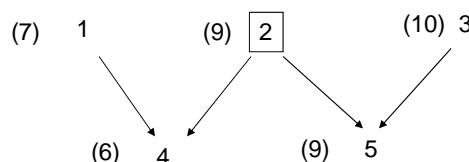
$$\begin{bmatrix} \mathbf{X}'\mathbf{X} & \mathbf{X}'\mathbf{Z} \\ \mathbf{Z}'\mathbf{X} & \mathbf{Z}'\mathbf{Z} + \frac{\sigma_e^2}{\sigma_a^2} \mathbf{A}^{-1} \end{bmatrix} \begin{bmatrix} \mathbf{b} \\ \mathbf{u} \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{Y} \\ \mathbf{Z}'\mathbf{Y} \end{bmatrix}$$

Only Estimate of Ratio is Needed

Only inverse is needed

1

## Example 2



$$\begin{bmatrix} 7 \\ 9 \\ 10 \\ 6 \\ 9 \end{bmatrix} = \begin{bmatrix} 1 \\ 1 \\ 1 \\ 1 \\ 1 \end{bmatrix} [\mu] + \begin{bmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} a_1 \\ a_2 \\ a_3 \\ a_4 \\ a_5 \end{bmatrix} + \begin{bmatrix} e_1 \\ e_2 \\ e_3 \\ e_4 \\ e_5 \end{bmatrix}$$

$$\mathbf{Y} = \mathbf{X}\mathbf{b} + \mathbf{Z}\mathbf{u} + \mathbf{e}$$

2

## Example 2

$$\mathbf{Y} = \begin{bmatrix} 7 \\ 9 \\ 10 \\ 6 \\ 9 \end{bmatrix} \quad b = [\mu]$$

(7)      1      (9)      2      (10) 3  
 (6)      4      (9)      5

$$\mathbf{X} = \begin{bmatrix} 1 \\ 1 \\ 1 \\ 1 \\ 1 \end{bmatrix} \quad Z = \begin{bmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{bmatrix} \quad \mathbf{u} = \begin{bmatrix} a_1 \\ a_2 \\ a_3 \\ a_4 \\ a_5 \end{bmatrix} \quad \mathbf{e} = \begin{bmatrix} e_1 \\ e_2 \\ e_3 \\ e_4 \\ e_5 \end{bmatrix}$$

3

(7)      1      (9)      2      (10) 3  
 (6)      4      (9)      5

$$\mathbf{A} = \begin{bmatrix} 1 & 0 & 0 & \frac{1}{2} & 0 \\ 0 & 1 & 0 & \frac{1}{2} & \frac{1}{2} \\ 0 & 0 & 1 & 0 & \frac{1}{2} \\ \frac{1}{2} & \frac{1}{2} & 0 & 1 & \frac{1}{4} \\ 0 & \frac{1}{2} & \frac{1}{2} & \frac{1}{4} & 1 \end{bmatrix}$$

Assume heritability=.5

$$\frac{\sigma_e^2}{\sigma_a^2} = 1$$

$$\mathbf{Z}'\mathbf{Z} + \frac{\sigma_e^2}{\sigma_a^2} \mathbf{A}^{-1} = \begin{bmatrix} \frac{5}{2} & \frac{1}{2} & 0 & -1 & 0 \\ \frac{1}{2} & 3 & \frac{1}{2} & -1 & -1 \\ 0 & \frac{1}{2} & \frac{5}{2} & 0 & -1 \\ -1 & -1 & 0 & 3 & 0 \\ 0 & -1 & -1 & 0 & 3 \end{bmatrix}$$

4

# MME

$$\begin{bmatrix} \mathbf{X}'\mathbf{X} & \mathbf{X}'\mathbf{Z} \\ \mathbf{Z}'\mathbf{X} & \mathbf{Z}'\mathbf{Z} + \frac{\sigma_e^2}{\sigma_a^2} \mathbf{A}^{-1} \end{bmatrix} \begin{bmatrix} \mathbf{b} \\ \mathbf{u} \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{Y} \\ \mathbf{Z}'\mathbf{Y} \end{bmatrix}$$

$$\begin{bmatrix} 5 & 1 & 1 & 1 & 1 & 1 \\ 1 & \frac{5}{2} & \frac{1}{2} & 0 & -1 & 0 \\ 1 & \frac{1}{2} & 3 & \frac{1}{2} & -1 & -1 \\ 1 & 0 & \frac{1}{2} & \frac{5}{2} & 0 & -1 \\ 1 & -1 & -1 & 0 & 3 & 0 \\ 1 & 0 & -1 & -1 & 0 & 3 \end{bmatrix} \begin{bmatrix} \mu \\ a_1 \\ a_2 \\ a_3 \\ a_4 \\ a_5 \end{bmatrix} = \begin{bmatrix} 41 \\ 7 \\ 9 \\ 10 \\ 6 \\ 9 \end{bmatrix}$$

5

$\mathbf{Y}$		$\mathbf{Z}$	$\mathbf{X}$	$\mathbf{X'}$
7		1 0 0 0 0	1	1 1 1 1 1
9		0 1 0 0 0	1	
10		0 0 1 0 0	1	
6		0 0 0 1 0	1	
9		0 0 0 0 1	1	
$\mathbf{XZ=}$	1 1 1 1 1			$\mathbf{XX=}$ 5
				$\text{sig(a)=}$ 1
				$\text{sig(e)=}$ 1
				$\text{lam=}$ 1
$\mathbf{ZX=}$	1 1	$\mathbf{A}$		
	1 1	1 0 0 0.5 0		
	1	0 1 0 0.5 0.5		
	1	0 0 1 0 0.5		
$\mathbf{XY=}$	41	0.5 0.5 0 1 0.25		
		0 0.5 0.5 0.25 1		
$\mathbf{ZY=}$	7 9	$\mathbf{Z'Z+INV(A)}$		
	10 6 9	2.5 0.5 0 -1 0		
		0.5 3 0.5 -1 -1		
		0 0.5 2.5 0 -1		
		-1 -1 0 3 0	$\text{INV(A)*Lam}$	
		0 -1 -1 0 3	0 0.5 1.5 0 -1	
			-1 -1 0 2 0	
			0 -1 -1 0 2	
$\mathbf{5}$	$\mathbf{1}$	$\mathbf{1}$	$\mathbf{1}$	$\mathbf{1}$
1	2.5	0.5	0	-1
1	0.5	3	0.5	-1
1	0	0.5	2.5	0
1	-1	-1	0	3
1	0	-1	-1	0
				u5
$\mathbf{b}$				$\mathbf{b}$
$\mathbf{u1}$		0.566038 -0.32075 -0.35849 -0.32075 -0.41509 -0.41509	41	41
$\mathbf{u2}$	='	-0.32075 0.645864 0.169811 0.184325 0.37881 0.224964	7	7
$\mathbf{u3}$		-0.35849 0.169811 0.660377 0.169811 0.396226 0.396226	9	9
$\mathbf{u4}$		-0.32075 0.184325 0.169811 0.645864 0.224964 0.37881	10	10
$\mathbf{u5}$		-0.41509 0.37881 0.396226 0.224964 0.730044 0.345428	6	6
		-0.41509 0.224964 0.396226 0.37881 0.345428 0.730044	9	9
				mean + bv
				8.301887
				-0.96081
				7.341074
				8.377358
				0.075472
				0.885341
				9.187228
				-1.06241
				7.239478
				8.854862
		Inv(LHS)	RHS	6

## R code Example 2

```

Y = matrix( c(7,
           9,
           10,
           6,
           9), 5,1)
lam = 1

Z = matrix( c(1, 0, 0, 0, 0,
              0, 1, 0, 0, 0,
              0, 0, 1, 0, 0,
              0, 0, 0, 1, 0,
              0, 0, 0, 0, 1 ),5,5)

X = matrix( c( 1,
               1,
               1,
               1,
               1),5,1)
A = matrix( c(1, 0, 0, .5, 0,
               0, 1, 0, -.5, 0,
               0, 0, 1, 0, .5,
               .5,.5,0, 1,.25,
               0,.5,.5,.25, 1 ),5,5)

```

7

## R code

```
LHS = rbind( cbind(t(X) %*% X , t(X) %*% Z ),
             cbind( t(Z) %*% X , ( t(Z) %*% Z ) + (lam * solve(A)) ))
```

```
RHS = rbind(t(X) %*% y,
            t(Z) %*% y)
```

```
C = solve(LHS)
```

```
BU = C %*% RHS
```

```
BU
```

```
[,1]
[1,] 8.3018868
[2,] -0.9608128
[3,] 0.0754717
[4,] 0.8853411
[5,] -1.0624093
[6,] 0.5529753
```

$$b = [\hat{\mu}]$$

$$\mathbf{U} = \begin{bmatrix} \hat{a}_1 \\ \hat{a}_2 \\ \hat{a}_3 \\ \hat{a}_4 \\ \hat{a}_5 \end{bmatrix}$$

8

```

proc iml;                                lam=1;
start main;
y={ 7,                                     Z={1 0 0 0 0,
      9,                                     0 1 0 0 0,
      10,                                    0 0 1 0 0,
      6,                                     0 0 0 1 0,
      9};                                    0 0 0 0 1};

X={1,                                     LHS=((X`*X)|| (X`*Z))//((Z`*X)|| (Z`*Z+INV(A)#
      1,                                     LAM));
      1,                                     RHS=(X`*Y)//(Z`*Y);
      1,                                     C=INV(HS);
      1};                                     BU=C*RHS;
A={1 0 0 .5 0,                           print C BU;
      0 1 0 .5 .5,                         finish main;
      0 0 1 0 .5,                         run;
      .5 .5 0 1 .25,                       quit;
      0 .5 .5 .25 1};

```

9

## Estimates

$$\begin{aligned}
 & \text{BU} & b = [\hat{\mu}] \\
 & 8.3018868 & \\
 & -0.960813 & \\
 & 0.0754717 & \\
 & 0.8853411 & \\
 & -1.062409 & \\
 & 0.5529753 & \\
 & & \mathbf{U} = \begin{bmatrix} \hat{a}_1 \\ \hat{a}_2 \\ \hat{a}_3 \\ \hat{a}_4 \\ \hat{a}_5 \end{bmatrix}
 \end{aligned}$$

10

## Missing Values (Sex Limited Traits)

Generation

$$\begin{array}{ccccccc}
 & 1 & (7) & 1 & M & 2 & (10) 3 \\
 & & & & \searrow & \downarrow & \\
 2 & & & (6) & 4 & 5 & \\
 & & & & & & \\
 \mathbf{Y} = \begin{bmatrix} 7 \\ 10 \\ 6 \end{bmatrix} & \mathbf{e} = \begin{bmatrix} e_1 \\ e_3 \\ e_4 \end{bmatrix} & & & & \mathbf{A} = \begin{bmatrix} 1 & 0 & 0 & \frac{1}{2} & 0 \\ 0 & 1 & 0 & \frac{1}{2} & \frac{1}{2} \\ 0 & 0 & 1 & 0 & \frac{1}{2} \\ \frac{1}{2} & \frac{1}{2} & 0 & 1 & \frac{1}{4} \\ 0 & \frac{1}{2} & \frac{1}{2} & \frac{1}{4} & 1 \end{bmatrix} \\
 & & & & & b = [\mu] & \\
 & & & & & & \\
 \mathbf{X} = \begin{bmatrix} 1 \\ 1 \\ 1 \end{bmatrix} & Z = \begin{bmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \end{bmatrix} & \mathbf{U} = \begin{bmatrix} a_1 \\ a_2 \\ a_3 \\ a_4 \\ a_5 \end{bmatrix} & & & & \text{Assume } h^2=.5 \\
 & & & & & & & \\
 & & & & & & & 11
 \end{array}$$

Y		Z	X	X
7	1	0	1	
10	0	0	1	
6	0	0	1	
XZ=	1	0	1	1
	1	0	0	0
	0	0	0	0
ZX=	1	0	1	0
	1	0	0	1
	0	0	0	0
ZY=	7		A	
	0	1	0	0.5
	10	0	1	0.5
	6	0	1	0
	0	0.5	0	1
	0.5	0.5	0.25	1
	0	0.5	0.5	0.25
	3	1	b	
	1	2.5	0	
	0	0.5	-1	
	1	0	0.5	
	1	-1	0	
	0	0	-1	
	23			
	7			
	0			
	10			
	6			
	0			
	LHS		RHS	
b	0.769231	-0.46154	-0.15385	-0.38462
u1	-0.46154	0.74359	0.025641	0.230769
u2	='	-0.15385	0.025641	0.897436
u3		-0.076923	0.076923	0.358974
u4		-0.230769	0.692308	0.230769
u5		-0.46154	0.410256	0.358974
	-0.26923	0.128205	0.487179	0.384615
				0.294872
				0.935897
				7.846154
				-0.64103
				7.205128
				-0.4359
				7.410256
				1.076923
				8.923077
				-0.97436
				6.871795
				0.320513
				8.166667
				12
				sex limited blup.xls

```

proc iml;                                lam=1;
start main;

y={ 7,                                     Z={1 0 0 0 0,
      10,                                    0 0 1 0 0,
      6};                                    0 0 0 0 1};

X={1,                                     LHS=((X`*X)||((X`*Z))//((Z`*X)||((Z`*
      1,                                         Z+INV(A)#LAM)));
      1};

A={1 0 0 .5  0,                           RHS=(X`*Y)//(Z`*Y);
   0 1 0 .5 .5,                           C=INV(LHS);
   0 0 1 0 .5,
   .5 .5 0 1 .25,
   0 .5 .5 .25 1};                         BU=C*RHS;
                                                print C BU;
                                                finish main;
                                                run;
                                                quit;

```

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## Estimates

$$\begin{aligned}
 b &= [\hat{\mu}] \\
 7.84 &\quad \leftarrow \\
 -0.64 & \\
 -0.43 & \\
 1.07 & \\
 -0.97 & \\
 0.32 & \\
 \end{aligned}
 \quad \left\{ \quad \mathbf{U} = \begin{bmatrix} \hat{a}_1 \\ \hat{a}_2 \\ \hat{a}_3 \\ \hat{a}_4 \\ \hat{a}_5 \end{bmatrix}$$

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## R code Example 3

```
Y = matrix( c( 7,
             10,
             6), 3,1)
lam = 1

Z = matrix( c(1, 0, 0, 0, 0,
              0, 0, 1, 0, 0,
              0, 0, 0, 1, 0), 3,5, byrow = TRUE)

X = matrix( c( 1,
               1,
               1), 3,1)

A = matrix( c(1, 0, 0, .5, 0,
              0, 1, 0, .5,.5,
              0, 0, 1, 0, .5,
              .5,.5,0, 1,.25,
              0,.5,.5,.25, 1 ), 5,5)
```

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## R code

```
LHS = rbind( cbind(t(X) %*% X , t(X) %*% Z ),
             cbind( t(Z) %*% X , ( t(Z) %*% Z ) + (lam * solve(A)) ))

RHS = rbind(t(X) %*% Y,
            t(Z) %*% Y)

C = solve(LHS)

BU = C %*% RHS

BU
```

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## Variance of the Estimates

$$\begin{bmatrix} \mathbf{C}_{11} & \mathbf{C}_{12} \\ \mathbf{C}_{21} & \mathbf{C}_{22} \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{X} & \mathbf{X}'\mathbf{Z} \\ \mathbf{Z}'\mathbf{X} & \mathbf{Z}'\mathbf{Z} + \frac{\sigma_e^2}{\sigma_a^2} \mathbf{A}^{-1} \end{bmatrix}^{-1}$$

$$V(\hat{\mathbf{b}}) = \mathbf{C}_{11}\sigma_e^2$$

$$V(\hat{\mathbf{u}} - \mathbf{u}) = C_{22}\sigma_e^2 \quad \text{Prediction Error Variance}$$

$$V(\hat{\mathbf{u}}) = \mathbf{A}\sigma_a^2 + \mathbf{C}_{22}\sigma_e^2 \quad \text{Prediction Error Variance Including Drift Variance}$$

Kennedy and Sorensen *Quantitative Genetics*

```

LHS=((X'*X)\|(X'*Z))\|((Z'*X)\|(Z'*Z+INV(A)\#LAM));
RHS=(X'*Y)\|(Z'*Y);
C=INV(LHS);
BU=C*RHS;
RMSE=(Y'*Y-BU'*RHS)\#(1/3);

print C BU RMSE;

CSUB=C[2:6,2:6];           Sub matrix with rows 2 through 6 and
PEV=CSUB#RMSE;             Columns 2 through 6 of C
SIGMA_A=RMSE*(1/LAM);
PV=A*SIGMA_A+PEV;

PRINT PEV PV;
finish main;
run;
quit;

```

Run "BLUP by proc iml.sas"

### PEV

~~1.12236 0.29509 0.32030 0.65827 0.39093  
0.29509 1.14758 0.29509 0.68854 0.68854  
0.32030 0.29509 1.12236 0.39093 0.65827  
0.65827 0.68854 0.39093 1.2686 0.60026  
0.39093 0.68854 0.65827 0.60026 1.2686~~

### EV

~~2.86014 0.29509 0.32030 1.52716 0.39093  
0.29509 2.88536 0.29509 1.5574 1.5574  
0.32030 0.29509 2.86014 0.39093 1.52716  
1.52716 1.5574 0.39093 3.00643 1.03471  
0.39093 1.5574 1.52716 1.03471 3.00643~~

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## Extensions of Model

- Inclusion of Dominance and Epistasis
  - Dominance
    - Dominance effects are the result of interaction of alleles within a locus
    - Dominance relationship matrix needed
    - Reflects the probability that individuals have the same pair of alleles in common at a locus
  - Epistasis
    - Epistatic genetic effects are the result of interactions between alleles at different loci
    - Epistatic relationship matrix needed
    - Reflects the probability that individuals have the same pair of alleles in common at different loci (4 possible pairings of 2 alleles at 2 loci)
  - Useful in crossbreeding programs but generally not useful in pure breeding programs
    - An individual does not pass on dominance or epistatic effects (without inbreeding or cloning), which are a function of both parents
    - Exception is Additive x Additive epistasis is a function of 2 alleles at different loci in the same gamete, but dissipates with recombination and/or segregation

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## Estimation of Variances Using all Data in a Pedigree

- **REML**

- EM-REML iterative process whereby
  - A value is assumed for additive variance
  - Estimates of breeding values found
  - Additive variance  $V(A)$  is estimated as variance of breeding values  $V(A) = (u' A^{-1} u + \text{stuff})/n$
  - The new value of  $V(A)$  is substituted into the MME
  - Estimates of breeding values ( $u$ ) are found
  - The process repeated until convergence
- DF-REML work by trial and error finding a value of  $V(A)$  that maximize the likelihood

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## Estimation of Effects and Parameters via Iteration and MCMC

### Distributions

$$b_i | \mathbf{b}_i, \mathbf{a}, \sigma_a^2, \sigma_\varepsilon^2, y \sim N\left(\hat{b}_i, \frac{\sigma_\varepsilon^2}{LHS_{ii}}\right)$$

$$a_i | \mathbf{b}, \mathbf{a}_i, \sigma_a^2, \sigma_\varepsilon^2, y \sim N\left(\hat{a}_i, \frac{\sigma_\varepsilon^2}{LHS_{ii}}\right)$$

$$\sigma_a^2 | \mathbf{b}, \mathbf{a}, \sigma_\varepsilon^2, y \sim \hat{v}_a \hat{S}_a^2 \chi_{\hat{v}_a}^{-2}$$

$$\sigma_\varepsilon^2 | \mathbf{b}, \mathbf{a}, \sigma_a^2, y \sim \hat{v}_\varepsilon \hat{S}_\varepsilon^2 \chi_{\hat{v}_\varepsilon}^{-2}$$

### Estimates

$$\hat{S}_a^2 = (\mathbf{a}' \mathbf{A}^{-1} \mathbf{a} + v_a S_a^2) / \hat{v}_a$$

$$\hat{v}_a = q + v_a$$

$$\hat{S}_\varepsilon^2 = (\boldsymbol{\varepsilon}' \boldsymbol{\varepsilon} + v_\varepsilon S_\varepsilon^2) / \hat{v}_\varepsilon$$

$$\hat{v}_\varepsilon = N + v_\varepsilon$$

$$\boldsymbol{\varepsilon} = \mathbf{Y} - \mathbf{X}\mathbf{B} - \mathbf{Z}\mathbf{a}$$

1. Solutions to MME are found using iterative approach (Gauss-Seidel)
2. With each Iteration a random amount is added to each solution based on the expected distribution
3. After processing all equations in the MME, new variances are computed and a random amount is added to each solution based on the expected distribution
4. After a burn in period, and many 1000 iterations, the average value of each parameter, with the empirical standard error is the best estimate of the effects and variances

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# Appendix 1

## Software packages for estimating EBVs, Variance Components, GWAS and genomic selection

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### Software engineering the mixed model for genome-wide association studies on large samples

<http://bib.oxfordjournals.org/content/10/6/664/T1.expansion.html>

Program	Web address (http)	Availability	Flexible modeling	Automatic GWAS	Sample size	Population structure	Build Kinship from pedigree	Build Kinship from marker	Number Random Effects
TASSEL	<a href="http://www.msizgenetics.net">www.msizgenetics.net</a>	Free	No	Yes	S	Yes	Yes	Yes	1
SAS	<a href="http://www.sas.com">www.sas.com</a>	Licensed	Yes	Yes	S	Yes	Yes	Yes	≥1
JMP Genomics	<a href="http://www.jmp.com/software/genomics">www.jmp.com/software/genomics</a>	Licensed	Yes	Yes	NA	Yes	NA	Yes	≥1
ASREML	<a href="http://www.vsni.co.uk/software/asreml">www.vsni.co.uk/software/asreml</a>	Licensed	Yes	Yes	NA	Yes	Yes	No	≥1
MIXTUREML	<a href="http://ipl.arsusda.gov/curtv/mixtureml.html">ipl.arsusda.gov/curtv/mixtureml.html</a>	Free	Yes	No	L	Yes	Yes	No	≥1
DMU	<a href="http://www.dmu.agrci.dk">www.dmu.agrci.dk</a>	Free	Yes	No	L	Yes	Yes	No	≥1
QxPak	<a href="http://ceads.nga.edu/~ignacy/newprograms.html">ceads.nga.edu/~ignacy/newprograms.html</a>	Free	Yes	Yes	L	Yes	Yes	No	≥1
WOMBAT	<a href="http://agbu.une.edu.au/~kmeyer/wombat">agbu.une.edu.au/~kmeyer/wombat</a>	Free	Yes	NA	L	Yes	Yes	No	≥1
EMMA(R)	<a href="http://mouse.cs.ucla.edu/emma">mouse.cs.ucla.edu/emma</a>	Free	No	Yes	M	No	No	Yes	1

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# Software

## Ignacy Misztal UGA

- Overview
  - <http://nce.ads.uga.edu/~ignacy/newprograms.html>
- General Documents
  - <http://nce.ads.uga.edu/wiki/lib/exe/fetch.php?media=blupf90.pdf>
  - <http://nce.ads.uga.edu/wiki/lib/exe/fetch.php?media=remlf90.pdf>
- **Binaries (UNIX, Windows, Max)**
  - <http://nce.ads.uga.edu/html/projects/programs/>
- **Programs, data, examples also at**
  - <http://www.biostat.washington.edu/suminst/sisg/computing>
  - Module 12

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## R packages

- QTL mapping
  - **onemap** – It is used to generate or rearrange genetic maps
  - **rqtI** – performs QTL mapping for bi-parental populations
  - **GAPIT** – most common package for Genome-Wide Association Mapping
- BLUP (Animal Model)
  - **pedigree** – Generates A matrix from sparse pedigree
  - **MCMCglmm** – Generalized Mixed Models incorporating pedigrees
  - **pedigreemm** - Fit mixed-effects models incorporating pedigrees
- Genomic Selection
  - **rrBLUP** – classic package to perform ridge regression BLUP and GBLUP
  - **BGLR** – whole genome regressions methods of genomic selection
  - **randomForest** – Random Forest Regression (non-parametric GS)
  - **brnn** – Bayesian Regularized Neural Network (non-parametric GS)
  - **parallel** – Allows the use of multiple cores for faster computation

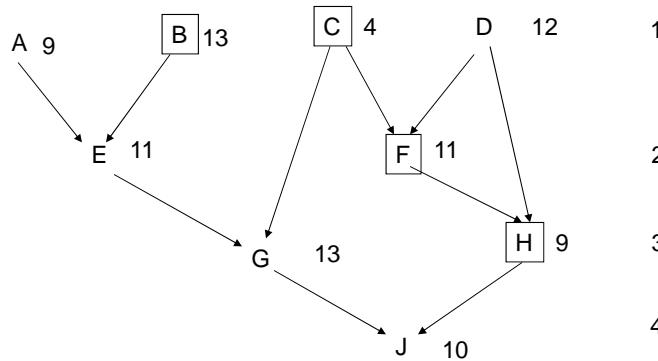
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## Appendix 2 Problems and Solutions

SAS IML  
BLUPF90

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### Problem 1



Find the best estimate of the genetic worth of each animal.  
Assume a heritability of .5. Work problem using either SAS IML and BLUPF90, also try REMLF90 to estimate variances

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### Answer Problem 1

```

proc iml;
start main;
A={1 0 0 0 0.5 0 0.25 0 0.125,
    0 1 0 0 0.5 0 0.25 0 0.125,
    0 0 1 0 0 0.5 0.5 0.25 0.375,
    0 0 0 1 0 0.5 0 0.75 0.375,
    0.5 0.5 0 0 1 0 0.5 0 0.25,
    0 0 0.5 0.5 0 1 0.25 0.75 0.5,
    0.25 0.25 0.5 0 0.5 0.25 1 0.125 0.5625,
    0 0 0.25 0.75 0 0.75 0.125 1.25 0.6875,
    0.125 0.125 0.375 0.375 0.25 0.5 0.5625 0.6875 1.0625};

10};
AINV=INV(A);
lam=1;
X={1,
1,
1,
1,
1,
1,
1,
1,
1,
1};

Z={1 0 0 0 0 0 0 0 0,
0 1 0 0 0 0 0 0 0,
0 0 1 0 0 0 0 0 0,
0 0 0 1 0 0 0 0 0,
0 0 0 0 1 0 0 0 0,
0 0 0 0 0 1 0 0 0,
0 0 0 0 0 0 1 0 0,
0 0 0 0 0 0 0 1 0,
0 0 0 0 0 0 0 0 1};

BU= 1.145
-0.31
1.689
-2.28
0.905
0.564
-0.19
0.105

LHS=((X`*X)||((Z`*Z)))/((Z`*X)||((Z`*Z+AINV#LAM)));
RHS=(X`*Y)/(Z`*Y);
C=INV(LHS);
BU=C*RHS;

```

Answer

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## Problem 1:BLUPF90 Data Files

**pedigree.txt**

```

1 0 0
2 0 0
3 0 0
4 0 0
5 2 1
6 3 4
7 3 5
8 6 4
9 8 7

```

**phenotypes.txt**

```

1 1 9
2 1 13
3 1 4
4 1 12
5 1 11
6 1 11
7 1 13
8 1 9
9 1 10

```

Genetic variance .00259  
Residual 2.389

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## par.txt

```
# Example of single-trait animal model with one fixed effect
DATAFILE
phenotypes.txt
NUMBER_OF_TRAITS
1
NUMBER_OF_EFFECTS
2
OBSERVATION(S)
3
WEIGHT(S)

EFFECTS: POSITIONS_IN_DATAFILE NUMBER_OF_LEVELS TYPE_OF_EFFECT [EFFECT NESTED]
1 9 cross
2 1 cross
RANDOM_RESIDUAL_VALUES
1.0
RANDOM_GROUP
1
RANDOM_TYPE
add_animal
FILE
pedigree.txt
(CO)VARIANCES
1.0
```

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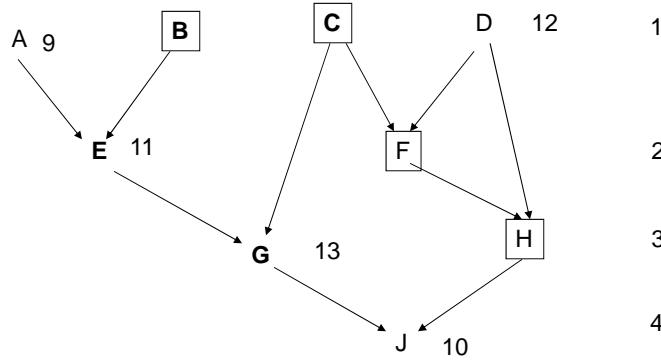
## run:BLUPF90 with par.txt

solutions

trait/effect	level	solution	
1	1	-0.31070241	
1	1	2	1.68929759
1	1	3	-2.28389748
1	1	4	0.90530229
1	1	5	1.14527490
1	1	6	-0.31432205
1	1	7	0.56530033
1	1	8	-0.19149873
1	1	9	0.09880650
1	2	1	10.07738212

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## Problem 2: Sex Limited Trait



Estimate breeding values for the males.

Assume a heritability of .5. Work problem using SAS and BLUPF90

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## Answer Problem 2

```

proc iml;
start main;
A={1 0 0 0 0.5 0 0.25 0 0.125,
     0 1 0 0 0.5 0 0.25 0 0.125,
     0 0 1 0 0 0.5 0.5 0.25 0.375,
     0 0 0 1 0 0 0.5 0 0.75 0.375,
     0.5 0.5 0 0 1 0 0.5 0 0.25 0.25,
     11, 0 0 0.5 0.5 0 1 0.25 0.75 0.5,
     13, 0.25 0.25 0.5 0 0.5 0.25 1 0.125 0.5625,
     10}; 0 0 0.25 0.75 0 0.75 0.125 1.25 0.6875,
     0.125 0.125 0.375 0.375 0.25 0.5 0.5625 0.6875 1.0625};

x={1,
  1,
  1,
  1,
  1};
AINV=INV(A);
lam=1;

Z={1 0 0 0 0 0 0 0 0,
   0 0 1 0 0 0 0 0,
   0 0 0 1 0 0 0 0,
   0 0 0 0 1 0 0,
   0 0 0 0 0 0 0 1};

LHS=((X`*X)|| (X`*Z))//((Z`*X)|| (Z`*Z+AINV#LAM));
RHS=(X`*Y)/(Z`*Y);
C=INV(LHS);
BU=C*RHS;
  
```

### Answer

11.03

-0.89

0.247

0.338

0.307

BU= -0.075

0.206

0.587

0.023

-0.102

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## Problem 2 BLUPF90 Data sets

pedigree.txt      phenotypes.txt

1 0 0	1 1 9
2 0 0	4 1 12
3 0 0	5 1 11
4 0 0	7 1 13
5 2 1	9 1 10
6 3 4	
7 3 5	
8 6 4	
9 8 7	

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## par.txt

```
# Example of single-trait animal model with one fixed effect
DATAFILE
phenotypes.txt
NUMBER_OF_TRAITS
1
NUMBER_OF_EFFECTS
2
OBSERVATION(S)
3
WEIGHT(S)

EFFECTS: POSITIONS_IN_DATAFILE NUMBER_OF_LEVELS TYPE_OF_EFFECT [EFFECT NESTED]
1 9 cross
2 1 cross
RANDOM_RESIDUAL_VALUES
1.0
RANDOM_GROUP
1
RANDOM_TYPE
add_animal
FILE
pedigree.txt
(CO)VARIANCES
1.0
```

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## Run: BLUPF90 with par.txt

solutions

trait/effect	level	solution
1	1	1
1	1	2
1	1	3
1	1	4
1	1	5
1	1	6
1	1	7
1	1	8
1	1	9
1	2	1

## Genomic Selection

### References

- Goddard (2008) Genomic selection: prediction of accuracy and maximization of long term response *Genetica* DOI 10.1007/s10709-008-9308-0
- NejatiJavaremi, A., C. Smith, and J. P. Gibson, 1997 Effect of total allelic relationship on accuracy of evaluation and response to selection. *Journal Of Animal Science* **75**: 1738-1745.
- VanRaden, P. M., 2008 Efficient Methods to Compute Genomic Predictions. *Journal Of Dairy Science* **91**: 4414-4423
- Meuwissen, T. H. E., B. J. Hayes, and M. E. Goddard, 2001 Prediction of total genetic value using genome-wide dense marker maps. *Genetics* **157**: 1819-1829

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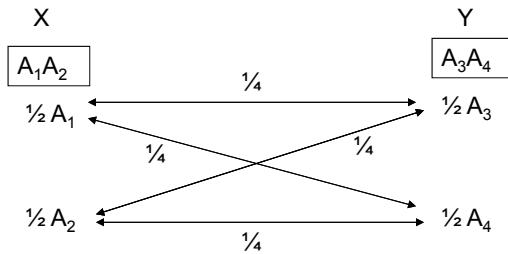
## Genomic Relationship Matrix

- Assumes
  - Dense markers evenly spaced across the genome
  - Assumes markers are in LD with QTL affecting trait(s) of interest
  - Alike in State (AIS) alleles were at one time a result of a single mutation, thus IBD when traced back in evolutionary time
  - Each marker accounts for an equal proportion of genetic variance (infinitesimal model)
  - Genetic Effects are Normally Distributed

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## AIS relationships

$TA_k$ =total allelic relationship at  $k^{\text{th}}$  locus  
 $TA_k=2x$  coefficient of relationship(Malecot. 1948)



$$TA_k = 2 \frac{\sum_{i=1}^2 \sum_{j=1}^2 I_{ij}}{4}$$

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## Compute (AIS) relationship matrix (G)

$$TA_k = 2 \frac{\sum_{i=1}^2 \sum_{j=1}^2 I_{ij}}{4} \quad \mathbf{G} = \sigma_{A^*}^2 \mathbf{G}^* \quad \sigma_{A^*}^2$$

$TA_k$ =total allelic relationship at  $k^{\text{th}}$  locus  
 $TA_k=2x$  coefficient of relationship  
(Malecot. 1948)

Is the additive genetic variance associated with the markers for the trait

$$G_{xy}^* = \frac{\sum_{k=1}^L TA_k}{L} = \frac{2 \sum_{k=1}^L \left( \frac{\sum_{i=1}^2 \sum_{j=1}^2 I_{ij}}{4} \right)}{L} \quad \sigma_{A^*}^2 < \sigma_A^2$$

Note: with low marker density the markers may not capture any genetic variance

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Individual	LOCUS										Pedigree
	A		B		C		D		E		
1	2	1	2	1	2	1	2	1	2	1	2
1	2	2	1	1	1	2	1	1	2	2	
2	1	2	1	2	2	2	1	2	1	1	
3	1	2	1	1	1	2	1	2	1	2	
4	2	2	1	1	2	2	1	1	2	1	
5	2	1	1	2	2	2	1	1	2	1	
6	2	2	1	1	2	2	1	1	2	1	

Individuals (X,Y)	Total	relationship=axy									
x=1	2      2										
y=1	2      2										
sum	4	4									
shared alleles	2	2									
x=2	2      2										
y=1	1      1										
sum	4	4									
shared alleles	2	2									
x=1	2      2										
y=2	1      1										
sum	4	4									
shared alleles	2	2									
AIS	G+GRM										
1	2	3	4	5	6		IBD	PEDIGREE	A		
1	1.8 0.8	0.8 1.4	1.2 1	1.6 1.2	1.2 1.2	1.6 1.2					
2	0.8 0.8	1.4 1.4	1 1.2	1.2 1.2	1 1.2	1.2 1.2					
3	1.2 1.2	1.2 1.2	1.2 1.2	1 1.2	1 1.2	1.2 1.2					
4	1.6 1.6	1.2 1.2	1.2 1.2	1.8 1.8	1.4 1.4	1.8 1.8					
5	1.2 1.2	1.2 1.2	1.4 1.4	1.4 1.4	1.4 1.4	1.4 1.4					
6	1.6 1.6	1.2 1.2	1.2 1.2	1.8 1.8	1.4 1.4	1.8 1.8					

Parents assumed not related (False)    Parents assumed non inbred (false)    Full sibs assumed = relationship (false)

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## G\* Computed Directly from M

Individual	LOCUS										code
	A		B		C		D		E		
1	2	1	2	1	2	1	2	1	2	1	2
1	2	2	1	1	1	2	1	1	2	2	
2	1	2	1	2	2	2	1	2	1	1	
3	1	2	1	1	1	2	1	2	1	2	
4	2	2	1	1	2	2	1	1	2	1	
5	2	1	1	2	2	2	1	1	2	1	
6	2	2	1	1	2	2	1	1	2	1	

M	N individuals x p markers	M*	p markers x N individuals
1	-1 0 0 0 0 1	1 -1 0 0 -1 0	0 -1 0 0 1 -1
2	0 0 -1 1 0 -1	0 -1 0 0 -1 	0 -1 0 1 1 -1
3	0 0 -1 -1 1 	0 -1 0 0 -1 0	0 -1 0 -1 -1 0
4	1 -1 1 0 0 	1 -1 0 0 -1 	1 -1 0 0 1 
5	0 0 0 -1 1 	0 -1 0 0 -1 0	0 -1 0 0 0 0
6	1 -1 1 -1 0 	1 -1 0 0 0 	1 -1 0 0 0 

0.8 -0.2 0.4 0.2 0.6 0.2 0.6	0.2 0.2 0.2 0.8 0.4 0.4 0.8	0.2 0.2 0.2 0.4 0.4 0.4 0.8	1.8 0.8 0.8 1.2 1.2 1.2 1.6
-0.2 0.4 0 0.2 0.2 0 0.2	0 0.2 0.2 0.8 0.4 0.4 0.8	0 0.2 0.2 0.4 0.4 0.4 0.8	1.2 1.2 1.2 1.8 1.4 1.4 1.8
0.2 0 0.2 0.2 0.6 0.2 0.6	0 0.2 0.2 0.8 0.4 0.4 0.8	0 0.2 0.2 0.4 0.4 0.4 0.8	1.2 1.2 1.2 1.8 1.4 1.4 1.8
0.6 0.2 0.2 0 0.4 0.2 0.4	0.8 0.4 0.4 0.4 0.4 0.4 0.8	0.8 0.4 0.4 0.4 0.4 0.4 0.8	1.2 1.2 1.2 1.8 1.4 1.4 1.8
0.2 0.6 0.2 0.2 0.8 0.4 0.8	0.2 0.6 0.2 0.2 0.4 0.4 0.8	0.2 0.6 0.2 0.2 0.4 0.4 0.8	1.6 1.2 1.2 1.8 1.4 1.4 1.8

MM/5 = G\*

dimension nxn

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## Mixed Model Equations

$$\mathbf{G} = \mathbf{MM}' / L$$

$\mathbf{M}$  (n individuals x p markers)  
 $\mathbf{M}(n,p)\mathbf{M}'(p,n)$   
 $\mathbf{MM}'(n,n)$

$$\begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z} + \frac{1}{\sigma_{A^*}^2} \mathbf{G}^{-1} \end{bmatrix} \begin{bmatrix} \mathbf{b} \\ \mathbf{u} \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{Y} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Y} \end{bmatrix}$$

Simplifications If  $\mathbf{R} = \mathbf{I}\sigma_e^2$  n effects to estimate

$$\begin{bmatrix} \mathbf{X}'\mathbf{X} & \mathbf{X}'\mathbf{Z} \\ \mathbf{Z}'\mathbf{X} & \mathbf{Z}'\mathbf{Z} + \frac{\sigma_e^2}{\sigma_{A^*}^2} \mathbf{G}^{-1} \end{bmatrix} \begin{bmatrix} \mathbf{b} \\ \mathbf{u} \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{Y} \\ \mathbf{Z}'\mathbf{Y} \end{bmatrix}$$

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G may not (usually does not) have an inverse

- G may not be positive definite
  - The G matrix is an estimate of the true genetic variance co-variance matrix
  - Genotyping errors and possible inclusion of individuals without all parents create inconsistency
  - Solution: multiply both sides of the second equation by G

$$\begin{bmatrix} \mathbf{X}'\mathbf{X} & \mathbf{X}'\mathbf{Z} \\ \sigma_{A^*}^2 \mathbf{GZ}'\mathbf{X} & \sigma_{A^*}^2 \mathbf{GZ}'\mathbf{Z} + \sigma_e^2 \mathbf{I} \end{bmatrix} \begin{bmatrix} \mathbf{b} \\ \mathbf{u} \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{Y} \\ \sigma_{A^*}^2 \mathbf{GZ}'\mathbf{Y} \end{bmatrix}$$

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### Example

$$\begin{aligned}
 \mathbf{Y} &= \begin{bmatrix} 7 \\ 9 \\ 10 \\ 6 \\ 9 \\ 11 \end{bmatrix} & \mathbf{X} &= \begin{bmatrix} 1 \\ 1 \\ 1 \\ 1 \\ 1 \\ 1 \end{bmatrix} & b &= [\mu_0] & Z &= \begin{bmatrix} 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{bmatrix} & \mathbf{u} &= \begin{bmatrix} u_1 \\ u_2 \\ u_3 \\ u_4 \\ u_5 \\ u_6 \end{bmatrix} \\
 \mathbf{M} &= \begin{bmatrix} 1 & -1 & 0 & -1 & 1 \\ 0 & 0 & 1 & 0 & -1 \\ 0 & -1 & 0 & 0 & 0 \\ 1 & -1 & 1 & -1 & 0 \\ 0 & 0 & 1 & -1 & 0 \\ 1 & -1 & 1 & -1 & 0 \end{bmatrix} & \mathbf{MM}' / L &= \begin{bmatrix} .8 & -.2 & .2 & .6 & .2 & .6 \\ -.2 & .4 & 0 & .2 & .2 & .2 \\ .2 & 0 & .2 & .2 & 0 & .2 \\ .6 & .2 & .2 & .8 & .4 & .8 \\ .2 & .2 & 0 & .4 & .4 & .4 \\ .6 & .2 & .2 & .8 & .4 & .8 \end{bmatrix} & \sigma_A^2 &= 10 & \\
 & & & & & & \sigma_{A^*}^2 &= 5 & \\
 & & & & & & \sigma_e^2 &= 20 &
 \end{aligned}$$

Note, only  $\frac{1}{2}$  the additive genetic variance was captured by the markers  
(missing heritability issue)

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Y		Z		V(A)=	5					
7	1	0	0	0						
9	0	1	0	0	V(E)=					
10	0	0	1	0	20					
6	0	0	0	1						
9	0	0	0	0						
11	0	0	0	0						
				XX						
				6						
X										
1	0.8	-0.2	0.2	0.6	MM'/5					
1	-0.2	0.4	0	0.2						
1	0.2	0	0.2	0						
1	0.6	0.2	0.2	0.8						
1	0.2	0.2	0	0.4						
1	0.6	0.2	0.2	0.8						
				XY	52					
$\sqrt{V(A^*)G^*ZX}$		$V(A^*)GZ + V(E)$		$V(A^*)GZY$						
11	24	-1	1	3	3					
4	-1	22	0	1	1					
4	1	0	21	1	0					
15	3	1	1	24	2					
8	1	1	0	2	22					
15	3	1	1	4	2					
				24	24					
					89					
					37					
					34					
					126					
					68					
					126					
6	1	1	1	1	b					
11	24	-1	1	3	52					
4	-1	22	0	1	89					
4	1	0	21	1	37					
15	3	1	1	24	34					
8	1	1	0	2	126					
15	3	1	1	4	68					
					126					
		LHS		RHS						
b	0.238268	-0.00798	-0.01022	-0.01037	-0.00629	-0.00886	-0.00629	52	8.762384	
u1	-0.07865	0.045659	0.005799	0.001807	-0.00248	0.001686	-0.00248		-0.25929	
u2	-0.03389	0.003561	0.047264	0.001527	-0.00087	-0.00061	-0.00087		0.094486	
u3	-0.03092	-0.00058	0.001379	0.04919	-0.00075	0.001505	-0.00075		-0.02194	
u4	='	-0.11254	-0.00078	0.003063	0.003334	0.046655	0.001074	-0.00335		-0.1648
u5	-0.06107	0.000807	0.000747	0.003012	-0.0015	0.048432	-0.0015	68	-0.05796	
u6	-0.11254	-0.00078	0.003063	0.003334	-0.00335	0.001074	0.046655	126	-0.1648	

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## R code Example 4

```
NL=5                               X = matrix( c( 1,
SigA=5                                1,
SigE=20                                1,
                                         1,
                                         1,
                                         1,
                                         1 ),
Y = matrix( c( 7,                      M = matrix( c( 1,-1,0,-1,1,
9,                                     0,0,1,0,-1,
10,                                    0,-1,0,0,
6,                                     1,-1,1,-1,0,
9,                                     0,0,1,-1,0,
11), 6,1)                         1,-1,1,-1,0),
Z = matrix( c( 1, 0, 0, 0, 0, 0,      6,5, byrow = TRUE)
0, 1, 0, 0, 0, 0,                   G=(1/NL)*M%*%t(M)
0, 0, 1, 0, 0, 0,
0, 0, 0, 1, 0, 0,
0, 0, 0, 0, 1, 0,
0, 0, 0, 0, 0, 1),6,6)
```

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## R code

```
LHS = rbind( cbind(t(X) %*% X , t(X) %*% Z ),
              cbind(SigA*G%*%t(Z) %*% X , SigA*G%*%t(Z)%*%Z + SigE*Z))

RHS = rbind(t(X)%*%Y,
            SigA*G%*%t(Z)%*%Y)

C = solve(LHS)

BU = C %*% RHS

BU [1] 8.76238422
[2] -0.25929249
[3] 0.09448802
[4] -0.02193502
[5] -0.16480447
[6] -0.05795688
[7] -0.16480447
```

Check G for inverse  
GI=solve(G)

gEBV

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## Equivalent Model Estimation of Marker effects

$$\begin{bmatrix} \mathbf{X}'_{1,N} \mathbf{X}_{N,1} & \mathbf{X}'_{1,N} \mathbf{M}_{N,p} \\ \mathbf{M}'_{p,N} \mathbf{X}_{N,1} & \mathbf{M}'_{p,N} \mathbf{M}_{N,p} + \frac{\sigma_e^2}{\sigma_g^2} \mathbf{I} \end{bmatrix} \begin{bmatrix} \boldsymbol{\beta}_{1,1} \\ \mathbf{g}_{p,1} \end{bmatrix} = \begin{bmatrix} \mathbf{X}'_{1,N} \mathbf{Y}_{N,1} \\ \mathbf{M}'_{p,N} \mathbf{Y}_{N,1} \end{bmatrix}$$

Assumption depends on method

- 1) (GBLUP, ssGBLUP) Genetic variance  $\sigma_g^2 = \left( \frac{\sigma_A^2}{L} \right)$  associated with each marker is equal
- 2) (Bayes A) sampled from a t distribution
- 3) (Bayes B and Bayes C  $\pi$ ) from a mixture of distributions (null and t)

$$\hat{u}_i = GEBV_i = \mathbf{M}\mathbf{g} = \sum_j M_{ij} \hat{g}_j$$

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M'		M						
1	0	-1	0	-1	1			
-1	0	-1	0	0	-1			
0	1	0	1	1	1			
-1	0	0	-1	-1	-1			
1	-1	0	0	0	0			
M'M		M'X	M'Y	Y	X			
3	-3	2	-3	1				
-3	4	-2	3	-1				
2	-2	4	-3	-1				
-3	3	-3	4	-1				
1	-1	-1	-1	2				
I		0	24	7	1			
1	0	0	0	0				
0	1	0	0	0				
0	0	1	0	0				
0	0	0	1	0				
0	0	0	0	1				
LHS		V(A)=	5	X'X				
6	3	-4	4	-4	B			
3	23	-3	2	-3	g1			
-4	-3	24	-2	3	-1			
4	2	-2	24	-3	g2			
-4	-3	3	3	24	='			
0	1	-1	-1	-1	g3			
RHS		52	24	7	1			
6	3	-4	4	-4	B			
3	23	-3	2	-3	g1			
-4	-3	24	-2	3	-1			
4	2	-2	24	-3	g2			
-4	-3	3	3	24	='			
0	1	-1	-1	-1	g3			
inverse(LHS)		52	24	7	1			
B	0.238268	-0.02055	0.030921	-0.03165	0.029414	0.002238	52	8.762384
g1	-0.02055	0.046795	0.002074	-0.00012	0.002068	-0.00194	24	-0.08491
g2	0.030921	0.002074	0.047716	-0.00139	-0.00057	0.001958	-34	0.021935
g3	-0.03165	-0.00012	-0.00139	0.047031	0.00085	0.002119	35	0.012177
g4	0.029414	0.002068	-0.00057	0.00085	0.047091	0.002059	-33	0.070134
g5	0.002238	-0.00194	0.001958	0.002119	0.002059	0.045822	-2	-0.08231
M								
u1	1	-1	0	-1	1	-0.08491	-0.25929	
u2	0	0	1	0	-1	0.021935	0.094486	
u3	0	-1	0	0	0	0.012177	-0.02194	same as before
u4	1	-1	1	-1	0	0.070134	-0.1648	
u5	0	0	1	-1	0	-0.08231	-0.05796	
u6	1	-1	1	-1	0	0	-0.1648	

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## R code Example 5

```
NL=5  
SigA=5  
Sigg=SigA/NL  
SigE=20  
  
y = matrix( c( 7,  
             9,  
             10,  
             6,  
             9,  
             11), 6,1)  
  
I = matrix( c( 1, 0, 0, 0, 0,  
              0, 1, 0, 0, 0,  
              0, 0, 1, 0, 0,  
              0, 0, 0, 1, 0,  
              0, 0, 0, 0, 1),5,5)  
  
X = matrix( c( 1,  
              1,  
              1,  
              1,  
              1,  
              1 ), 6,1)  
  
M = matrix( c( 1,-1,0,-1,1,  
              0,0,1,0,-1,  
              0,-1,0,0,0,  
              1,-1,1,-1,0,  
              0,0,1,-1,0,  
              1,-1,1,-1,0,6,5, byrow = TRUE)
```

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## R code

```
LHS = rbind( cbind(t(X) %*% X , t(X) %*% M ),  
            cbind( t(M) %*% X , t(M)%*%M + (SigE/Sigg)*I))  
  
RHS = rbind(t(X)%*% y,  
            t(M)%*%y)  
  
C = solve(LHS)  
  
Bg = C %*% RHS  
  
Bg  
[.1]  
[1.] 8.76238422  
[2.] -0.08491256  
[3.] 0.02193502  
[4.] 0.01217705  
[5.] 0.07013393  
[6.] -0.08231097  
>
```

Marker effects

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## R code

gEBV

```
[,1]
[1,] -0.25929249
[2,] 0.09448802
[3,] -0.02193502
[4,] -0.16480447
[5,] -0.05795688
[6,] -0.16480447
```

g=Bg[2:6]  
U=M%\*%g  
U

Compare to Slide 13

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## Single Step ssGBLUP

- Merge G matrix into regular A matrix
  - Aguilar, I., I. Misztal, D. L. Johnson, A. Legarra, S. Tsuruta *et al.* 2010 Hot topic: A unified approach to utilize phenotypic, full pedigree, and genomic information for genetic evaluation of Holstein final score. *Journal Of Dairy Science* **93**: 743-752.
  - Corrects for multi-trait selection bias
    - Vitezica, Z. G., I. Aguilar, I. Misztal, and A. Legarra, 2011 Bias in genomic predictions for populations under selection. *Genetics Research* **93**: 357-366.
  - Uses all information
    - Phenotypes of animals without genotypes
      - J. Anim Sci. 2011. 89:23-28. doi:10.2527/jas.2010-3071
- Software
  - <http://nce.ads.uga.edu/~ignacy/genomic-blupf90/>
  - <http://snp.toulouse.inra.fr/~alegarra/>

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## ssGBLUP

GBLUP only animals genotyped included in analysis

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

ssGBLUP all animals with phenotypes included

$$\begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z} + \mathbf{H}^{-1} \end{bmatrix} \begin{bmatrix} \mathbf{b} \\ \mathbf{u} \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{Y} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Y} \end{bmatrix}$$

$$\mathbf{H}^{-1} = \mathbf{A}^{-1} + \begin{bmatrix} 0 & 0 \\ 0 & \mathbf{G}^{-1} - \mathbf{A}_{22}^{-1} \end{bmatrix}$$

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$$\mathbf{g} = \mathbf{Z}(\mathbf{Z}\mathbf{Z}')^{-1}\mathbf{u} \quad \text{GWAS}$$

GBLUP

SNP effects using only genotyped individuals

$$\begin{bmatrix} \mathbf{X}'_{1,N} \mathbf{X}_{N,1} & \mathbf{X}'_{1,N} \mathbf{M}_{N,p} \\ \mathbf{M}'_{p,N} \mathbf{X}'_{N,1} & \mathbf{M}'_{p,N} \mathbf{M}_{N,p} + \frac{\sigma_e^2}{\sigma_g^2} \mathbf{I} \end{bmatrix} \begin{bmatrix} \boldsymbol{\beta}_{1,1} \\ \mathbf{g}_{p,1} \end{bmatrix} = \begin{bmatrix} \mathbf{X}'_{1,N} \mathbf{Y}_{N,1} \\ \mathbf{M}'_{p,N} \mathbf{Y}_{N,1} \end{bmatrix}$$

ssGBLUP

SNP effects using all information

$$\begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z} + \mathbf{H}^{-1} \end{bmatrix} \begin{bmatrix} \mathbf{b} \\ \mathbf{u} \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{Y} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Y} \end{bmatrix}$$

$$g = \frac{\sigma_u^2}{\sigma_a^2} \mathbf{D} \mathbf{Z}' \mathbf{H}^{-1} \mathbf{u}$$

Wang, H., I. Misztal, I. Aguilar, A. Legarra, and W. M. Muir. Genome-wide association mapping including phenotypes from relatives without genotypes. 2012. Genetics Research 94:73-83

20

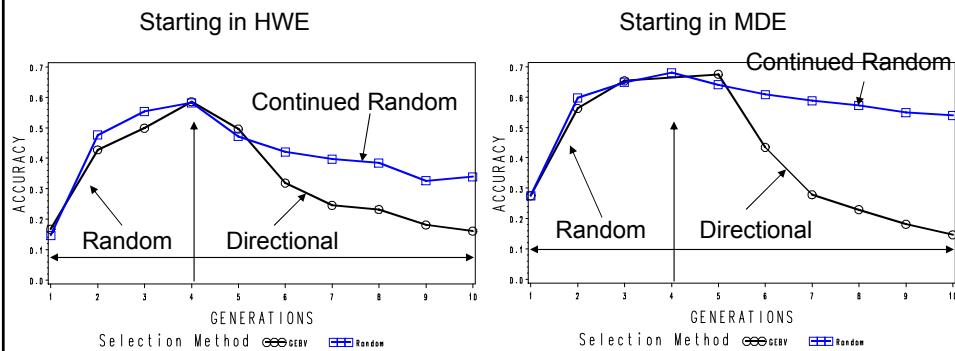
# Issues

## Genomic Selection and GWAS

- Admixture (Walsh Lectures)
  - Major problem
  - False Positives
  - Spurious Correlations
  - Correlation does not mean Causation
  - Partial Solution
    - Use of Igenstrat to correct for structure
    - Use of Structure to correct for structure
    - Scaling of G to combine all populations and cross in common relationship matrix
- Pedigree errors
  - More costly in terms of accuracy with G than A matrix
- Cost
  - Use dense SNP genotyping all breeders (parents)
  - Low Density on all candidates
    - Reducing the number of markers down to those that are most predictive
    - Going from 60,000 SNP to 384 SNP for genotyping
    - GWAS SNP selection
- Selection (See next slide)
  - Allele frequencies change
  - Older data becomes a liability

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### Effect of Random vs. Directional Selection on Accuracy



$h^2=.1$   $N=256$ ,  $Ne=32$ , 100/100 Marker/QTL loci distributed on 100cM.  
(average over 60 replicates, SEM=.02).

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# Appendix 1

## Example use of GS3 to do GWAS and Genomic Selection

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- Programs and data
  - <http://snp.toulouse.inra.fr/~alegarra/>
  - <http://www.biostat.washington.edu/suminst/sis/g/computing>
    - Legarra GS3
      - Gibbs Sampling
      - Genomic Selection
      - Gauss Seidel
      - BayesCpi
      - Bayesian Lasso
    - See manualgs3\_6.pdf

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## Exo\_data.txt

T1	t2	t3	t4	ID	sex	cage
1	2	3	4	5	6	7
20.3	1.08004	0.952123	1.45443	345	1	69
26.7	0.99726	1.01302	1.13901	346	2	27
19.5	1.08285	0.900454	1.33243	347	2	43
22.2	1.02697	1.01719	0.92849	348	2	2
17.3	1.05095	0.958695	1.42519	349	1	218
18.1	1.0204	1.05445	0.384847	350	2	17
25.6	0.95566	0.947974	2.06488	351	2	57
20.6	1.01382	0.921759	1.59988	352	2	36
.	.	.	.	.	.	.

Values of the trait of -9999 are treated as missing values.

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## exo\_genotypes.txt

The SNP effects have to be in one single column, coded as 0/1/2 for aa/Aa/AA (i.e., no letters, no triallelic SNP); a value of 5 implies a missing value (see below). No space is allowed among SNPs.

ID

345 1111212111212111021111211101011120210000002022.....  
346 11211112112110211112111211101120120210001120200.....  
347 20222222020220202222222202020020220000002022....  
...

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## pedigri.dat

Renumbered sequential

0 for unknown parents

Animal sire dam

1	0	0
2	0	0
3	0	0
4	0	0
5	0	0
6	0	0

...

2266	152	325
2267	119	292
2268	8	180
2269	64	236
2270	5	177
2271	156	329
2272	34	206

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## Parameter File

- DATAFILE  
./exo\_data.txt ← Any file name with data
- PEDIGREE FILE  
./pedigri.dat ← Any file name with pedigree
- GENOTYPE FILE  
./exo\_genotypes.txt ← Any file name with genotypes blank line otherwise
- NUMBER OF LOCI (might be 0)  
10946 ← Loci If have genomic information
- METHOD (BLUP/MCMCBLUP/VCE/PREDICT)
- BLUP ← BLUP=phenotypic BLUP or GBLUP
- SIMULATION
- F ← VCE=Variance component estimation  
REML or Gibbs sampling

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## Parameter File (cont1)

- GIBBS SAMPLING PARAMETERS
  - NITER
  - 10000
  - BURNIN
  - 200
  - THIN
  - 10
  - CONV\_CRIT (MEANINGFUL IF BLUP)
  - 1d-8
  - CORRECTION (to avoid numerical problems)
  - 1000
  - VARIANCE COMPONENTS SAMPLES
  - var2
- 
- Even if not doing GIBBs or variance estimation must include
- File name to store estimates

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## Parameter File (cont2)

- SOLUTION FILE
  - solutions2
  - TRAIT AND WEIGHT COLUMNS
  - 1 0 #weight
  - NUMBER OF EFFECTS
  - 5
  - POSITION IN DATA FILE TYPE OF EFFECT NUMBER OF LEVELS
  - 6 cross 1
  - 5 add\_animal 2272
  - 7 perm\_diagonal 2000
  - 8 add\_SNP 0
  - 8 dom\_SNP 0
- 
- File name to store solutions
- 0 for weight means no weight
- cross= fixed effect  
cov= covariable  
add SNP= additive SNP effect  
dom SNP=dominant SNP effect  
add anima=additive infinitesimal (polygenic)  
perm diagonal=common environmental effect
- Position in data file
- Number of levels except for SNP effects which was given by number of loci

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## Parameter File (cont4)

- VARIANCE COMPONENTS (fixed for any BLUP, starting values for VCE)
- vara
- 2.52d-04 2
- vard
- 1.75d-06                                  Even if not in your model
- varg    must include key word and
- 3.56 2                                        value
- varp
- 2.15 2
- vare
- 0.19 2

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## Parameter File (cont5)

- RECORD ID                                      The ID in the data file that corresponds to the animal ID in pedigree file
- 5
- CONTINUATION (T/F)                              For GIBBS sampling if want to continue sampling
- F    ←
- MODEL (T/F for each effect)                      Can be used to add or ignore effects rather than changing the other parameters
- T T T T T
- A PRIORI a                                      a priori distributions (inverted chi squared) for variance components. The first value=expectation, the second value
- 1 1    are the degrees of freedom. If the degrees of freedom = -2, flat distribution assumed (roughly) equivalent to REML.
- a PRIORI D
- 1 1
- USE MIXTURE                                      USE MIXTURE (BAYESC) statement starts (if
- F    VCE) the BayesCPi method
- ^
- #OPTION BayesianLasso Tibshirani
- #OPTION SNP\_weights myfile 1
- # OPTION BinaryTrait

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## Run GS3

- ./gs3 together.031210.par
- Now Try This
  - Change parameter file to estimate additive SNP only effects (remove dominance and polygenic)
  - How much of the genetic variation was accounted for by the SNPs?

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## How Adequate was the SNP chip, is it dense enough

- Additive variance
  - Add\_animal
    - 4.56
  - Add\_SNP
    - .914
- 10,946 SNPs were able to capture  
 $.914/4.56 = 20.0\%$  of additive genetic variation
- No

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## Do the SNPs account for any variation not accounted for by polygenic

- Model including polygenic and add\_SNP
  - Polygenic variance= 3.41
  - Add\_SNP variance=.924
  - Total=4.33
- Polygenic only=4.56
- NO, adding genotypic information did not increase the amount of variation that could be accounted for

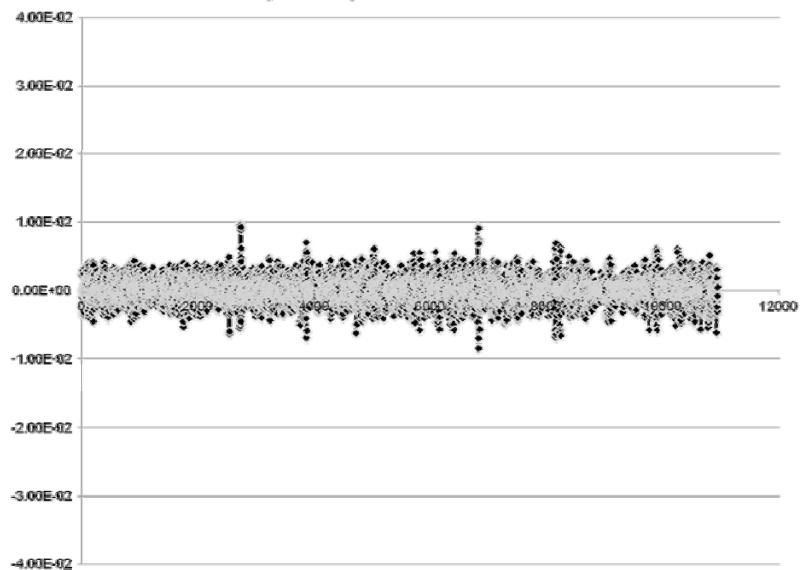
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## GWAS

- Change parameter file to do GWAS via BayesCpi,
- Then fix pi by setting mixture to true and
  - A PRIORI a
    - 1 20
    - 1 1
  - Graph SNP effects
- Solution
  - BayesPiC
    - $\pi=.04$
    - proportion of the mixture for non-null additive locus effects

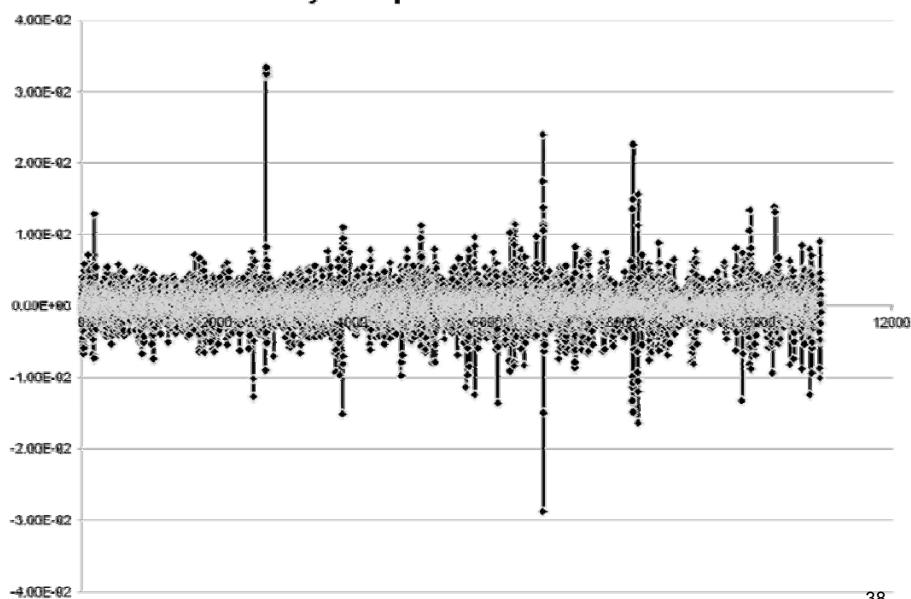
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### BayesB a priori 1-1 SNP effect



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### BayesB a-priori 1-20 SNP effects



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# Lecture 6

## QTL and Association Mapping with Mixed Models

Bruce Walsh lecture notes  
SISG -Mixed Model Course  
Seattle, 16 - 18 July 2014

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## QTL & Association mapping

- We would like to know both the genomic locations (map positions) and effects (either genotypic means or variances) for genes underlying quantitative trait variation
- QTL mapping
  - Using linkage information on a set of known relatives
- Association mapping
  - Using very fine scale LD to map genes in a set of random individuals from a population

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# Outline

- Basics of QTL mapping
  - Line crosses
    - typically fixed effects models
  - Outbred populations
    - Random effects family models
    - General pedigree methods
- High parameter models
  - Shrinkage approaches for detecting epistasis
- Association mapping

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## Inbred Line Cross QTL mapping

- Most powerful design
  - Cross two fully inbred lines, look at marker trait segregation in the  $F_2$  (or other, such as  $F_n$ ) generations
  - P1: MMQQ, P2:mmqq
  - All  $F_1$  same genotype/phase: MQ/mq
  - Hence, in the  $F_1$ , all parents have the same genotype
  - At most only two alleles, each with freq 1/2
  - Idea: Does the mean trait value of (say) MM individuals differ from (say) mm
    - Different marker genotypes have different mean trait values

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# Conditional Probabilities of QTL Genotypes

The basic building block for all QTL methods is  $\Pr(Q_k | M_j)$  --- the probability of QTL genotype  $Q_k$  given the marker genotype is  $M_j$ .

$$\Pr(Q_k | M_j) = \frac{\Pr(Q_k M_j)}{\Pr(M_j)}$$

Consider a QTL linked to a marker (recombination fraction =  $c$ ). Cross  $MMQQ \times mmqq$ . In the F1, all gametes are  $MQ$  and  $mq$

In the F2,  $\text{freq}(MQ) = \text{freq}(mq) = (1-c)/2$ ,  
 $\text{freq}(mQ) = \text{freq}(Mq) = c/2$

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## Expected Marker Means

The expected trait mean for marker genotype  $M_j$  is just

$$\mu_{M_j} = \sum_{k=1}^N \mu_{Q_k} \Pr(Q_k | M_j)$$

For example, if  $QQ = 2a$ ,  $Qq = a(1+k)$ ,  $qq = 0$ , then in the F2 of an  $MMQQ/mmqq$  cross,

$$(\mu_{MM} - \mu_{mm})/2 = a(1 - 2c)$$

- If the trait mean is significantly different for the genotypes at a marker locus, it is linked to a QTL
- A small  $MM-mm$  difference could be (i) a tightly-linked QTL of small effect or (ii) loose linkage to a large QTL

# Linear Models for QTL Detection

The use of differences in the mean trait value for different marker genotypes to detect a QTL and estimate its effects is a use of [linear models](#).

One-way ANOVA.

Value of trait in kth individual of marker genotype type i

$$z_{ik} = \mu + b_i + e_{ik}$$

↑  
Effect of marker genotype i on trait value

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$$z_{ik} = \mu + b_i + e_{ik}$$

[Detection](#): a QTL is linked to the marker if at least one of the  $b_i$  is significantly different from zero

[Estimation](#): (QTL effect and position): This requires relating the  $b_i$  to the QTL effects and map position

# Detecting epistasis

One major advantage of linear models is their flexibility. To test for epistasis between two QTLs, use ANOVA with an interaction term

$$z = \mu + a_i + b_k + d_{ik} + e$$

Effect from marker genotype at first marker set (can be > 1 loci)

Effect from marker genotype at second marker set

Interaction between marker genotypes  $i$  in 1st marker set and  $k$  in 2nd marker set

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# Detecting epistasis

$$z = \mu + a_i + b_k + d_{ik} + e$$

- At least one of the  $a_i$  significantly different from 0  
---- QTL linked to first marker set
- At least one of the  $b_k$  significantly different from 0  
---- QTL linked to second marker set
- At least one of the  $d_{ik}$  significantly different from 0  
---- interactions between QTL in sets 1 and two

Problem: Huge number of potential interaction terms (order  $m^2$ , where  $m$  = number of markers)

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# Model selection

- With (say) 300 markers, we have (potentially) 300 single-marker terms and  $300 \times 299/2 = 44,850$  epistatic terms
  - Hence, a model with up to  $p=45,150$  possible parameters
  - $2^P$  possible submodels =  $10^{13,600}$  ouch!
- The issue of **Model selection** becomes very important.
- How do we find the best model?
  - Stepwise regression approaches
    - Forward selection (add terms one at a time)
    - Backwards selection (delete terms one at a time)
  - Try all models, assess best fit
  - Mixed-model approaches (SSVS)

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## Model Selection

**Model Selection:** Use some criteria to choose among a number of candidate models. Weight goodness-of-fit ( $L$ , value of the likelihood at the MLEs) vs. number of estimated parameters ( $k$ )

AIC = Akaike's information criterion

$$AIC = 2k - 2 \ln(L)$$

BIC = Bayesian information criterion (Schwarz criterion)

$$BIC = k \ln(n)/n - 2 \ln(L)/n$$

BIC penalizes free parameters more strongly than AIC

Other measures. Smaller is better

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# Model averaging

**Model averaging:** Generate a composite model by weighting (averaging) the various models, using AIC, BIC, or other

Idea: Perhaps no "best" model, but several models all extremely close. Better to report this "distribution" rather than the best one

One approach is to average the coefficients on the "best-fitting" models using some scheme to return a composite model

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## Supersaturated Models

A problem with many QTL approaches is that there are far more parameters ( $p$ ) to estimate than there are independent samples ( $n$ ).

Case in point: epistasis

Such supersaturated models arise commonly in Genomics. How do we deal with them?

One approach is to have all parameters included, but some are shrunk back (regressed) towards zero by assigning them a very small posterior variance

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## Shrinkage estimators

**Shrinkage estimates:** Rather than adding interaction terms one at a time, a shrinkage method starts **with all interactions included**, and then shrinks most back to zero.

Under a Bayesian analysis, any effect is *random*. One can assume the effect for (say) interaction  $ij$  is drawn from a normal with mean zero and variance  $\sigma^2_{ij}$

Further, the interaction-specific variances are themselves random variables drawn from a hyperparameter distribution, such as an inverse chi-square.

One then estimates the hyperparameters and uses these to predict the variances, with effects with small variances shrinking back to zero, and effects with large variances remaining in the model.

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## What is a "QTL"

- A detected "QTL" in a mapping experiment is a region of a chromosome detected by linkage.
- Usually large (typically 10-40 cM)
- When further examined, most "large" QTLs turn out to be a linked collection of locations with increasingly smaller effects
- The more one localizes, the more subregions that are found, and the smaller the effect in each subregion
- This is called **fractionation**

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# Limitations of QTL mapping

- Poor resolution (~20 cM or greater in most designs with sample sizes in low to mid 100's)
  - Detected "QTLs" are thus large chromosomal regions
- Fine mapping requires either
  - Further crosses (recombinations) involving regions of interest (i.e., RILs, NILs)
  - Enormous sample sizes
    - If marker-QTL distance is 0.5cM, require sample sizes in excess of 3400 to have a 95% chance of 10 (or more) recombination events in sample
    - 10 recombination events allows one to separate effects that differ by ~ 0.6 SD

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# Limitations of QTL mapping (cont)

- "Major" QTLs typically fractionate
  - QTLs of large effect (accounting for > 10% of the variance) are routinely discovered.
  - However, a large QTL peak in an initial experiment generally becomes a series of smaller and smaller peaks upon subsequent fine-mapping.
- The Beavis effect:
  - When power for detection is low, marker-trait associations declared to be statistically significant significantly overestimate their true effects.
  - This effect can be very large (order of magnitude) when power is low.

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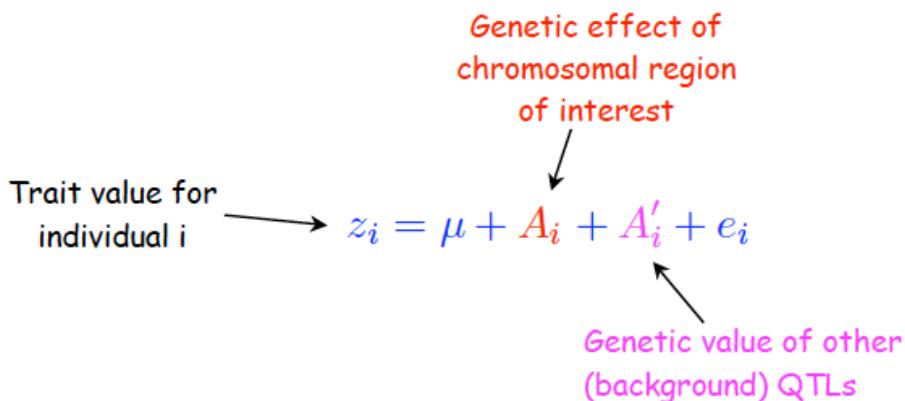
# Outbred populations

- When we move from the simple framework of an inbred line cross QTL design to a set of parents from an outbred population, complications arise as the parents don't all have the same genotypes
  - Differences in linkage phase
  - Many uninformative as to linkage (varies over makers)
  - Possibility of multiple alleles
- Result: express marker effects in terms of the variance in trait value it explains, rather than in terms of mean marker effects

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# General Pedigree Methods

Random effects (hence, variance component) method for detecting QTLs in general pedigrees



The model is rerun for each marker

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$$z_i = \mu + A_i + A'_i + e_i$$

The covariance between individuals i and j is thus

$$\sigma(z_i, z_j) = R_{ij} \sigma_A^2 + 2\Theta_{ij} \sigma_{A'}^2$$

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Assume  $\mathbf{z}$  is MVN, giving the covariance matrix as

$$\mathbf{V} = \mathbf{R} \sigma_A^2 + \mathbf{A} \sigma_{A'}^2 + \mathbf{I} \sigma_e^2$$

Here

$$R_{ij} = \begin{cases} 1 & \text{for } i = j \\ \hat{R}_{ij} & \text{for } i \neq j \end{cases}, \quad A_{ij} = \begin{cases} 1 & \text{for } i = j \\ 2\Theta_{ij} & \text{for } i \neq j \end{cases}$$

Estimated from marker data	Estimated from the pedigree
-------------------------------	--------------------------------

The resulting likelihood function is

$$\ell(\mathbf{z} | \mu, \sigma_A^2, \sigma_{A'}^2, \sigma_e^2) = \frac{1}{\sqrt{(2\pi)^n |\mathbf{V}|}} \exp \left[ -\frac{1}{2} (\mathbf{z} - \mu)^T \mathbf{V}^{-1} (\mathbf{z} - \mu) \right]$$

A significant  $\sigma_A^2$  indicates a linked QTL.

# Association & LD mapping

Mapping major genes (LD mapping) vs. trying to Map QTLs (Association mapping)

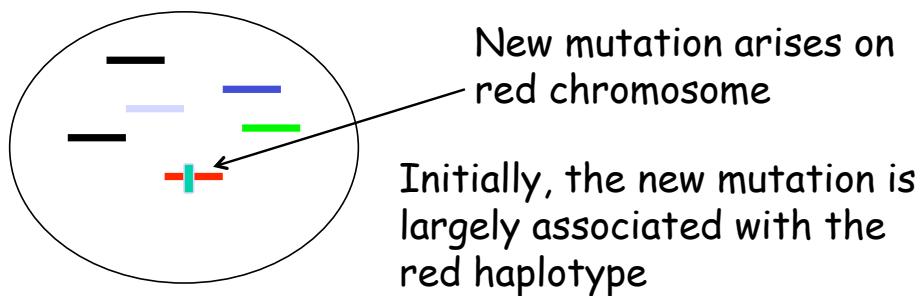
Idea: Collect random sample of individuals, contrast trait means over marker genotypes

If a dense enough marker map, likely population level linkage disequilibrium (LD) between closely-linked genes

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## Fine-mapping genes

Suppose an allele causing an effect on the trait arose as a single mutation in a closed population



Hence, markers that define the red haplotype are likely to be associated (i.e. in LD) with the mutant allele

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## Background: Association mapping

- If one has a very large number of SNPs, then new mutations (such as those that influence a trait) will be in LD with very close SNPs for hundreds to thousands of generations, generating a marker-trait association.
  - Association mapping looks over all sets of SNPs for trait -SNP associations. GWAS = genome-wide association studies.
  - This is also the basis for genomic selection
- Main point from extensive human association studies
  - Almost all QTLs have very small effects
  - Marker-trait associations do not fully recapture all of the additive variance in the trait (due to incomplete LD)
  - This has been called the "missing heritability problem" by human geneticists, but not really a problem at all (more shortly).

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## Association mapping

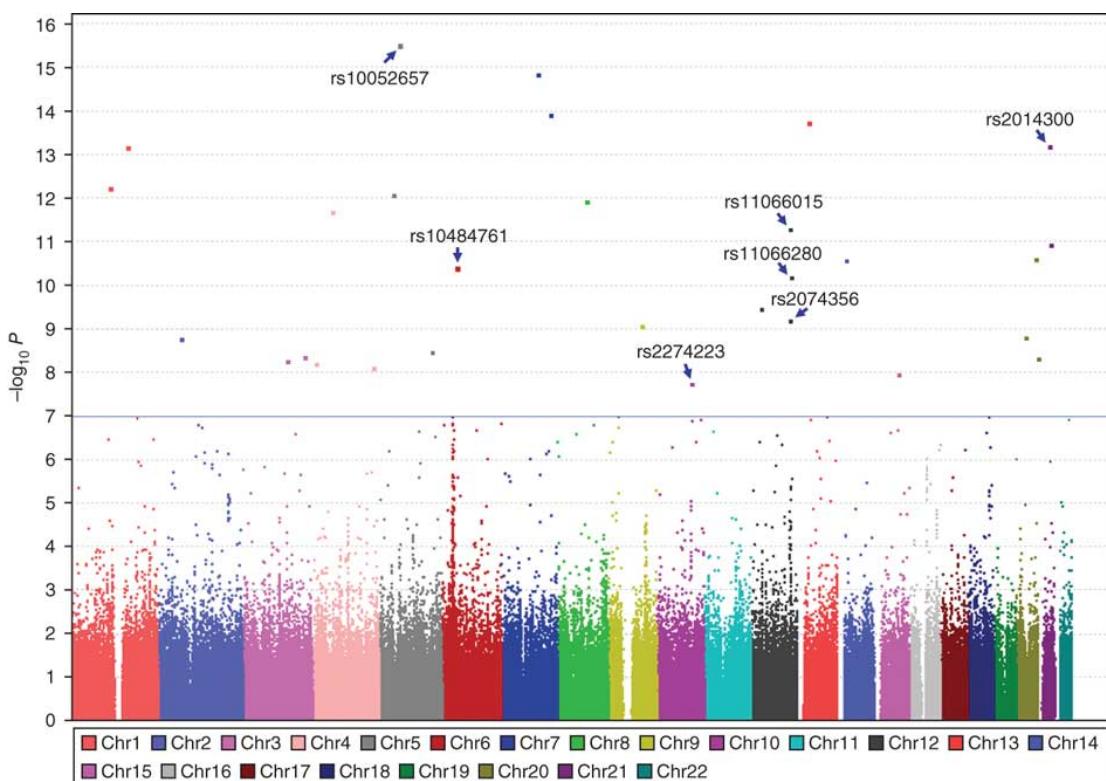
- Marker-trait associations within a population of unrelated individuals
- Very high marker density (~ 100s of markers/cM) required
  - Marker density no less than the average track length of linkage disequilibrium (LD)
- Relies on very slow breakdown of initial LD generated by a new mutation near a marker to generate marker-trait associations
  - LD decays very quickly unless very tight linkage
  - Hence, resolution on the scale of LD in the population(s) being studied (1 ~ 40 KB)
- Widely used since mid 1990's. Mainstay of human genetics, strong inroads in breeding, evolutionary genetics
- Power a function of the genetic variance of a QTL, not its mean effects

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# Manhattan plots

- The results for a **Genome-wide Association study** (or **GWAS**) are typically displayed using a **Manhattan plot**.
  - At each SNP,  $-\ln(p)$ , the negative log of the p value for a significant marker-trait association is plotted. Values above a threshold indicate significant effects
  - Threshold set by Bonferroni-style multiple comparisons correction
  - With n markers, an overall false-positive rate of p requires each marker be tested using  $p/n$ .
  - With  $n = 10^6$  SNPs, p must exceed  $0.01/10^6$  or  $10^{-8}$  to have a control of 1% of a false-positive

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# Population Stratification

When population being sampled actually consists of several distinct subpopulations we have lumped together, marker alleles may provide information as to which group an individual belongs. If there are other risk factors in a group, this can create a false association btw marker and trait

Example. The *Gm* marker was thought (for biological reasons) to be an excellent candidate gene for diabetes in the high-risk population of Pima Indians in the American Southwest. Initially a very strong association was observed:

<i>Gm</i> <sup>+</sup>	Total	% with diabetes
Present	293	8%
Absent	4,627	29%

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<i>Gm</i> <sup>+</sup>	Total	% with diabetes
Present	293	8%
Absent	4,627	29%

Problem: freq(*Gm*<sup>+</sup>) in Caucasians (lower-risk diabetes Population) is 67%, *Gm*<sup>+</sup> rare in full-blooded Pima

The association was re-examined in a population of Pima that were 7/8th (or more) full heritage:

<i>Gm</i> <sup>+</sup>	Total	% with diabetes
Present	17	59%
Absent	1,764	60%

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# Linkage vs. Association

The distinction between linkage and association is subtle, yet critical

Marker allele M is **associated** with the trait if  
 $\text{Cov}(M, y) \neq 0$

While such associations can arise via linkage, they can also arise via population structure.

Thus, association DOES NOT imply linkage, and linkage is not sufficient for association

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## Accounting for population structure

- Three classes of approaches proposed
  - 1) Attempts to correct for common pop structure signal (**regression/PC methods**)
  - 2) Attempts to first assign individuals into subpopulations and then perform association mapping in each set (**Structure**)
  - 3) **Mixed models** that use all of the marker information (Tassel, EMMA, many others)
    - These can also account for cryptic relatedness in the data set, which also causes false-positives.

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# Regression Approaches

One approach to control for structure is simply to include a number of markers, outside of the SNP of interest, chosen because they are expected to vary over any subpopulations

How might you choose these in a sample? Try those markers (read STRs) that show the largest departure from Hardy-Weinberg, as this is expected in markers that vary the most over subpopulations.

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Indicator (0 / 1) Variable  
for SNP genotype k. Typically  
 $k = 3$ , i.e. AA, Aa aa

$$y = \mu + \sum_{k=1}^n \beta_k M_k + \sum_{j=1}^m \gamma_j b_j + e$$

↑  
SNP marker under consideration

Significant  $\beta$  indicates marker-trait association

m unlinked markers that vary across subpopulations.  
 $b_j$  = marker genotype indicator variable

Variations on this theme (**eigenstrat**) --- use all of the marker information to extract a set of significant PCs, which are then included in the model as cofactors

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# Structured Association Mapping

Pritchard and Rosenberg (1999) proposed **Structured Association Mapping**, wherein one assumes k subpopulations (each in Hardy-Weinberg).

Given a large number of markers, one then attempts to assign individuals to groups using an MCMC Bayesian classifier

Once individuals assigned to groups, association mapping without any correction can occur in each group.

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# Mixed-model approaches

- Mixed models use marker data to
  - Account for population structure
  - Account for cryptic relatedness
- Three general approaches:
  - Treat a single SNP as fixed
    - TASSLE, EMMA
  - Treat a single SNP as random
    - General pedigree method
  - Fit all of the SNPs at once
    - GBLUP

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# Structure plus Kinship Methods

Association mapping in plants offer occurs by first taking a large collection of lines, some closely related, others more distantly related. Thus, in addition to this collection being a series of subpopulations (derivatives from a number of founding lines), there can also be additional structure within each subpopulation (groups of more closely related lines within any particular lineage).

$$Y = X\beta + Sa + Qv + Zu + e$$

Fixed effects in blue, random effects in red

This is a mixed-model approach. The program TASSEL runs this model.

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## Q-K method

$$Y = X\beta + Sa + Qv + Zu + e$$

$\beta$  = vector of fixed effects

$a$  = SNP effects

$v$  = vector of subpopulation effects (STRUCTURE)

$Q_{ij}$  = Prob(individual i in group j). Determined from STRUCTURE output

$u$  = shared polygenic effects due to kinship.

$Cov(u) = \text{var}(A)^*A$ , where the relationship matrix

$A$  estimated from marker data matrix  $K$ , also called a GRM - a genomic relationship matrix

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# Which markers to include in K?

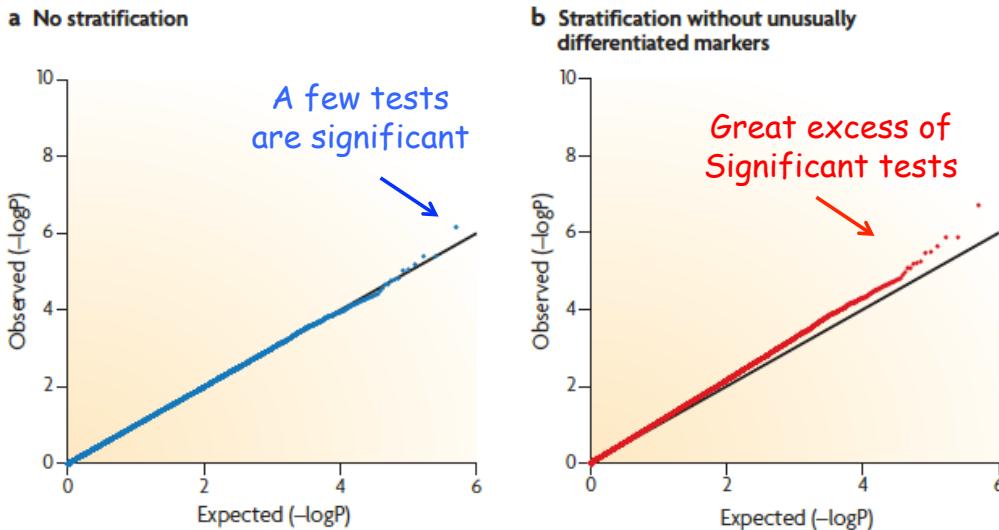
- Best approach is to leave out the marker being tested (and any in LD with it) when construction the genomic relationship matrix
  - **LOCO approach** - leave out one chromosome (which the tested marker is linked to)
- Best approach seems to be to use most of the markers
- Other mixed-model approaches along these lines

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## P – P plots

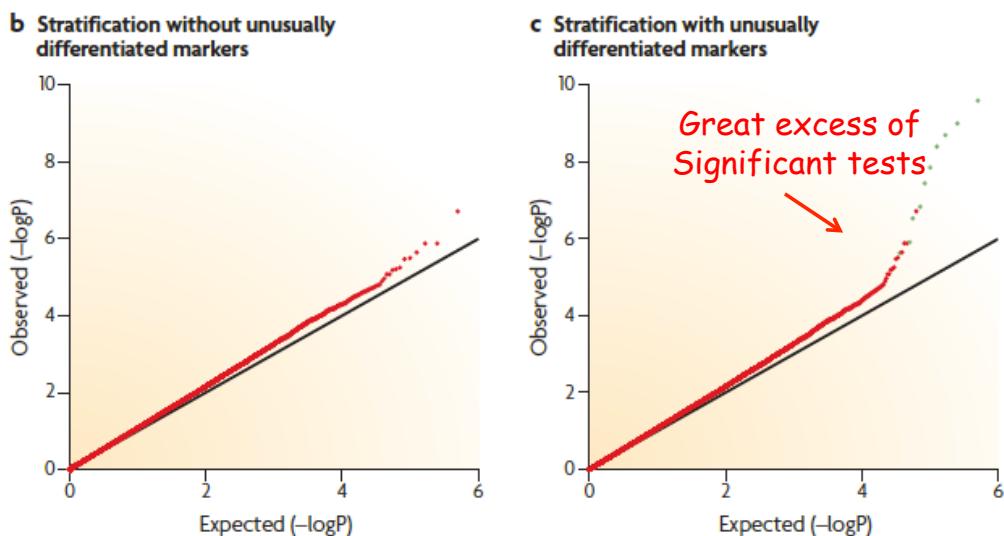
- Another powerful diagnostic tool is the **p-p plot**.
- If all tests are drawn from the null, then the distribution of p values should be uniform.
  - There should be a slight excess of tests with very low p indicating true positives
- This gives a straight line of a log-log plot of observed (seen) and expected (uniform) p values with a slight rise near small values
  - If the fraction of true positives is high (i.e., many sites influence the trait), this also bends the p-p plot

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Price et al. 2010 Nat Rev Gene 11: 459

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As with using  $\lambda$ , one should construct p-p following some approach to correct for structure & relatedness to see if they look unusual.

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## GBLUP

- The Q-K method tests SNPs one at a time, treating them as fixed effects
- The general pedigree method (slides 24-26) also tests one marker at a time, treating them as random effects
- Genomic selection can be thought as estimating all of the SNP effects at once and hence can also be used for GWAS

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## BLUP, GBLUP, and GWAS

- Pedigree information gives EXPECTED value of shared sites (i.e.,  $\frac{1}{2}$  for full-sibs)
  - A matrix in BLUP
  - The actual **realization** of the fraction of shared genes for a particular pair of relatives can be rather different, due to sampling variance in segregation of alleles
  - GRM (or K or marker matrix M)
  - Hence "identical" relatives can differ significantly in fraction of shared regions
  - Dense marker information can account for this

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# The general setting

- Suppose we have **n measured individuals** (the  $n \times 1$  vector  $\mathbf{y}$  of trait values)
- The  $n \times n$  **relationship matrix  $A$**  gives the relatedness among the sampled individuals, where the elements of  $A$  are obtained from the pedigree of measured individuals
- We may also have  $p (\gg n)$  SNPs per individual, where the  $n \times p$  **marker information matrix  $M$**  contains the marker data, where  $M_{ij} = \text{score for SNP } j \text{ (i.e., 0 for 00, 1 for 10, 2 for 11) in individual } i$ .

## Covariance structure of random effects

- A critical element specifying the mixed model is the covariance structure (matrix) of the vector  $\mathbf{u}$  of random effects
- Standard form is that  $\text{Cov}(\mathbf{u}) = \text{variance component} * \text{matrix of known constants}$ 
  - This is the case for pedigree data, where  $\mathbf{u}$  is typically the vector of breeding values, and the pedigree defines a **relationship matrix  $A$** , with  $\text{Cov}(\mathbf{u}) = \text{Var}(A) * \mathbf{A}$ , the additive variance times the relationship matrix
  - With marker data, the covariance of random effects are functions of the marker information matrix  $M$ .
    - If  $\mathbf{u}$  is the vector of  $p$  marker effects, then  $\text{Cov}(\mathbf{u}) = \text{Var}(m) * M^T M$ , the marker variance times the covariance structure of the markers.

$$\mathbf{Y} = \mathbf{X}\beta + \mathbf{Z}\mathbf{u} + \mathbf{e}$$

Pedigree-based BV estimation: (BLUP)

$\mathbf{u}_{nx1}$  = vector of BVs,  $\text{Cov}(\mathbf{u}) = \text{Var}(A) \mathbf{A}_{nxn}$

Marker-based BV estimation: (GBLUP)

$\mathbf{u}_{nx1}$  = vector of BVs,  $\text{Cov}(\mathbf{u}) = \text{Var}(m) \mathbf{M}^T \mathbf{M}$  ( $n \times n$ )

GWAS:  $\mathbf{u}_{px1}$  = vector of marker effects,  
 $\text{Cov}(\mathbf{u}) = \text{Var}(m) \mathbf{M} \mathbf{M}^T$  ( $p \times p$ )

Genomic selection: predicted vector of breeding values from marker effects,  $\text{GBV}_{nx1} = \mathbf{M}_{nxp} \mathbf{u}_{px1}$ .  
Note that  $\text{Cov}(\text{GBV}) = \text{Var}(m) \mathbf{M}^T \mathbf{M}$  ( $n \times n$ )

Lots of variations of these general ideas by adding additional assumptions on covariance structure.

## Association mapping (cont)

Q/q is the polymorphic site contributing to trait variation, M/m alleles (at a SNP) used as a marker

Let p be the frequency of M, and assume that Q only resides on the M background (**complete disequilibrium**)

Haplotype	Frequency	effect
QM	rp	a
qM	(1-r)p	0
qm	1-p	0

Halotype	Frequency	effect	
QM	rp	a	Effect of m = 0
qM	(1-r)p	0	Effect of M = ar
qm	1-p	0	

Genetic variation associated with Q =  $2(rp)(1-rp)a^2$   
 $\sim 2rpa^2$  when Q rare. Hence, little power if Q rare

Genetic variation associated with marker M is  
 $2p(1-p)(ar)^2 \sim 2pa^2r^2$

Ratio of marker/true effect variance is  $\sim r$

Hence, if Q rare within the A class, even less power, as M only captures a fraction of the associated QTL.

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## Common variants

- Association mapping is only powerful for common variants
  - freq(Q) moderate
  - freq (r) of Q within M haplotypes modest to large
- Large effect alleles ( $a$  large) can leave small signals.
- The fraction of the actual variance accounted for by the markers is no greater than  $\sim \text{ave}(r)$ , the average frequency of Q within a haplotype class
- Hence, don't expect to capture all of  $\text{Var}(A)$  with markers, esp. when QTL alleles are rare but markers are common (e.g. common SNPs,  $p > 0.05$ )
- Low power to detect  $G \times G$ ,  $G \times E$  interactions

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"How wonderful that we have met with a paradox. Now we have some hope of making progress" -- Neils Bohr



The case of the missing heritability

Infamous figure from *Nature* on the angst of human geneticists over the finding that all of their discovered SNPs still accounted for only a fraction of relative-based heritability estimates of human disease. 51

## The "missing heritability" pseudo paradox

- A number of GWAS workers noted that the sum of their significant marker variances was much less (typically 10%) than the additive variance estimated from biometrical methods
- The "missing heritability" problem was birthed from this observation.
- Not a paradox at all
  - **Low power** means small effect (i.e. variance) sites are unlikely to be called as significant, esp. given the high stringency associated with control of false positives over tens of thousands of tests
  - Further, even if all markers are detected, only a fraction  $\sim r$  (the frequency of the causative site within a marker haplotype class) of the underlying variance is accounted for.

# Models with multiple random effects: Repeated Measures and Maternal effects

Bruce Walsh lecture notes  
SISG -Mixed Model Course  
Seattle, 16 - 18 July 2014

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Often there are several vectors of random effects

- Repeatability models
  - Multiple measures
- Common family effects
  - Cleaning up residual covariance structure
- Maternal effects models
  - Maternal effect has a genetic (i.e., breeding value) component

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# Multiple random effects

$$\mathbf{y} = \mathbf{X}\beta + \mathbf{Z}\mathbf{a} + \mathbf{W}\mathbf{u} + \mathbf{e}$$

$\mathbf{y}$  is a  $n \times 1$  vector of observations

$\beta$  is a  $q \times 1$  vector of fixed effects

$\mathbf{a}$  is a  $p \times 1$  vector of random effects

$\mathbf{u}$  is a  $m \times 1$  vector of random effects

$\mathbf{X}$  is  $n \times q$ ,  $\mathbf{Z}$  is  $n \times p$ ,  $\mathbf{W}$  is  $n \times m$

$\mathbf{y}, \mathbf{X}, \mathbf{Z}, \mathbf{W}$  observed.  $\beta, \mathbf{a}, \mathbf{u}, \mathbf{e}$  to be estimated

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## Covariance structure

$$\mathbf{y} = \mathbf{X}\beta + \mathbf{Z}\mathbf{a} + \mathbf{W}\mathbf{u} + \mathbf{e}$$

*Defining the covariance structure key in any mixed-model*

Suppose  $\mathbf{e} \sim (0, \sigma_e^2 \mathbf{I})$ ,  $\mathbf{u} \sim (0, \sigma_u^2 \mathbf{I})$ ,  $\mathbf{a} \sim (0, \sigma_A^2 \mathbf{A})$ ,  
as with breeding values

These covariances matrices are still not sufficient, as we have yet to give describe the relationship between  $\mathbf{e}$ ,  $\mathbf{a}$ , and  $\mathbf{u}$ . If they are independent:

$$\begin{pmatrix} \mathbf{a} \\ \mathbf{u} \\ \mathbf{e} \end{pmatrix} \sim \begin{pmatrix} 0 \\ 0 \\ 0 \end{pmatrix}, \begin{pmatrix} \sigma_A^2 \cdot \mathbf{A} & 0 & 0 \\ 0 & \sigma_u^2 \cdot \mathbf{I} & 0 \\ 0 & 0 & \sigma_e^2 \cdot \mathbf{I} \end{pmatrix}$$

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$$\mathbf{y} = \mathbf{X}\beta + \mathbf{Z}\alpha + \mathbf{W}\mathbf{u} + \mathbf{e} \quad \begin{pmatrix} \mathbf{a} \\ \mathbf{u} \\ \mathbf{e} \end{pmatrix} \sim \begin{pmatrix} \mathbf{0} \\ \mathbf{0} \\ \mathbf{0} \end{pmatrix}, \begin{pmatrix} \sigma_A^2 \cdot \mathbf{A} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \sigma_u^2 \cdot \mathbf{I} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \sigma_e^2 \cdot \mathbf{I} \end{pmatrix}$$

Covariance matrix for the vector of observations  $\mathbf{y}$

$$\text{Var}(\mathbf{y}) = \mathbf{V} = \mathbf{Z}\mathbf{A}\mathbf{Z}^T\sigma_A^2 + \mathbf{W}\mathbf{W}^T\sigma_u^2 + \mathbf{I}\sigma_e^2$$

Note that if we ignored the second vector  $\mathbf{u}$  of random effects, and assumed  $\mathbf{y} = \mathbf{X}\beta + \mathbf{Z}\alpha + \mathbf{e}^*$ , then  $\mathbf{e}^* = \mathbf{W}\mathbf{u} + \mathbf{e}$ , with  $\text{Var}(\mathbf{e}^*) = \sigma_e^2 \mathbf{I} + \sigma_u^2 \mathbf{W}\mathbf{W}^T$

Consequence of ignoring random effects is that these are incorporated into the residuals, potentially compromising its covariance structure

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## Mixed-model Equations

$$\begin{pmatrix} \mathbf{X}^T \mathbf{X} & \mathbf{X}^T \mathbf{Z} & \mathbf{X}^T \mathbf{W} \\ \mathbf{Z}^T \mathbf{X} & \mathbf{Z}^T \mathbf{Z} + \lambda_A \mathbf{A}^{-1} & \mathbf{Z}^T \mathbf{W} \\ \mathbf{W}^T \mathbf{X} & \mathbf{W}^T \mathbf{Z} & \mathbf{W}^T \mathbf{W} + \lambda_u \mathbf{I} \end{pmatrix} \begin{pmatrix} \hat{\beta} \\ \hat{\alpha} \\ \hat{\mathbf{u}} \end{pmatrix} = \begin{pmatrix} \mathbf{X}^T \mathbf{y} \\ \mathbf{Z}^T \mathbf{y} \\ \mathbf{W}^T \mathbf{y} \end{pmatrix}$$

where

$$\lambda_A = \frac{\sigma_e^2}{\sigma_A^2} \quad \text{and} \quad \lambda_u = \frac{\sigma_e^2}{\sigma_u^2}$$

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# The repeatability model

- Often, multiple measurements (aka "records") are collected on the same individual
- Such a record for individual k has three components
  - Breeding value  $a_k$
  - Common (permanent) environmental value  $p_k$
  - Residual value for ith observation  $e_{ki}$
- Resulting observation is thus
  - $Z_{ki} = \mu + a_k + p_k + e_{ki}$
- The repeatability of a trait is  $r = (\sigma_A^2 + \sigma_p^2)/\sigma_z^2$
- Resulting variance of the residuals is  $\sigma_e^2 = (1-r) \sigma_z^2$

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## Resulting mixed model

$$\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}\mathbf{a} + \mathbf{Z}\mathbf{p} + \mathbf{e}$$

$$\begin{pmatrix} \mathbf{a} \\ \mathbf{p} \\ \mathbf{e} \end{pmatrix} \sim \begin{pmatrix} \mathbf{0} \\ \mathbf{0} \\ \mathbf{0} \end{pmatrix}, \begin{pmatrix} \sigma_A^2 \cdot \mathbf{A} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \sigma_p^2 \cdot \mathbf{I} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \sigma_e^2 \cdot \mathbf{I} \end{pmatrix}$$

Notice that we could also write this model as

$$\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}(\mathbf{a} + \mathbf{p}) + \mathbf{e} = \mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}\mathbf{v} + \mathbf{e}, \mathbf{v} = \mathbf{a} + \mathbf{p}$$

In class question: Why can we obtain separate estimates of  $\mathbf{a}$  and  $\mathbf{p}$ ?

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The careful reader might notice that the two vectors of random effects, the breeding values  $\mathbf{a}$  and permanent environment effects  $\mathbf{p}$ , enter the model as  $\mathbf{Z}\mathbf{a}$  and  $\mathbf{Z}\mathbf{p}$ , respectively. Why then do we simply not combine these, e.g.,  $\mathbf{Z}\mathbf{u}$  where  $\mathbf{u} = \mathbf{a} + \mathbf{p}$ ? The reason we cannot do this (and indeed the reason we can estimate  $\mathbf{a}$  and  $\mathbf{p}$  separately!) is that  $\mathbf{a}$  and  $\mathbf{p}$  have *different covariance structures*,  $\sigma_A^2 \mathbf{A}$  versus  $\sigma_p^2 \mathbf{I}$ . Thus, we assume that permanent environment effects are uncorrelated across individuals and are homoscedastic. On the other hand, breeding values generate covariances in relatives. Again, the critical importance of the covariance matrix to a mixed model analysis is apparent.

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## The incident matrix $\mathbf{Z}$

Suppose we have a total of 7 observations/records, with 3 measures from individual 1, 2 from individual 2, and 2 from individual 3. Then:

$$\mathbf{y} = \begin{pmatrix} y_{11} \\ y_{12} \\ y_{13} \\ y_{21} \\ y_{22} \\ y_{31} \\ y_{32} \end{pmatrix}, \quad \mathbf{Z} = \begin{pmatrix} 1 & 0 & 0 \\ 1 & 0 & 0 \\ 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \\ 0 & 0 & 1 \end{pmatrix}, \quad \mathbf{a} = \begin{pmatrix} A_1 \\ A_2 \\ A_3 \end{pmatrix}, \quad \mathbf{p} = \begin{pmatrix} p_1 \\ p_2 \\ p_3 \end{pmatrix}$$

Why? Matrix multiplication. Consider  $y_{21}$ .

$$y_{21} = \mu + A_2 + p_2 + e_{21}$$

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# Consequences of ignoring p

- Suppose we ignored the permanent environment effects and assumed the model  $\mathbf{y} = \mathbf{X}\beta + \mathbf{Z}\mathbf{a} + \mathbf{e}^*$ 
  - Then  $\mathbf{e}^* = \mathbf{Z}\mathbf{p} + \mathbf{e}$ ,
  - $\text{Var}(\mathbf{e}^*) = \sigma_e^2 \mathbf{I} + \sigma_p^2 \mathbf{Z}\mathbf{Z}^\top$
- Assuming that  $\text{Var}(\mathbf{e}^*) = \sigma_e^2 \mathbf{I}$  gives an incorrect model
- We could either
  - use  $\mathbf{y} = \mathbf{X}\beta + \mathbf{Z}\mathbf{a} + \mathbf{e}^*$  with the correct error structure (covariance) for  $\mathbf{e}^* = \sigma_e^2 \mathbf{I} + \sigma_p^2 \mathbf{Z}\mathbf{Z}^\top$
  - Or use  $\mathbf{y} = \mathbf{X}\beta + \mathbf{Z}\mathbf{a} + \mathbf{Z}\mathbf{p} + \mathbf{e}$ , where  $\mathbf{e} = \sigma_e^2 \mathbf{I}$

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The repeatability model was used by Estany et al. (1989) to examined the selection response for litter size in rabbits. Their model assumed two groups of fixed effects,  $d_t$  the year-season (environmental) effect which had 22 levels in this experiment and the reproductive state  $l_i$  of the doe ( $l$  has three levels:  $l_1$  for primiparous does,  $l_2$  for lactating does, and  $l_3$  for non-primaparous and non-lactating does). Since only two of these  $l_x$  factors are estimable,  $l_1$  was assigned a value zero. Their model had three random effects,  $a_k$  and  $p_k$  for the additive genetic and permanent environmental effect of the  $k$ th doe, and the residual  $e$ , giving the overall model as

$$y_{tkli} = \mu + l_i + d_t + a_k + p_k + e_{tkli}$$

where  $y_{tkli}$  denotes the litter size for the  $\ell$ th litter of doe  $k$  in reproductive state  $i$  in season-year  $t$ .

In matrix form, the mixed-model becomes

$$\mathbf{y} = \mathbf{X}\beta + \mathbf{Z}\mathbf{a} + \mathbf{Z}\mathbf{p} + \mathbf{e}$$

where  $\mathbf{a}$  and  $\mathbf{p}$  are  $n \times 1$  vectors corresponding to the  $n$  does,  $\text{Var}(\mathbf{a}) = \sigma_A^2 \mathbf{A}$ ,  $\text{Var}(\mathbf{p}) = \sigma_p^2 \mathbf{I}$ , and  $\text{Var}(\mathbf{e}) = \sigma_e^2 \mathbf{I}$ .  $\mathbf{X}$  and  $\mathbf{Z}$  are incident matrices, and the vector of fixed effects is

$$\beta = \begin{pmatrix} \mu \\ l_1 \\ l_2 \\ d_1 \\ \vdots \\ d_{22} \end{pmatrix}$$

## Resulting mixed-model equations

$$\begin{pmatrix} \mathbf{X}^T \mathbf{X} & \mathbf{X}^T \mathbf{Z} & \mathbf{X}^T \mathbf{Z} \\ \mathbf{Z}^T \mathbf{X} & \mathbf{Z}^T \mathbf{Z} + \lambda_A \mathbf{A}^{-1} & \mathbf{Z}^T \mathbf{Z} \\ \mathbf{Z}^T \mathbf{X} & \mathbf{Z}^T \mathbf{Z} & \mathbf{Z}^T \mathbf{Z} + \lambda_u \mathbf{I} \end{pmatrix} \begin{pmatrix} \hat{\boldsymbol{\beta}} \\ \hat{\mathbf{a}} \\ \hat{\mathbf{p}} \end{pmatrix} = \begin{pmatrix} \mathbf{X}^T \mathbf{y} \\ \mathbf{Z}^T \mathbf{y} \\ \mathbf{Z}^T \mathbf{y} \end{pmatrix}$$

where

$$\lambda_A = \frac{\sigma_e^2}{\sigma_A^2} = \frac{1-r}{h^2} \quad \text{and} \quad \lambda_u = \frac{\sigma_e^2}{\sigma_p^2} = \frac{1-r}{r-h^2}$$

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## Common family effects

- Sibs in the same family also share a common environment
  - $\text{Cov}(\text{full sibs}) = \sigma_A^2/2 + \sigma_D^2/4 + \sigma_{ce}^2$
- Hence, if the model assumes  $\mathbf{y}_i = \mu + \mathbf{a}_i + \mathbf{c}_i + \mathbf{e}_i$ , with  $\mathbf{a} \sim 0$ ,  $\sigma_A^2 \mathbf{A}$ ,  $\mathbf{c} \sim 0$ ,  $\sigma_{cf}^2 \mathbf{I}$ . If there are records for different sibs from the same family,  $\text{Var}(\mathbf{e})$  is no longer  $\sigma_e^2 \mathbf{I}$
- $\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}\mathbf{a} + \mathbf{W}\mathbf{c} + \mathbf{e}$
- Again, if common family effect ignored (we assume  $\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}\mathbf{a} + \mathbf{e}^*$ ) the error structure is  $\mathbf{e}^* = \sigma_e^2 \mathbf{I} + \sigma_{cf}^2 \mathbf{W}\mathbf{W}^T$ 
  - Where  $\sigma_{cf}^2 = \sigma_D^2/4 + \sigma_{ce}^2$
  - The common family effect may contain both environment and non-additive genetic components

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Example: Measure 7 individuals, first five are from family one, last two from family 2

$$\mathbf{y} = \mathbf{X}\beta + \mathbf{Z}\mathbf{a} + \mathbf{W}\mathbf{c} + \mathbf{e}$$

$$\mathbf{y} = \begin{pmatrix} y_{11} \\ y_2 \\ y_3 \\ y_4 \\ y_5 \\ y_6 \\ y_7 \end{pmatrix}, \quad \mathbf{Z} = \mathbf{I}, \quad \mathbf{a} = \begin{pmatrix} A_1 \\ A_2 \\ A_3 \\ A_4 \\ A_5 \\ A_6 \\ A_7 \end{pmatrix}, \quad \mathbf{W} = \begin{pmatrix} 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 0 & 1 \\ 0 & 1 \end{pmatrix}, \quad \mathbf{c} = \begin{pmatrix} c_1 \\ c_2 \end{pmatrix}$$

$\mathbf{Z} = \mathbf{I}$  as every individual has a single record.  
 If there are missing and/or repeated records,  
 $\mathbf{Z}$  does not have this simple structure

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$$\mathbf{y} = \mathbf{X}\beta + \mathbf{Z}\mathbf{a} + \mathbf{W}\mathbf{c} + \mathbf{e}$$

$$\mathbf{y} = \begin{pmatrix} y_{11} \\ y_2 \\ y_3 \\ y_4 \\ y_5 \\ y_6 \\ y_7 \end{pmatrix}, \quad \mathbf{Z} = \mathbf{I}, \quad \mathbf{a} = \begin{pmatrix} A_1 \\ A_2 \\ A_3 \\ A_4 \\ A_5 \\ A_6 \\ A_7 \end{pmatrix}, \quad \mathbf{W} = \begin{pmatrix} 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 0 & 1 \\ 0 & 1 \end{pmatrix}, \quad \mathbf{c} = \begin{pmatrix} c_1 \\ c_2 \end{pmatrix}$$

Again, matrix multiplication gives us the form of the  $\mathbf{Z}$  and  $\mathbf{W}$  matrices. Consider  $y_6$ :

$$y_6 = \mu + A_6 + c_2 + e_6$$

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# Maternal effects with genetic components

- The phenotype of an offspring can be influenced by its mother beyond her genetic contribution
- For example, two offspring with identical genotypes will still show potentially significant differences in size if they receive different amounts of milk from their mothers
- Such **maternal effects** can be quite important
- While we have just discussed models with common family effects, these are potentially rather different than maternal effects models
  - Common family environmental effects are assumed not to be inherited across generations.

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- Consider milk yield. The heritability for this trait is around 30% and the milk yield of the mother has a significant impact on the weight of her offspring
- Offspring with high breeding values for milk will tend to have daughters with above-average milk yield, and hence above-average maternal effects
- The value of an offspring can be considered to consist of two components
  - A direct effect (intrinsic breeding value)
  - A maternal contribution

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Phenotypic value = direct value + maternal value

$$P_z = P_d + P_m$$

```

    graph TD
      Pz[P_z] --> Pd[P_d]
      Pz --> Pm[P_m]
      Pd --- Observable[Observable]
      Pm --- Latent[Latent (unseen) values]
  
```

Both of the latent values can be further decomposed into breeding plus residual (environmental + non-additive genetic) values

$$P_d = \mu + A_d + E_d, \quad P_m = \mu + A_m + E_m,$$

The direct breeding value  $A_d$  appears in the phenotype of its carrier

The maternal breeding value  $A_m$  DOES NOT appear in the phenotype of its carrier, but rather in the phenotype of her offspring

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## Direct vs. maternal breeding values

- The direct and maternal contributions are best thought of as two separate, but potentially correlated traits.
  - Hence, we need to consider  $\sigma(A_d, A_m)$  in addition to  $\sigma^2(A_d)$  and  $\sigma^2(A_m)$ . This changes the form of the mixed-model equations
- The direct BV ( $A_d$ ) is expressed in the individual carrying it
- The maternal BV ( $A_m$ ) is only expressed in the offspring trait value (and only mom's  $A_m$  appears)

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## Covariance structure

$$\begin{pmatrix} \mathbf{a}_d \\ \mathbf{a}_m \end{pmatrix} \sim \begin{pmatrix} \mathbf{0} \\ \mathbf{0} \end{pmatrix}, \begin{pmatrix} \sigma^2(A_d) \mathbf{A} & \sigma(A_d, A_m) \mathbf{A} \\ \sigma(A_d, A_m) \mathbf{A} & \sigma^2(A_m) \mathbf{A} \end{pmatrix}$$

This is often written using the Kronecker (or direct) product:

$$\mathbf{A} \otimes \mathbf{B} = \begin{pmatrix} a_{11} \mathbf{B} & \cdots & a_{1n} \mathbf{B} \\ \vdots & \ddots & \vdots \\ a_{m1} \mathbf{B} & \cdots & a_{mn} \mathbf{B} \end{pmatrix}$$

Giving

$$\begin{pmatrix} \mathbf{a}_d \\ \mathbf{a}_m \end{pmatrix} \sim \begin{pmatrix} \mathbf{0} \\ \mathbf{0} \end{pmatrix}, \mathbf{G} \otimes \mathbf{A} \quad \mathbf{G} = \begin{pmatrix} \sigma^2(A_d) & \sigma(A_d, A_m) \\ \sigma(A_d, A_m) & \sigma^2(A_m) \end{pmatrix}$$

The mixed-model becomes

$$\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}_d \mathbf{a}_d + \mathbf{Z}_m \mathbf{a}_m + \mathbf{e}$$

↑  
Direct effects  
breeding values

↑  
Maternal effects  
breeding values

The error structure needs a little care, as the direct  $E_d$  and maternal  $E_m$  residual values can be correlated\*. Initially, we will assume  $\text{Var}(\mathbf{e}) \sim \sigma_e^2 \mathbf{I}$

\*See Bijma 2006 J. Anim. Sci. 84:800-806 for treatment of correlated environmental residuals under this model

The resulting mixed-model equations become

$$\begin{pmatrix} \mathbf{X}^T \mathbf{X} & \mathbf{X}^T \mathbf{Z}_d & \mathbf{X}^T \mathbf{Z}_s \\ \mathbf{Z}_d \mathbf{X}^T & \mathbf{Z}_d^T \mathbf{Z}_d + \lambda_1 \mathbf{A}^{-1} & \mathbf{Z}_d^T \mathbf{Z}_m + \lambda_2 \mathbf{A}^{-1} \\ \mathbf{Z}_m \mathbf{X}^T & \mathbf{Z}_m^T \mathbf{Z}_d + \lambda_2 \mathbf{A}^{-1} & \mathbf{Z}_m^T \mathbf{Z}_m + \lambda_3 \mathbf{A}^{-1} \end{pmatrix} \begin{pmatrix} \boldsymbol{\beta} \\ \mathbf{a}_d \\ \mathbf{a}_m \end{pmatrix} = \begin{pmatrix} \mathbf{X}^T \mathbf{y} \\ \mathbf{Z}_d^T \mathbf{y} \\ \mathbf{Z}_m^T \mathbf{y} \end{pmatrix}$$

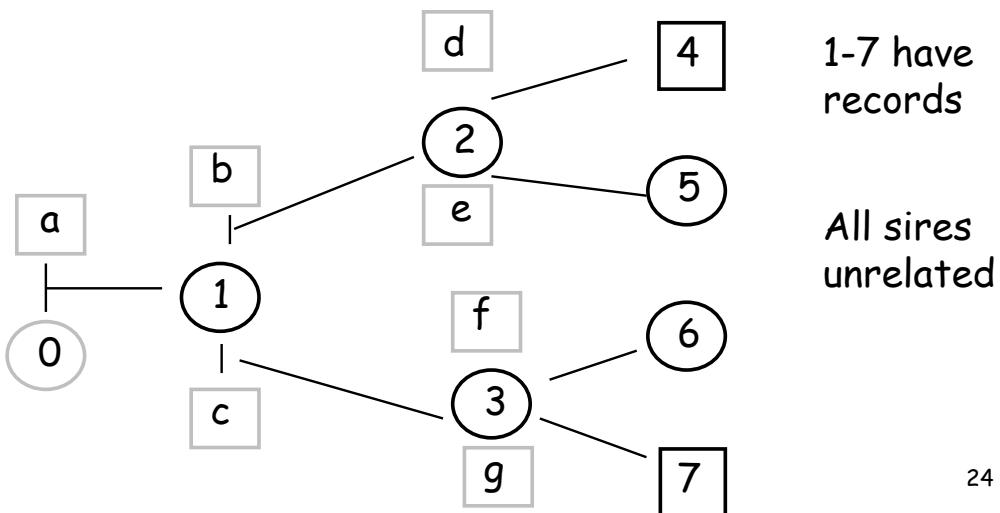
where the weights  $\lambda_i$  are related to elements in the inverse of  $\mathbf{G}$ , viz.,

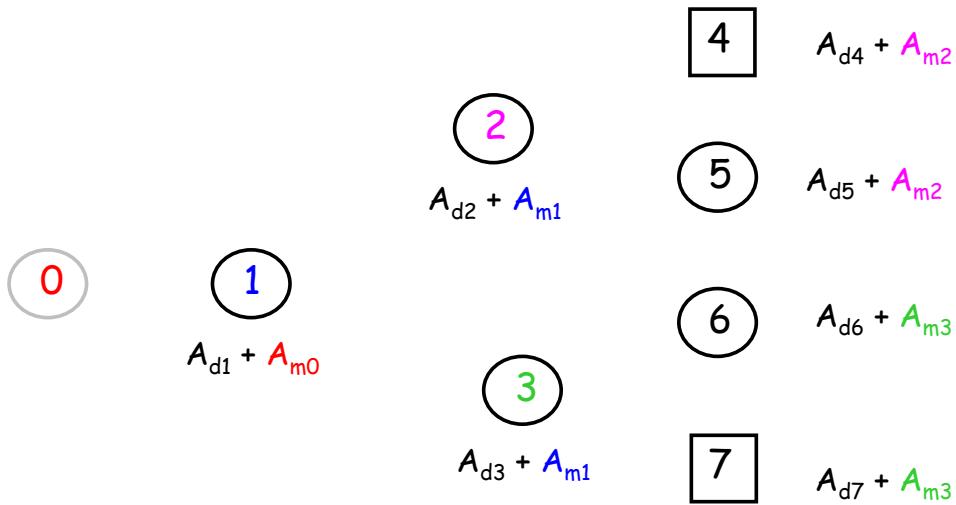
$$\begin{pmatrix} \lambda_1 & \lambda_2 \\ \lambda_2 & \lambda_3 \end{pmatrix} = \sigma_e^2 \mathbf{G}^{-1} = \sigma_e^2 \begin{pmatrix} \sigma^2(A_d) & \sigma(A_d, A_m) \\ \sigma(A_d, A_m) & \sigma^2(A_m) \end{pmatrix}^{-1}$$

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## Filling out the maternal effects incident matrix $\mathbf{Z}_m$

A little bookkeeping care is needed when filling out  $\mathbf{Z}_m$ , because the  $A_m$  associated with a record (measured individual) is that of their mother.





The observed values are  $y_1$  through  $y_7$ .  
 What we can estimate are  $A_{d1}$  through  $A_{d7}$ ,  
 $A_{m0}$  through  $A_{m3}$

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$$\mathbf{y} = \begin{pmatrix} y_1 \\ y_2 \\ y_3 \\ y_4 \\ y_5 \\ y_6 \\ y_7 \end{pmatrix}, \quad \mathbf{a}_d = \begin{pmatrix} A_{d,1} \\ A_{d,2} \\ A_{d,3} \\ A_{d,4} \\ A_{d,5} \\ A_{d,6} \\ A_{d,7} \end{pmatrix}, \quad \mathbf{Z}_d = \mathbf{I}, \quad \mathbf{a}_m = \begin{pmatrix} A_{m,0} \\ A_{m,1} \\ A_{m,2} \\ A_{m,3} \end{pmatrix}$$

Note that we estimate  $A_{m0}$  even though we don't have a record (observation) on her.

Since  $\mathbf{Z}_m \mathbf{a}_m$  must be a  $7 \times 1$  matrix,  $\mathbf{Z}_m$  is  $7 \times 4$  (as  $\mathbf{a}_m$  is  $4 \times 1$ )

Record 1 is associated with  $A_{m0}$

Records 2 and 3 are associated with  $A_{m1}$

Records 4 and 5 are associated with  $A_{m2}$

Records 6 and 7 are associated with  $A_{m3}$

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Record 1 is associated with  $A_{m0}$

Records 2 and 3 are associated with  $A_{m1}$

Records 4 and 5 are associated with  $A_{m2}$

Records 6 and 7 are associated with  $A_{m3}$

$$\mathbf{Z}_m = \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 1 \end{pmatrix}, \quad \text{as} \quad \mathbf{Z}_m \mathbf{a}_m = \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} A_{m,0} \\ A_{m,1} \\ A_{m,1} \\ A_{m,2} \\ A_{m,2} \\ A_{m,3} \\ A_{m,3} \end{pmatrix} = \begin{pmatrix} A_{m,0} \\ A_{m,1} \\ A_{m,1} \\ A_{m,2} \\ A_{m,2} \\ A_{m,3} \\ A_{m,3} \end{pmatrix}$$

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## What about $A_{m4}$ through $A_{m7}$ ?

Although we have records that only directly relate  $A_{m0}$  to  $A_{m3}$ , through the use of  $\mathbf{A}$  we can (in theory) also estimate the maternal breeding values for individuals 4 through 7. Note this includes the maternal BVs for the two males (5 & 7), as they can pass this onto their daughters.

$$\mathbf{Z}_m^* = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \end{pmatrix}, \quad \mathbf{a}_m^* = \begin{pmatrix} A_{m,0} \\ A_{m,1} \\ A_{m,2} \\ A_{m,3} \\ A_{m,4} \\ A_{m,5} \\ A_{m,6} \\ A_{m,7} \end{pmatrix}$$

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Note that

$$\mathbf{Z}_m^* \mathbf{a}_m^* = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \end{pmatrix} \begin{pmatrix} A_{m,0} \\ A_{m,1} \\ A_{m,2} \\ A_{m,3} \\ A_{m,4} \\ A_{m,5} \\ A_{m,6} \\ A_{m,7} \end{pmatrix} = \begin{pmatrix} A_{m,0} \\ A_{m,1} \\ A_{m,1} \\ A_{m,1} \\ A_{m,2} \\ A_{m,2} \\ A_{m,3} \\ A_{m,3} \end{pmatrix}$$

All this raises the question about what can, and cannot, be estimated from the data ( $\mathbf{y}$ ) and the design ( $\mathbf{Z}_m, \mathbf{Z}_d$ )?

First issue: Is the structure of the design such that we can estimate all of the variance components. This is the issue of **identifiability**

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## Estimability vs. Identifiability

### Details: Identifiability of Variance Components

Due to potential confounding of effects, any particular design might not allow for all variables of interest to be uniquely estimated. For the vector  $\beta$  of fixed effects, this is the concept of **estimability** (LW Chapter 26). For  $\mathbf{z} \sim (\mathbf{X}\beta, \mathbf{V})$ , the vector of fixed effects is estimable (all have unique values) if  $(\mathbf{X}^T \mathbf{V}^{-1} \mathbf{X})^{-1}$  exists. Otherwise, some of the fixed effects are confounded and cannot be separated by the design ( $\mathbf{X}$ ) being used. With (co)variance components (often called **dispersal parameters**), a similar concept, **identifiability**, also exists. If variance components are not identifiable in the design, then BLUPs for their associated vectors of random effects do not exist.

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Conditions for identifiability of REML estimates of (co)variance components are given by Rothenberg (1971), Jiang (1996), and Cantet and Cappa (2008). Before presenting these, we first review a few details about REML. Recall (LW Chapter 27) that REML estimates are those that maximize that part of the likelihood function that is independent of the fixed effects (this is often stated as being the **translation invariant** part). Let  $\mathbf{V}$  be the covariance matrix of  $\mathbf{z}$ , which is a function of its variance components. As detailed in LW Chapter 27, Harville (1977) shows that (if it exists) the transformation provided by the matrix

$$\mathbf{P} = \mathbf{V}^{-1} - \mathbf{V}^{-1} \mathbf{X} (\mathbf{X}^T \mathbf{V}^{-1} \mathbf{X})^{-1} \mathbf{X}^T \mathbf{V}^{-1} \quad (1a)$$

plays a critical role in REML estimates. That this matrix can remove fixed effects can be seen by noting that

$$\mathbf{P}\mathbf{z} = \mathbf{V}^{-1} (\mathbf{z} - \mathbf{X}\hat{\boldsymbol{\beta}}) \quad (1b)$$

yields a vector that is the data vector adjusted by the (estimated) fixed effects. Now consider covariance structures of the form

$$\mathbf{V} = \sum_{i=1}^n \mathbf{V}_i \theta_i \quad (2a)$$

where  $\mathbf{V}_i$  is a matrix of known constants and the  $\theta_i$  are unknown variances and covariances to be estimated.

The equations to maximize the likelihood over the restricted space (the REML estimates) are given by LW Equations 27.18 and 27.19, and are solved iteratively. These equations involve the **trace** (sum of the diagonal elements) of matrix products involving  $\mathbf{P}$  and the  $\mathbf{V}_i$ . Recall (LW Appendix 4) that for a vector  $\boldsymbol{\Theta}$  of  $n$  unknowns, the Fisher information matrix  $\mathbf{F}$  (the matrix of second partial derivatives of the likelihood with respect to the parameters) can be used to provide large-sample standard errors. The resulting  $n \times n$  information matrix for REML estimates of the unknown  $\theta_i$  in Equation 2a is

$$F_{ij} = \text{trace}(\mathbf{P}\mathbf{V}_i \mathbf{P}\mathbf{V}_j) \quad (2b)$$

Much in the same fashion that the existence of  $(\mathbf{X}^T \mathbf{V}^{-1} \mathbf{X})^{-1}$  informs us that all fixed effects are estimable in a given design, all variance components  $\theta_i$  are identifiable if all of the eigenvalues of  $\mathbf{F}$  are positive, that is, that  $\mathbf{F}$  is positive-definite (Rothenberg 1971, Jiang 1996). For the maternal effects mixed model, Equation 2a becomes

$$\mathbf{V} = \mathbf{V}_1 \sigma^2(A_d) + \mathbf{V}_2 \sigma(A_d, A_s) + \mathbf{V}_3 \sigma^2(A_s) + \mathbf{V}_4 \sigma_e^2 \quad (3a)$$

where

$$\mathbf{V}_1 = \mathbf{Z}_d \mathbf{A} \mathbf{Z}_d^T, \quad \mathbf{V}_2 = \left( \mathbf{Z}_d \mathbf{A} \mathbf{Z}_m^T + \mathbf{Z}_m \mathbf{A} \mathbf{Z}_d^T \right), \quad \mathbf{V}_3 = \mathbf{Z}_m \mathbf{A} \mathbf{Z}_s^T, \quad \mathbf{V}_4 = \mathbf{I} \quad (3b)$$

Substituting Equations 1a and 3b into Equation 2b fills out the  $\mathbf{F}$  matrix (which is only  $4 \times 4$  in this case given the four unknown variance components). For any particular design, the eigenvalues of this matrix can be computed to determine if the variance components are all identifiable.

## Second issue, connectivity

Even if the design is such that we can estimate all the genetic variances, whether we can estimate all of the  $\beta$ ,  $a_d$ , and  $a_m$  in the model depends on whether a unique inverse exists for the MME

$$\begin{pmatrix} \mathbf{X}^T \mathbf{X} & \mathbf{X}^T \mathbf{Z}_d & \mathbf{X}^T \mathbf{Z}_s \\ \mathbf{Z}_d \mathbf{X}^T & \mathbf{Z}_d^T \mathbf{Z}_d + \lambda_1 \mathbf{A}^{-1} & \mathbf{Z}_d^T \mathbf{Z}_m + \lambda_2 \mathbf{A}^{-1} \\ \mathbf{Z}_m \mathbf{X}^T & \mathbf{Z}_m^T \mathbf{Z}_d + \lambda_2 \mathbf{A}^{-1} & \mathbf{Z}_m^T \mathbf{Z}_m + \lambda_3 \mathbf{A}^{-1} \end{pmatrix} \begin{pmatrix} \beta \\ a_d \\ a_m \end{pmatrix} = \begin{pmatrix} \mathbf{X}^T \mathbf{y} \\ \mathbf{Z}_d^T \mathbf{y} \\ \mathbf{Z}_m^T \mathbf{y} \end{pmatrix}$$

Unique estimates of all the  $\beta$  require  $(\mathbf{X}^T \mathbf{V}^{-1} \mathbf{X})^{-1}$  exists

If  $(\mathbf{X}^T \mathbf{V}^{-1} \mathbf{X})^{-1}$  does not exist, a generalized inverse is used which can uniquely estimate k linear combinations of the  $\beta$  where k is the rank of  $\mathbf{X}^T \mathbf{V}^{-1} \mathbf{X}$

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Likewise, if the MME equation does not have an inverse (and this is not due to constraints on  $\beta$ ), then a generalized inverse can be used to estimate unique estimates of certain linear combinations of the  $a_d$  and  $a_m$ .

$$\begin{pmatrix} \mathbf{X}^T \mathbf{X} & \mathbf{X}^T \mathbf{Z}_d & \mathbf{X}^T \mathbf{Z}_s \\ \mathbf{Z}_d \mathbf{X}^T & \mathbf{Z}_d^T \mathbf{Z}_d + \lambda_1 \mathbf{A}^{-1} & \mathbf{Z}_d^T \mathbf{Z}_m + \lambda_2 \mathbf{A}^{-1} \\ \mathbf{Z}_m \mathbf{X}^T & \mathbf{Z}_m^T \mathbf{Z}_d + \lambda_2 \mathbf{A}^{-1} & \mathbf{Z}_m^T \mathbf{Z}_m + \lambda_3 \mathbf{A}^{-1} \end{pmatrix} \begin{pmatrix} \beta \\ a_d \\ a_m \end{pmatrix} = \begin{pmatrix} \mathbf{X}^T \mathbf{y} \\ \mathbf{Z}_d^T \mathbf{y} \\ \mathbf{Z}_m^T \mathbf{y} \end{pmatrix}$$

A key role in ensuring that unique estimates of  $a_d$  and  $a_m$  exist is played by the relationship matrix A. If individuals with records and individuals without records are sufficiently well connected (non-zero entries in A for their pair-wise relatedness), then we usually can estimate values of un-observed individuals (although their precision is another issue)

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## Correlated Residuals Common Environmental Effects

- Environmental effects common within a group partial between groups
  - Agronomy
    - Common fields among multiple fields



1

## Correlated Residuals Common Environmental Effects

- Animals
  - Multiple pens, cages, or locations
  - Shared maternal effects
    - Common litter

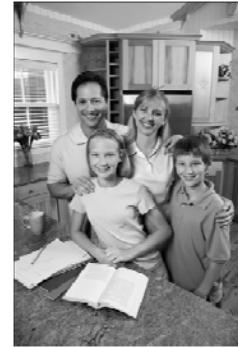


2

## Correlated Residuals Common Environmental Effects

### – Humans

- Shared family environment
  - Nutrition
  - Nurturing
  - Social economic factors



3

## Common Environmental Effects

- In humans, confounds genetic effects with social economic factors
- In plant or animal breeding, reduces response to selection
  - Common environmental effects are included with the phenotype
  - Errors in selection decisions

4

## Solution

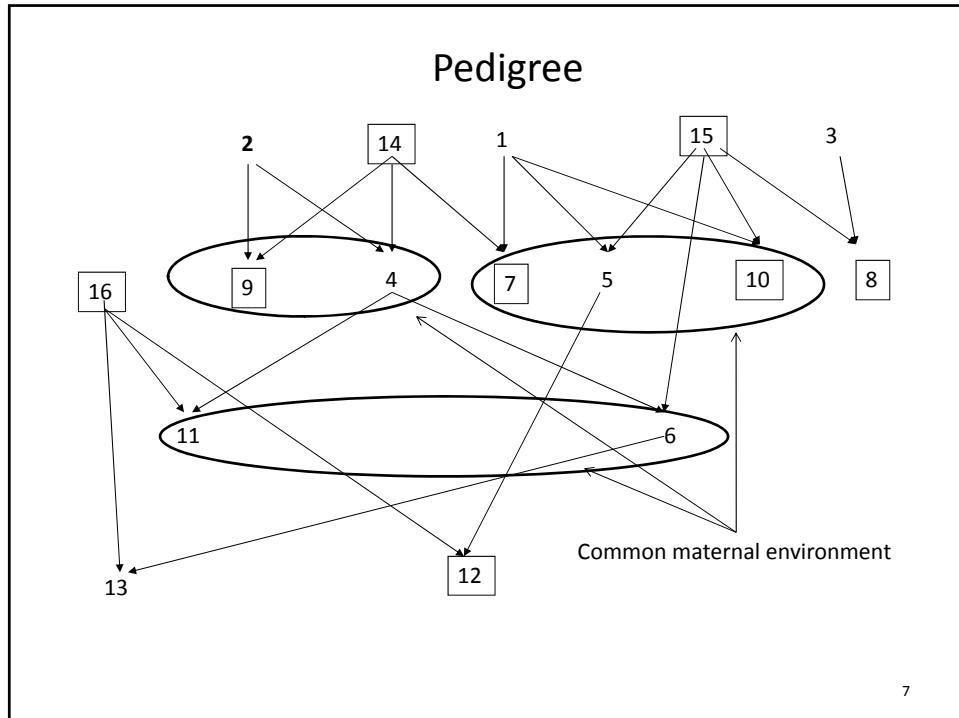
- Experimental design
  - Randomized Complete Block (RCB)
    - all treatments in all blocks
    - Best design
  - Randomized Incomplete Block
    - Incomplete block design messy
  - Not possible with human (no randomization) and most plant and animal breeding programs (not practical)
- Breeders in the past
  - Performed within and between family selection
  - Tried to adjust for herd/Y/S as fixed effects then solved for breeding values
  - Problem: best genetics confounded with herd (adjusting for fixed removed some genetic effects)
- Mixed models
  - Empirical Bayesian approach to estimate and adjust for the effect
    - First use of mixed models
    - recovery of inter-block information
    - Yates, 1939; Cox, 1958

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## Example 1

- 10 calves, 5 male and 5 female, from 3 sires and 6 dams, were sampled over 3 years and weaning weight recorded. Some dams were used more than once.
- Remove the fixed effects of year and sex and the random effect of common maternal environment. Then estimate the breeding values of all animals for weaning weight.

6

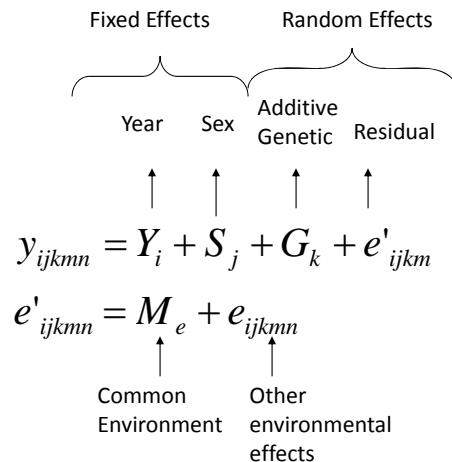


## Correlated Residual Example

Schaeffer Table 8.7

Animal	Sire	Dam	Year	Sex	Wean Wt
7	14	1	86	M	400
4	14	2	86	F	380
8	15	3	86	M	410
5	15	1	87	F	350
9	14	2	87	M	420
6	15	4	87	F	360
10	15	1	88	M	390
11	16	4	88	F	390
12	16	5	88	M	430
13	16	6	88	F	370

## Model solution 1



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## Variance-covariance solution 1

$$\mathbf{V} \begin{bmatrix} \mathbf{G} \\ \mathbf{e}' \end{bmatrix} = \begin{bmatrix} \mathbf{A}\sigma_G^2 & 0 \\ 0 & \mathbf{R}\sigma_{e'}^2 \end{bmatrix}$$

$$\sigma_{e'}^2 = \sigma_m^2 + \sigma_e^2$$

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## Correlated Residuals

Animals in a common group (pen, herd, or **mother**) share a common environmental effect. Let  $\rho$  be the correlation between residuals due to shared environment.

A covariance within groups is reflected in a between group variance  
Principle for estimating heritability via ANOVA (between and within sire variances)

$\rho$  is the intra-class environmental correlation

$$\rho = \frac{\sigma_b^2}{\sigma_b^2 + \sigma_e^2}$$

$$\mathbf{R} = (\sigma_b^2 + \sigma_e^2) \begin{bmatrix} 1 & \rho & \rho & \cdots & 0 & 0 & 0 \\ \rho & 1 & \rho & \cdots & 0 & 0 & 0 \\ \rho & \rho & 1 & \cdots & 0 & 0 & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots & \vdots \\ 0 & 0 & 0 & \cdots & 1 & \rho & \rho \\ 0 & 0 & 0 & \cdots & \rho & 1 & \rho \\ 0 & 0 & 0 & \cdots & \rho & \rho & 1 \end{bmatrix} = \begin{bmatrix} \sigma_b^2 + \sigma_e^2 & \sigma_b^2 & \sigma_b^2 & \cdots & 0 & 0 & 0 \\ \sigma_b^2 & \sigma_b^2 + \sigma_e^2 & \sigma_b^2 & \cdots & 0 & 0 & 0 \\ \sigma_b^2 & \sigma_b^2 & \sigma_b^2 + \sigma_e^2 & \cdots & 0 & 0 & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots & \vdots \\ 0 & 0 & 0 & \cdots & \sigma_b^2 + \sigma_e^2 & \sigma_b^2 & \sigma_b^2 \\ 0 & 0 & 0 & \cdots & \sigma_b^2 & \sigma_b^2 + \sigma_e^2 & \sigma_b^2 \\ 0 & 0 & 0 & \cdots & \sigma_b^2 & \sigma_b^2 & \sigma_b^2 + \sigma_e^2 \end{bmatrix}$$

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## Genetic Parameters

$$\mathbf{G} = \mathbf{A}\sigma_G^2$$

$$\sigma_G^2 = 2000$$

$$\sigma_{m_e}^2 = 500$$

$$\sigma_e^2 = 6500$$

$$\rho = \frac{500}{500 + 6500} = .0714$$

The shared environmental effect is small, but real

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Shared Maternal Environment			Environmental Correlation Matrix ( $R$ )									
An	Sire	Dam	animals 7, 5, 10 shared mother 1									
7	14	1	7	4	8	5	9	6	10	11	12	13
4	14	2	1	0	0	$\rho$	0	0	$\rho$	0	0	0
8	15	3	0	1	0	0	$\rho$	0	0	0	0	0
5	15	1	0	0	1	0	0	0	0	0	0	0
9	14	2	$\rho$	0	0	1	0	0	$\rho$	0	0	0
6	15	4	0	$\rho$	0	0	1	0	0	0	0	0
10	15	1	0	0	0	0	1	0	$\rho$	0	0	0
11	16	4	$\rho$	0	0	$\rho$	0	0	1	0	0	0
12	16	5	0	0	0	0	$\rho$	0	1	0	0	0
13	16	6	0	0	0	0	0	0	0	1	0	0
												$\sigma_e^2$

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MME Residual Correlation Structure

$$\mathbf{y} = \mathbf{X}\mathbf{b} + \mathbf{Z}\mathbf{u} + \mathbf{e}$$

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

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All animals have a genetic effect but only animals with a record contribute to the phenotype

Note that these animals did not have records and are missing

An	Sire	Dam
7	14	1
4	14	2
8	15	3
5	15	1
9	14	2
6	15	4
10	15	1
11	16	4
12	16	5
13	16	6

$$\mathbf{Z} = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \end{bmatrix}$$

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Year sex  
86 87 88 m

$$\mathbf{X} = \begin{bmatrix} 1 & 0 & 0 & 1 \\ 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 1 \\ 0 & 1 & 0 & 0 \\ 0 & 1 & 0 & 1 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 1 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 1 & 1 \\ 0 & 0 & 1 & 0 \end{bmatrix}$$

$$\mathbf{B} = \begin{bmatrix} b_1 \\ b_2 \\ b_3 \\ b_4 \end{bmatrix}$$

Herd  
Year  
Sex

$$\mathbf{Y} = \begin{bmatrix} 400 \\ 380 \\ 410 \\ 350 \\ 420 \\ 360 \\ 390 \\ 390 \\ 430 \\ 370 \end{bmatrix}$$

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## R code Example 6

```

Sig_m=500
Sig_e=6500
Sig_g=2000
m=Sig_m/(Sig_m+Sig_e)

Ainv=matrix(c(2.5,.5,1,0,0,0,-1,-1,0,0,-1,0,0,0,0,0,
Y=matrix(c(400,.5,2.5,0,1,0,0,-1,0,0,-1,0,0,-1,0,0,0,
380,1,0,2,0,0,0,0,-1,0,0,-1,0,0,0,0,0,
410,0,1,0,3,.5,0,0,.5,-1,-1,0,-1,-1,0,0,0,0,
350,0,0,0,.5,1.5,0,0,0,-1,0,0,0,0,0,0,0,0,
420,0,0,0,0,2.5,0,.5,0,.5,0,-1,-1,-1,0,0,0,0,
360,-1,-1,0,0,0,2,0,0,0,0,0,0,0,0,0,0,0,
390,-1,0,-1,.5,0,.5,0,3,0,0,0,-1,0,-1,0,0,
390,0,0,-1,-1,0,0,2,0,0,0,0,0,0,0,0,0,0,
430,0,-1,0,-1,0,.5,0,0,0,2.5,0,0,0,0,-1,0,
370),10,1);
X=matrix(c(1,0,0,1,0,-1,0,-1,0,0,0,0,0,0,0,-1,
1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,
1,0,0,1,0,0,0,-1,0,-1,0,0,0,0,0,2,0,0,
0,1,0,0,0,0,0,0,-1,0,0,0,-1,0,0,0,0,2,0,
0,1,0,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,2),16,16)

0,1,0,1,
0,1,0,0,
0,0,1,1,
0,0,1,0,
0,0,1,1,
0,0,1,0),
0,0,1,0),10,4,byrow = TRUE )

```

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```

Z= matrix(c
(0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0,
0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0,
0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0,
0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0,
0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0,
0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0,
0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0,
0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0,
0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0,
0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0,
0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1),
10,16,byrow=TRUE);

R=matrix(c(1, 0, 0, m, 0, 0, m, 0, 0, 0,
0, 1, 0, 0, m, 0, 0, 0, 0, 0, 0,
0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0,
m, 0, 0, 1, 0, 0, m, 0, 0, 0,
0, m, 0, 0, 1, 0, 0, 0, 0, 0,
0, 0, 0, 0, 1, 0, 0, m, 0, 0,
m, 0, 0, m, 0, 0, 1, 0, 0, 0,
0, 0, 0, 0, 0, m, 0, 1, 0, 0,
0, 0, 0, 0, 0, 0, 0, 1, 0, 0,
0, 0, 0, 0, 0, 0, 0, 0, 1, 0),
10,10)

```

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```

RINV=solve(R)

LHS=rbind(
  cbind( t(X) %*% RINV %*% X, t(X) %*% RINV %*% Z) ,
  cbind( t(Z) %*% RINV %*% X, t(Z) %*% RINV %*% Z+Ainv*(1/Sig_g)) )

RHS=rbind(
  t(X) %*% RINV %*% Y,
  t(Z) %*% RINV %*% Y)

C=solve(LHS)
BU=C %*% RHS
BU

```

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```

[,1]
[1,] 366.914758
[2,] 362.433866
[3,] 371.047672
[4,] 46.065237
[5,] 3.924541
[6,] -17.066236
[7,] 10.326070
[8,] -11.796658
[9,] 1.944260
[10,] 12.668024
[11,] -12.972376
[12,] 13.080473
[13,] -2.981939
[14,] -12.428131
[15,] 11.496208
[16,] -2.434303
[17,] -27.099471
[18,] 18.946256
[19,] 12.874337
[20,] -1.041514

```

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## Solution 2 Correlated Residuals

Directly model the data structure

Add another random effect due to shared environment  
(mother, cage, herd)

$$y_{ijkmn} = Y_i + S_j + G_k + M_e + e_{ijkmn}$$

↑      ↑      ↗      ↗      ↗  
 Year    Sex    Additive    Common Group    Random  
 {Fixed Effects}    {Genetic}    {Environment}    {error}

21

## MME Correlated Residuals

$$\mathbf{y} = \mathbf{X}\mathbf{b} + \mathbf{Z}_1\mathbf{G} + \mathbf{Z}_2\mathbf{m} + \mathbf{e}$$

↗      ↗  
 Genetic effect    Shared Group Environmental effect

$$V \begin{bmatrix} \mathbf{G} \\ \mathbf{m} \\ \mathbf{e} \end{bmatrix} = \begin{bmatrix} \mathbf{A}\sigma_G^2 & 0 & 0 \\ 0 & \mathbf{I}\sigma_{m_e}^2 & 0 \\ 0 & 0 & \mathbf{I}\sigma_e^2 \end{bmatrix}$$

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Year 86 87 88	sex m
------------------	----------

$$\mathbf{X} = \begin{bmatrix} 1 & 0 & 0 & 1 \\ 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 1 \\ 0 & 1 & 0 & 0 \\ 0 & 1 & 0 & 1 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 1 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 1 & 1 \\ 0 & 0 & 1 & 0 \end{bmatrix}$$

$$\mathbf{B} = \begin{bmatrix} b_1 \\ b_2 \\ b_3 \\ b_4 \end{bmatrix}$$

Herd  
Year  
Sex

$$\mathbf{Y} = \begin{bmatrix} 400 \\ 380 \\ 410 \\ 350 \\ 420 \\ 360 \\ 390 \\ 390 \\ 430 \\ 370 \end{bmatrix}$$

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**Animal Direct Genetic Effect**

Note that sires and dams did not have records and are missing

An	Sire	Dam
7	14	1
4	14	2
8	15	3
5	15	1
9	14	2
6	15	4
10	15	1
11	16	4
12	16	5
13	16	6

$$\mathbf{Z}_l = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

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Common Maternal Environmental effect

Animal 1 was the mother of animals 7, 5, 10

An	Sire	Dam		1 2 3 4 5 6	Shared groups (Mothers)
7	14	1		1 0 0 0 0 0	
4	14	2		0 1 0 0 0 0	
8	15	3		0 0 1 0 0 0	
5	15	1		1 0 0 0 0 0	
9	14	2		0 1 0 0 0 0	
6	15	4		0 0 0 1 0 0	
10	15	1		1 0 0 0 0 0	
11	16	4		0 0 0 1 0 0	
12	16	5		0 0 0 0 1 0	
13	16	6		0 0 0 0 0 1	

$Z_2 =$

$$\begin{bmatrix} 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{bmatrix}$$

$I =$

$$\begin{bmatrix} 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{bmatrix}$$

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MME

$$\begin{bmatrix} \mathbf{X}'\mathbf{X} & \mathbf{X}'\mathbf{Z}_1 & \mathbf{X}'\mathbf{Z}_2 \\ \mathbf{Z}_1'\mathbf{X} & \mathbf{Z}_1'\mathbf{Z}_1 + \mathbf{A}^{-1}k_{11} & \mathbf{Z}_1'\mathbf{Z}_2 \\ \mathbf{Z}_2'\mathbf{X} & \mathbf{Z}_2'\mathbf{Z}_1 & \mathbf{Z}_2'\mathbf{Z}_2 + \mathbf{I}k_{22} \end{bmatrix} \begin{bmatrix} \hat{\mathbf{b}} \\ \hat{\mathbf{G}} \\ \hat{\mathbf{M}}_e \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{y} \\ \mathbf{Z}_1'\mathbf{y} \\ \mathbf{Z}_2'\mathbf{y} \end{bmatrix}$$

$$\begin{bmatrix} k_{11} & k_{12} \\ k_{21} & k_{22} \end{bmatrix} = \begin{bmatrix} \sigma_G^2 & 0 \\ 0 & \sigma_{m_e}^2 \end{bmatrix}^{-1} \sigma_e^2$$

$$\begin{bmatrix} k_{11} & k_{12} \\ k_{21} & k_{22} \end{bmatrix} = \begin{bmatrix} 2000 & 0 \\ 0 & 500 \end{bmatrix}^{-1} 6500 = \begin{bmatrix} 3.25 & 0 \\ 0 & 13 \end{bmatrix}$$

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## R code Example 7

```

Sig_m=500
Sig_e=6500
Sig_g=2000

Y=matrix(c(400,
          380,
          410,
          350,
          420,
          360,
          390,
          390,
          430,
          370),10,1);
Ainv=matrix(c(2.5,.5,1,0,0,0,-1,-1,0,0,-1,0,0,0,0,0,
            .5,2.5,0,1,0,0,-1,0,0,-1,0,0,-1,0,0,0,0,
            1,0,2,0,0,0,0,-1,0,0,-1,0,0,0,0,0,0,
            0,1,0,.3,.5,0,0,.5,-1,-1,0,-1,-1,0,0,0,0,0,
            0,0,0,.5,1.5,0,0,0,-1,0,0,0,0,0,0,0,0,0,
            0,0,0,0,2.5,0,.5,0,.5,0,-1,-1,-1,0,0,0,0,0,
            0,0,0,0,0,0,2,0,0,0,0,0,0,0,0,0,0,0,
            -1,-1,0,0,0,0,2,0,0,0,0,0,0,0,0,0,0,0,
            -1,0,-1,.5,0,.5,0,.3,0,0,0,-1,0,-1,0,0,0,
            0,0,0,-1,-1,0,0,0,2,0,0,0,0,0,0,0,0,0,
            0,-1,0,-1,0,.5,0,0,0,2.5,0,0,0,0,-1,0,
            -1,0,-1,0,0,0,0,0,0,0,0,2,0,0,0,0,0,0,
            0,0,0,-1,0,0,0,0,0,0,0,0,0,0,0,0,0,-1,
            1,0,0,0,0,-1,0,-1,0,0,0,0,0,0,0,2,0,0,0,
            1,0,0,1,0,0,0,-1,0,-1,0,0,0,0,0,2,0,0,
            0,1,0,0,0,0,0,-1,0,0,0,-1,0,0,0,0,2,0,
            0,1,0,1,0,0,0,0,0,-1,0,0,0,-1,0,0,0,2,0,
            0,1,0,0,0,0,0,0,0,0,0,0,0,0,0,-1,0,0,0,
            0,0,1,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,
            0,0,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,
            0,0,1,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0),
          10,16,byrow = TRUE )

X=matrix(c(1,0,0,1,
          1,0,0,0,
          1,0,0,1,
          0,1,0,0,
          0,1,0,1,
          0,1,0,0,
          0,0,1,1,
          0,0,1,0,
          0,0,1,1,
          0,0,1,0),10,4,byrow = TRUE )

```

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```

Z1= matrix(c
(0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0,
0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0,
0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0,
0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0,
0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0,
0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0,
0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0,
0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0,
0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0,
0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0,
0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1),
10,16,byrow=TRUE)

Z2=matrix(c
(1 , 0 , 0 , 0 , 0 , 0 ,
0 , 1 , 0 , 0 , 0 , 0 ,
0 , 0 , 1 , 0 , 0 , 0 ,
1 , 0 , 0 , 0 , 0 , 0 ,
0 , 1 , 0 , 0 , 0 , 0 ,
0 , 0 , 0 , 1 , 0 , 0 ,
1 , 0 , 0 , 0 , 0 , 0 ,
0 , 0 , 0 , 1 , 0 ,
0 , 0 , 0 , 0 , 1 ,
0 , 0 , 0 , 0 , 0 , 1 ),
10,6,byrow=TRUE)

I=matrix(c
(1, 0, 0, 0, 0, 0,
0, 1, 0, 0, 0, 0,
0, 0, 1, 0, 0, 0,
0, 0, 0, 1, 0, 0,
0, 0, 0, 0, 1, 0,
0, 0, 0, 0, 0, 1),
6,6)

```

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```

P=matrix(c(Sig_g, 0,
           0, Sig_m),2,2)

K=solve(P)*Sig_e

LHS=rbind(
  cbind(t(X) %*% X, t(X) %*% Z1, t(X) %*% Z2),
  cbind(t(Z1) %*% X, t(Z1) %*% Z1+Ainv*K[1,1], t(Z1) %*% Z2),
  cbind(t(Z2) %*% X, t(Z2) %*% Z1, t(Z2) %*% Z2+I*K[2,2]))

RHS=rbind(t(X) %*% Y,
           t(Z1) %*% Y,
           t(Z2) %*% Y)
C=solve(LHS)
BU=C %*% RHS
BU

```

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### Solutions

<b>B</b>	<b>G</b>	Animal	<b>M̂_e</b>	Dam
369.87	1.81	14	-2.365897	1
363.57	-3.80	1 2	1.226796	2
375.03	2.783	3	0.0671247	3
40.76 ← Sex	-3.56	15	0.5146638	4
	0.13	3	0.9262775	5
	2.63	16		6
	-1.96	7	-0.368965	
	3.46	4		
	-1.57	8		
	-3.88	5		
	3.91	9		
	-0.90	6		
	-6.31	10		
	4.56	11		
	1.22	12		
	0.12	13		

Note: results are same as using correlated residual matrix

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## How are the results used?

- The model separates Nature from Nurture
  - Human experimenters maybe interested in both effects
    - Example: How much of the variation in infant weight at 4 weeks post delivery, is due to the genes of the child vs. the nurture of the mother and perhaps the cause of the nurture effects
  - Breeders are only interested in making maximal genetic improvement
    - Use the additive genetic effects to select best animals

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## Impact of Fixed vs. Random Effect

- The data was collected over 3 years, the researcher was concerned about a common environmental effect due to years but could not decide if years should be a fixed or random effect. What difference does it really make?
  1. Model 1: Include fixed effect for sex and year; Animal as random
    - Additive genetic (2000)
    - Residual (6500).
  2. Model 2: Same as above but now assume the effect of years is random
    - Between year variance (500)
    - Residual (6500)
    - What are the best estimates of the breeding value of each animal? What are the year effects?
  3. Model 3: Same as Model 2 but increase between year variance to (100,000)
  - What impact does fixed vs. random year effect have on the results?

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## Years Fixed

$$\mathbf{y} = \mathbf{X}\mathbf{b} + \mathbf{Z}_1\mathbf{G} + \mathbf{e}$$

↑                      ↑  
Fixed effects      Additive Genetic effects

$$V \begin{bmatrix} \mathbf{G} \\ \mathbf{e} \end{bmatrix} = \begin{bmatrix} \mathbf{A}\sigma_G^2 & 0 \\ 0 & \mathbf{I}\sigma_e^2 \end{bmatrix}$$

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Year    sex 86 87 88 m	$\mathbf{X} = \begin{bmatrix} 1 & 0 & 0 & 1 \\ 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 1 \\ 0 & 1 & 0 & 0 \\ 0 & 1 & 0 & 1 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 1 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 1 & 1 \\ 0 & 0 & 1 & 0 \end{bmatrix}$	$\mathbf{B} = \begin{bmatrix} b_1 \\ b_2 \\ b_3 \\ b_4 \end{bmatrix}$	{ Herd Year Sex	$\mathbf{Y} = \begin{bmatrix} 400 \\ 380 \\ 410 \\ 350 \\ 420 \\ 360 \\ 390 \\ 390 \\ 430 \\ 370 \end{bmatrix}$
---------------------------	---	---	-----------------------	---

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## R code Example 8

Sig\_e=6500  
Sig\_g=2000

```

Y=matrix(c(400,
380,           Ainv=matrix(c(2.5,.5,1,0,0,0,-1,-1,0,0,-1,0,0,0,0,0,
410,             .5,2.5,0,1,0,0,-1,0,0,-1,0,0,-1,0,0,0,0,
350,               1,0,2,0,0,0,0,-1,0,0,-1,0,0,0,0,0,0,
420,                 0,1,0,3,.5,0,0,.5,-1,-1,0,-1,-1,0,0,0,0,
360,                   0,0,0,.5,1.5,0,0,0,-1,0,0,0,0,0,0,0,0,
390,                     0,0,0,0,2.5,0,.5,0,.5,0,-1,-1,-1,0,0,0,0,
390,                     -1,-1,0,0,0,2,0,0,0,0,0,0,0,0,0,0,0,
430,                     -1,0,-1,.5,0,.5,0,3,0,0,0,-1,0,-1,0,0,
370),10,1);
X=matrix(c(1,0,0,1,
1,0,0,0,
1,0,0,1,
0,1,0,0,
0,1,0,1,
0,1,0,0,
0,0,1,1,
0,0,1,0,
0,0,1,1,
0,0,1,0),10,4, byrow = TRUE )

```

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```

Z1= matrix(c
(0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0,
0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0,
0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0,
0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0,
0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0,
0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0,
0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0,
0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0,
0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0,
0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0,
0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1),
10,16,byrow=TRUE)

```

```

LHS=rbind(cbind(t(X)%%X, t( X) %%Z1),
          cbind(t(Z1) %%X, t(Z1) %%Z1+Ainv*(Sig_e/Sig_g)) )

```

```
RHS=rbind(t( X) %%Y, t( Z1) %%Y)
```

```
C=solve(LHS)
```

```
BU=C%*%RHS
```

```
BU
```

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## Solutions: Years Fixed

	Additive Genetic Effect
	1.96
	-4.39
Fixed effects	3.16
year	-3.78
369.59	0.20
363.39	2.84
374.79	-2.41
sex	3.94
40.63	-1.58
	-4.44
Note for Slide 48	4.35
$y_1+y_2+y_3/3=u=369.26$	-0.72
$Y_1-u=.33$	-6.93
$Y_2-u=-5.86$	4.97
$Y_3-u=5.53$	1.24
Come back to this	0.28

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## Years Random

$$\mathbf{y} = \mathbf{X}\mathbf{b} + \mathbf{Z}_1\mathbf{G} + \mathbf{Z}_2\mathbf{T} + \mathbf{e}$$

↑                      ↑  
 Genetic effect      Year effect

$$V \begin{bmatrix} \mathbf{G} \\ \mathbf{T} \\ \mathbf{e} \end{bmatrix} = \begin{bmatrix} \mathbf{A}\sigma_G^2 & 0 & 0 \\ 0 & \mathbf{I}\sigma_T^2 & 0 \\ 0 & 0 & \mathbf{I}\sigma_e^2 \end{bmatrix}$$

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$$\begin{array}{c}
 \text{overall} \\
 \text{mean sex} \\
 \downarrow \quad \downarrow \\
 \mathbf{X} = \begin{bmatrix} 1 & 1 \\ 1 & 0 \\ 1 & 1 \\ 1 & 0 \\ 1 & 1 \\ 1 & 0 \\ 1 & 1 \\ 1 & 0 \\ 1 & 1 \\ 1 & 0 \end{bmatrix} \quad \mathbf{B} = \begin{bmatrix} b_0 \\ b_1 \end{bmatrix} \quad \begin{array}{l} \text{Mean} \\ \text{Sex effect} \end{array} \quad \mathbf{Y} = \begin{bmatrix} 400 \\ 380 \\ 410 \\ 350 \\ 420 \\ 360 \\ 390 \\ 390 \\ 430 \\ 370 \end{bmatrix}
 \end{array}$$

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## Animal Additive Genetic Effect

Same as before

An	Sire	Dam	14	1	2	15	3	16	7	4	8	5	9	6	10	11	12	13
7	14	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
4	14	2	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0
8	15	3	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
5	15	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
9	14	2	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
6	15	4	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
10	15	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
11	16	4	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
12	16	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
13	16	6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1

$$\mathbf{Z}_1 = \begin{bmatrix} 14 & 1 & 2 & 15 & 3 & 16 & 7 & 4 & 8 & 5 & 9 & 6 & 10 & 11 & 12 & 13 \end{bmatrix}^T$$

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Common Year Effect		
An	Year	Year(T)
7	86	1 0 0
4	86	1 0 0
8	86	1 0 0
5	87	0 1 0
9	87	0 1 0
6	87	0 1 0
10	88	0 0 1
11	88	0 0 1
12	88	0 0 1
13	88	0 0 1

$\mathbf{Z}_2 = \begin{bmatrix} 1 & 0 & 0 \\ 1 & 0 & 0 \\ 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 1 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \\ 0 & 0 & 1 \\ 0 & 0 & 1 \end{bmatrix}$

$\mathbf{I} = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}$

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### MME

$$\begin{bmatrix} \mathbf{X}'\mathbf{X} & \mathbf{X}'\mathbf{Z}_1 & \mathbf{X}'\mathbf{Z}_2 \\ \mathbf{Z}_1'\mathbf{X} & \mathbf{Z}_1'\mathbf{Z}_1 + \mathbf{A}^{-1}k_{11} & \mathbf{Z}_1'\mathbf{Z}_2 \\ \mathbf{Z}_2'\mathbf{X} & \mathbf{Z}_2'\mathbf{Z}_1 & \mathbf{Z}_2'\mathbf{Z}_2 + \mathbf{I}k_{22} \end{bmatrix} \begin{bmatrix} \hat{\mathbf{b}} \\ \hat{\mathbf{G}} \\ \hat{\mathbf{T}} \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{y} \\ \mathbf{Z}_1'\mathbf{y} \\ \mathbf{Z}_2'\mathbf{y} \end{bmatrix}$$

$$\begin{bmatrix} k_{11} & k_{12} \\ k_{21} & k_{22} \end{bmatrix} = \begin{bmatrix} \sigma_g^2 & 0 \\ 0 & \sigma_e^2 \end{bmatrix}^{-1} \sigma_e^2$$

$$\begin{bmatrix} k_{11} & k_{12} \\ k_{21} & k_{22} \end{bmatrix} = \begin{bmatrix} 2000 & 0 \\ 0 & 500 \end{bmatrix}^{-1} 6500 = \begin{bmatrix} 3.25 & 0 \\ 0 & 13 \end{bmatrix}$$

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## R code Example 9

```

Sig_e=6500
Sig_g=2000
Sig_y=500

Y=matrix(c(400,
          380,
          410,
          350,
          420,
          360,
          390,
          390,
          430,
          370),10,1);
Ainv=matrix(c(2.5,.5,1,0,0,0,-1,-1,0,0,-1,0,0,0,0,0,
            .5,2.5,0,1,0,0,-1,0,0,-1,0,0,-1,0,0,0,0,
            1,0,2,0,0,0,0,-1,0,0,-1,0,0,0,0,0,0,
            0,1,0,.3,.5,0,0,.5,-1,-1,0,-1,-1,0,0,0,0,0,
            0,0,0,.5,1.5,0,0,0,-1,0,0,0,0,0,0,0,0,0,
            0,0,0,0,2.5,0,.5,0,.5,0,-1,-1,-1,0,0,0,0,0,
            -1,-1,0,0,0,2,0,0,0,0,0,0,0,0,0,0,0,0,
            -1,0,-1,.5,0,.5,0,3,0,0,0,-1,0,-1,0,0,0,
            0,0,0,-1,-1,0,0,0,2,0,0,0,0,0,0,0,0,0,0,
            0,-1,0,-1,0,.5,0,0,0,2.5,0,0,0,0,-1,0,
            -1,0,-1,0,0,0,0,0,0,0,2,0,0,0,0,0,0,0,
            0,0,0,-1,0,0,0,0,0,0,0,0,0,0,0,0,0,-1,
            1,0,0,-1,0,.5,-1,0,0,0,0,0,0,0,0,0,0,-1,
            1,1,0,0,0,-1,0,-1,0,0,0,0,0,0,0,0,0,0,
            1,0,0,0,0,-1,0,0,0,-1,0,0,0,0,0,0,0,0,
            1,1,0,0,0,-1,0,0,0,0,-1,0,0,0,0,0,0,0,
            1,0,0,0,0,-1,0,0,0,0,0,0,0,-1,0,0,0,0),
          16,16)

X=matrix(c(1,1,
          1,0,
          1,1,
          1,0,
          1,1,
          1,0,
          1,1,
          1,0,
          1,1,
          1,0,10,2,byrow = TRUE)

```

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```

Z1= matrix(c
(0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0,
 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0,
 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0,
 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0,
 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0,
 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0,
 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0,
 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0,
 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0,
 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0,
 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1,
 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0),
 10,16,byrow=TRUE)

Z2=matrix(c
(1, 0, 0,
 1, 0, 0,
 1, 0, 0,
 0, 1, 0,
 0, 1, 0,
 0, 1, 0,
 0, 0, 1,
 0, 0, 1,
 0, 0, 1,
 0, 0, 1),
 10,3,byrow=TRUE)

I= matrix(c
(1, 0, 0,
 0, 1, 0,
 0, 0, 1),
 3,3)

```

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```

P=matrix(c(Sig_g , 0,
           0,  Sig_y=500),2,2)
K=solve(P)*Sig_e

LHS=rbind(
  cbind(t(X)%%X, t(X) %%Z1, t(X) %%Z2) ,
  cbind(t(Z1) %%X , t(Z1) %%Z1+Ainv*K[1,1] , t(Z1) %%Z2),
  cbind(t(Z2) %%X, t(Z2) %%Z1, t(Z2) %%Z2+I*K[2,2])) 

RHS=rbind(t(X) %%Y,
           t(Z1) %%Y,
           t(Z2) %%Y)
C=solve(LHS)
BU=C %*% RHS
BU

```

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## Solutions Years random (var=500)

	Additive Genetic Effect
Fixed effects	1.40
	-4.41
	2.67
369.07 mean	-4.14
41.94 Sex effect	0.13
	4.35
	-2.77
	3.65
	-1.87
Year Effects	-5.06
	3.09
	-1.38
-0.008	-6.64
-0.988	6.12
0.996	2.09
	1.27

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## Years random (var=100000)

```

P=matrix(c(Sig_g , 0,
           0, Sig_y=100000),2,2)
K=solve(P)*Sig_e

LHS=rbind(
  cbind(t(X)%*%X, t(X) %*%Z1, t(X) %*%Z2) ,
  cbind(t(Z1) %*%X , t(Z1) %*%Z1+Ainv*K[1,1] , t(Z1) %*%Z2) ,
  cbind(t(Z2) %*%X, t(Z2) %*%Z1, t(Z2) %*%Z2+l*K[2,2])) 

RHS=rbind(t(X) %*%Y,
           t(Z1) %*%Y,
           t(Z2) %*%Y)
C=solve(LHS)
BU=C %*% RHS
BU

```

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## Solutions

### Additive Genetic Effect

	1.95	
	-4.39	
Fixed effects	3.15	Additive effects near identical to previous example where years were fixed
	-3.79	
369.25 mean	0.20	
40.67 Sex effect	2.88	
	-2.42	
	3.94	
Year Effects	-1.58	
0.32	-4.46	
-5.72	4.31	
5.40	-0.74	
Note the effect of years increased and near identical to slide 37 with years fixed	-6.93	
	5.00	
	1.27	
	0.30	

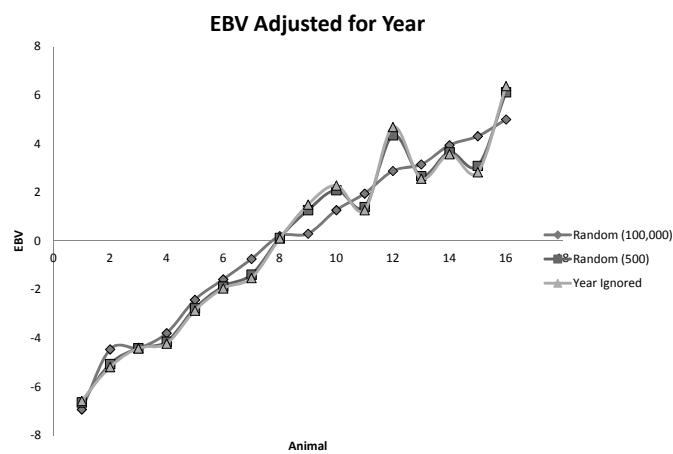
48

## Model Comparisons

	Fixed	Random (100,000)	Random (500)	Animal		EBV			
Year Effect					Fixed	Random (100,00)	Random (500)	Year Ignored	
	1	0.33	0.32	-0.008	1	1.96	1.95	1.4	1.27
2	5.86	-5.72	-0.988		2	-4.39	-4.39	-4.41	-4.42
3	5.53	5.4	0.996		3	3.16	3.15	2.67	2.57
					4	-3.78	-3.79	-4.14	-4.22
					5	0.2	0.2	0.13	0.11
					6	2.84	2.88	4.35	4.69
					7	-2.41	-2.42	-2.77	-2.86
					8	3.94	3.94	3.65	3.57
					9	-1.58	-1.58	-1.87	-1.95
					10	-4.44	-4.46	-5.06	-5.19
					11	4.35	4.31	3.09	2.83
					12	-0.72	-0.74	-1.38	-1.52
					13	-6.93	-6.93	-6.64	-6.58
					14	4.97	5	6.12	6.37
					15	1.24	1.27	2.09	2.28
					16	0.28	0.3	1.27	1.50

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How much should the EBV be adjusted for year?



When Year is fit as a random effect, the data tells us how much to adjust

Setting a factor as fixed is equivalent to assuming the intra-class correlation is 1

$$\rho = \frac{\sigma_b^2}{\sigma_b^2 + \sigma_e^2}$$

$$\rho = \frac{500}{500 + 6500} = .07 \quad \text{First Example}$$

$$\rho = \frac{100000}{100000 + 6500} \approx 1 \quad \text{Second Example}$$

Setting a factor at random allows the residual correlation, and amount of adjustment for that factor, to be estimated from the data

For a random factor the intra-class correlation is used as a regressor, how much to adjust for the factor; a correlation of 1, totally adjust (regress) for the factor, a correlation of 0, the factor is ignored

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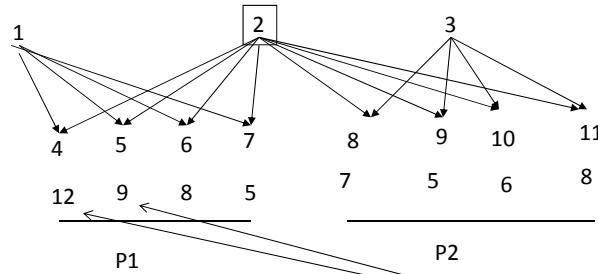
## Appendix 1

### Problems

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### Problem 1

#### Impact of maternal effect on breeding values



In the above data, if maternal effects are ignored, animals 4 and 5 would be chosen. If maternal effects are accounted for, which 2 animals would be selected?

For this trait the maternal effect variance was 10 times as large as the genetic variance which was the same as the residual variance

53

```

proc iml;
start main; Z1={0 0 0 1 0 0 0 0 0 0,
                    0 0 0 0 1 0 0 0 0 0,
                    0 0 0 0 0 1 0 0 0 0,
y={12, 0 0 0 0 0 1 0 0 0 0,
  9, 0 0 0 0 0 0 1 0 0 0,
  8, 0 0 0 0 0 0 0 1 0 0,
  5, 0 0 0 0 0 0 0 0 1 0,
  7, 0 0 0 0 0 0 0 0 0 1};
  5,
  6, Z2={1 0, A={1 0 0 .5 .5 .5 .5 0 0 0 0,
  8}; 1 0, 0 1 0 .5 .5 .5 .5 .5 .5 .5,
        1 0, 0 0 1 0 0 0 0 .5 .5 .5 .5,
X={1, 1 0, .5 .5 0 1 .5 .5 .25 .25 .25,
  1, 0 1, .5 .5 0 .5 1 .5 .5 .25 .25 .25,
  1, 0 1, .5 .5 0 .5 .5 1 .5 .25 .25 .25,
  1, 0 1}; .5 .5 .25 .25 .25 .25 1 .5 .5 .5,
  1, 1, 0 5 .5 .25 .25 .25 .25 .5 1 .5 .5,
  1, 0 1}; 0 5 .5 .25 .25 .25 .25 .5 .5 .5 1};

AINV=INV(A);

```

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## Genetic Parameters

```

P={10  0,
   0  100};

K=inv(P)#10;

LHS=((X`*X)|| (X`*Z1)|| (X`*Z2))
 //((Z1`*X)|| (Z1`*Z1+AINV#K[1,1])||(Z1`*Z2))
 //((Z2`*X)|| (Z2`*Z1)|| (Z2`*Z2+I#K[2,2]));
RHS=(X`*Y)/(Z1`*Y)/(Z2`*Y);
C=INV(LHS);
BU=C*RHS;
RMSE=(Y`*Y-BU`*RHS)#{1/6};
print BU ;
finish main;
run;
quit;

```

Run "BLUP Maternal Environmental.SAS"

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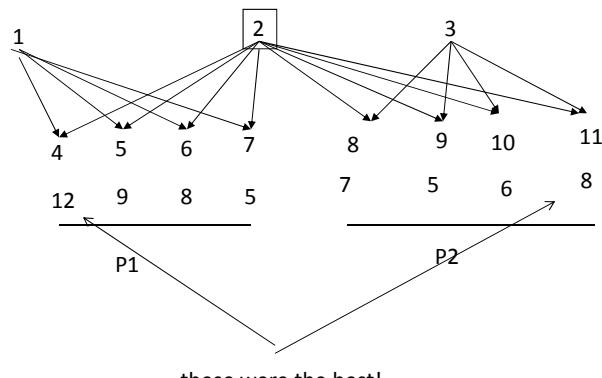
## Solutions

Dam

		1.201	1
	4	0.201	
1	5	-0.131	
	6		
	7	-1.131	
	8	0.131	
	9	-0.535	
	10	-0.201	
3	11	0.464	2

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### Selection after adjustment



Within Family Selection

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## Appendix 2

SAS IML Code for most Examples

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```

proc iml;                                Example 1
start main;

Sig_m=500;
Sig_e=6500+Sig_m;
Sig_g=2000;
LAM=1/2000;

y={400,
  380,
  410,
  350,
  420,
  360,
  390,
  390,
  430,
  370};

Z= {0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0,
     0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0,
     0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0,
     0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0,
     0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0,
     0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0,
     0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0,
     0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0,
     0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0,
     0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0,
     0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0,
     0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0,
     0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0,
     0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0};

R= { 1 0 0 .0714 0 0 .0714 0 0 0 ,
      0 1 0 0 .0714 0 0 0 0 0 ,
      0 0 1 0 0 0 0 0 0 0 ,
      .0714 0 0 1 0 0 .0714 0 0 0 ,
      0 .0714 0 0 1 0 0 0 0 0 ,
      0 0 0 0 0 1 0 .0714 0 0 ,
      .0714 0 0 .0714 0 0 1 0 0 0 ,
      0 0 0 0 0 .0714 0 1 0 0 ,
      0 0 0 0 0 0 0 0 1 0 ,
      0 0 0 0 0 0 0 0 0 1 }#Sig_e;

X={1 0 0 1,
  1 0 0 0,
  1 0 0 1,
  0 1 0 0,
  0 1 0 1,
  0 1 0 0,
  0 0 1 1,
  0 0 1 0,
  0 0 1 1,
  0 0 1 0};

RINV=INV(R);


```

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Ainv={2.5 .5 1 0 0 0 -1 -1 0 0 -1 0 0 0 0 0 0,	BU
.5 2.5 0 1 0 0 -1 0 0 -1 0 0 -1 0 0 0 0 0,	369.8741
1 0 2 0 0 0 0 -1 0 0 -1 0 0 0 0 0 0 0,	363.578
0 1 0 3 .5 0 0 .5 -1 -1 0 -1 -1 0 0 0 0,	375.0397
0 0 0 .5 1.5 0 0 0 -1 0 0 0 0 0 0 0 0,	40.76463
0 0 0 0 0 2.5 0 .5 0 .5 0 .5 0 -1 -1 -1,	
-1 -1 0 0 0 0 2 0 0 0 0 0 0 0 0 0 0,	1.813526
-1 0 -1 .5 0 .5 0 3 0 0 0 -1 0 -1 0 0,	-3.80565
0 0 0 -1 -1 0 0 0 2 0 0 0 0 0 0 0 0,	2.783858
0 -1 0 -1 0 .5 0 0 0 2.5 0 0 0 0 -1 0,	
-1 0 -1 0 0 0 0 0 0 2 0 0 0 0 0 0,	-3.56012
0 0 0 -1 0 .5 0 -1 0 0 0 2.5 0 0 0 -1,	0.13427
0 -1 0 -1 0 0 0 0 0 0 0 0 2 0 0 0,	2.634119
0 0 0 0 -1 0 -1 0 0 0 0 0 2 0 0,	-1.96639
0 0 0 0 0 -1 0 0 0 0 -1 0 0 0 0 2 0,	3.464949
0 0 0 0 0 -1 0 0 0 0 0 -1 0 0 0 0 2},	-1.5786
LHS=((X*RINV*X) (X*RINV*Z))//((Z*RINV*X) (Z*RINV*Z+Ainv#LAM));	6 -3.88408
RHS=(X*RINV*Y)/(Z*RINV*Y);	3.916292
C=INV(LHS);	-0.90666
BU=C*RHS;	-6.31701
print BU ;	4.569
finish main;run;quit;	1.227599
	0.1258

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## Example 2

```

proc iml;
start main;
y={400,
380,
410,
350,
420,
360,
390,
390,
430,
370};
Z1={0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0,
     0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0,
     0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0,
     0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0,
     0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0,
     0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0,
     0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0,
     0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0,
     0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0,
     0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0,
     0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0,
     0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0,
     0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1};

X={1 0 0 1,
  1 0 0 0,
  1 0 0 1,
  0 1 0 0,
  0 1 0 1,
  0 1 0 0,
  0 1 0 0,
  0 0 1 1,
  0 0 1 0,
  0 0 1 1,
  0 0 1 0};

Z2={ 1 0 0 0 0 0,
      0 1 0 0 0 0,
      0 0 1 0 0 0,
      1 0 0 0 0 0,
      0 1 0 0 0 0,
      0 0 0 1 0 0,
      0 1 0 0 0 0,
      0 0 0 1 0 0,
      0 0 0 0 1 0,
      1 0 0 0 0 0,
      0 0 0 1 0 0,
      0 0 0 0 1 0,
      0 0 0 0 0 1};

I= { 1 0 0 0 0 0,
      0 1 0 0 0 0,
      0 0 1 0 0 0,
      0 0 0 1 0 0,
      0 0 0 0 1 0,
      0 0 0 0 0 1};

```

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```

Ainv={2.5 .5 1 0 0 0 -1 -1 0 0 -1 0 0 0 0 0 0,
      .5 2.5 0 1 0 0 -1 0 0 -1 0 0 -1 0 0 0 0 0,
      1 0 2 0 0 0 0 -1 0 0 -1 0 0 0 0 0 0 0 0,
      0 1 0 3 .5 0 0 .5 -1 -1 0 -1 -1 0 0 0 0 0 0,
      0 0 0 .5 1.5 0 0 0 -1 0 0 0 0 0 0 0 0 0 0,
      0 0 0 0 0 2.5 0 .5 0 .5 0 .5 0 -1 -1 -1,
      -1 -1 0 0 0 0 2 0 0 0 0 0 0 0 0 0 0 0 0,
      -1 0 -1 .5 0 .5 0 3 0 0 0 -1 0 -1 0 0 0 0,
      0 0 0 -1 -1 0 0 0 2 0 0 0 0 0 0 0 0 0 0,
      0 -1 0 -1 0 .5 0 0 0 2.5 0 0 0 0 -1 0 0 0,
      -1 0 -1 0 0 0 0 0 0 2 0 0 0 0 0 0 0 0 0,
      0 0 0 -1 0 .5 0 -1 0 0 0 2.5 0 0 0 -1,
      0 -1 0 -1 0 0 0 0 0 0 0 0 2 0 0 0 0 0,
      0 0 0 0 0 -1 0 0 0 -1 0 0 0 0 2 0 0 0,
      0 0 0 0 0 -1 0 0 0 0 -1 0 0 0 0 2 0 0 0};

```

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```

P={2000 0,
   0 500};

K=inv(P)#6500;

LHS=((X`*X)|| (X`*Z1)|| (X`*Z2))
    //((Z1`*X)|| (Z1`*Z1+AINV#K[1,1])|| (Z1`*Z2))
    //((Z2`*X)|| (Z2`*Z1)|| (Z2`*Z2+I#K[2,2]));

RHS=(X`*Y)/(Z1`*Y)/(Z2`*Y);
C=INV(LHS);
BU=C*RHS;
print BU ;
finish main;
run;
quit;

```

“BLUP Maternal Environmental ex1.sas”

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### Example 3: SAS IML Code Years Fixed

```

proc iml;
start main;
y={400,
  380,
  410,
  350,
  420,
  360,
  390,
  390,
  430,
  370};
Z1={0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0,
      0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0,
      0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0,
      0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0,
      0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0,
      0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0,
      0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0,
      0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0,
      0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0,
      0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0,
      0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0,
      0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0};

Ainv={2.5 .5 1 0 0 0 -1 -1 0 0 -1 0 0 0 0 0 0,
      .5 2.5 0 1 0 0 -1 0 0 -1 0 0 -1 0 0 0 0 0,
      1 0 2 0 0 0 0 -1 0 0 -1 0 0 0 0 0 0 0 0,
      0 1 0 3 .5 0 0 5 -1 -1 0 -1 -1 0 0 0 0 0,
      0 0 0 .5 1.5 0 0 0 -1 0 0 0 0 0 0 0 0 0 0,
      0 0 0 0 0 2.5 0 .5 0 .5 0 .5 0 -1 -1 -1,
      -1 -1 0 0 0 0 2 0 0 0 0 0 0 0 0 0 0 0 0,
      -1 0 -1 .5 0 .5 0 3 0 0 0 -1 0 -1 0 0 0,
      0 0 0 -1 -1 0 0 0 2 0 0 0 0 0 0 0 0 0 0 0,
      0 -1 0 -1 0 .5 0 0 0 2.5 0 0 0 0 -1 0 0 0,
      -1 0 -1 0 0 0 0 0 0 2 0 0 0 0 0 0 0 0 0 0,
      0 0 0 -1 0 .5 0 -1 0 0 0 2.5 0 0 0 -1 0 0 0,
      0 -1 0 -1 0 0 0 0 0 0 0 0 2 0 0 0 0 0 0 0 0,
      0 0 0 0 0 -1 0 0 0 -1 0 0 0 0 0 0 0 0 0 0 0,
      0 0 0 0 0 -1 0 0 0 0 0 0 -1 0 0 0 0 0 0 0 0 2};

X={1 0 0 1,
  1 0 0 0,
  1 0 0 1,
  0 1 0 0,
  0 1 0 1,
  0 1 0 0,
  0 0 1 1,
  0 0 1 0,
  0 0 1 1,
  0 0 1 0};

As before

```

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```

Sig_e=6500;
Sig_g=2000;
LHS=((X`*X) || (X`*Z1))
//((Z1`*X) || (Z1`*Z1+AINV#(sig_e/sig_g)));
RHS=(X`*Y)/(Z1`*Y);
C=INV(LHS);
BU=C*RHS;
print BU;

finish main;run;quit;

```

“BLUP Common year fixed.sas”

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#### Example 4: Years Random

```

proc iml;
start main;
y={400,
 380,
 410,
 350,
 420,
 360,
 390,
 390,
 430,
 370};
Z1={0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0,
      0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0,
      0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0,
      0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0,
      0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0,
      0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0,
      0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0,
      0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0,
      0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0,
      0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0,
      0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0};

Z2={ 1 0 0 ,
      1 0 0 ,
      1 0 0 ,
      0 1 0 ,
      0 1 0 ,
      0 1 0 ,
      0 1 0 ,
      0 0 1 ,
      0 0 1 ,
      0 0 1 };

X={1 1,
  1 0,
  1 1,
  1 0,
  1 1,
  1 0,
  1 1,
  1 0,
  1 1,
  1 0};

I= {1 0 0 ,
      0 1 0 ,
      0 0 1 };

```

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```
Ainv={2.5 .5 1 0 0 0 -1 -1 0 0 -1 0 0 0 0 0,
      .5 2.5 0 1 0 0 -1 0 0 -1 0 0 -1 0 0 0,
      1 0 2 0 0 0 0 -1 0 0 -1 0 0 0 0 0 0,
      0 1 0 3 .5 0 0 0 .5 -1 -1 0 -1 -1 0 0 0,
      0 0 0 .5 1.5 0 0 0 -1 0 0 0 0 0 0 0 0,
      0 0 0 0 0 2.5 0 .5 0 .5 0 .5 0 -1 -1 -1,
      -1 -1 0 0 0 0 2 0 0 0 0 0 0 0 0 0 0,
      -1 0 -1 .5 0 .5 0 3 0 0 0 -1 0 -1 0 0,
      0 0 0 -1 -1 0 0 0 2 0 0 0 0 0 0 0 0,
      0 -1 0 -1 0 .5 0 0 0 2.5 0 0 0 0 -1 0,
      -1 0 -1 0 0 0 0 0 0 0 2 0 0 0 0 0 0,
      0 0 0 -1 0 .5 0 -1 0 0 0 2.5 0 0 0 -1,
      0 -1 0 -1 0 0 0 0 0 0 0 0 2 0 0 0 0,
      0 0 0 0 0 -1 0 -1 0 0 0 0 0 0 2 0 0,
      0 0 0 0 0 -1 0 0 0 -1 0 0 0 0 0 2 0,
      0 0 0 0 0 -1 0 0 0 0 -1 0 0 0 0 0 2};
```

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```
P={2000 0,
   0 500};

K=inv(P)#6500;

LHS=((X`*X)|| (X`*Z1)|| (X`*Z2))
    //((Z1`*X)|| (Z1`*Z1+AINV#K[1,1])|| (Z1`*Z2))
    //((Z2`*X)|| (Z2`*Z1)|| (Z2`*Z2+l#K[2,2]));

RHS=(X`*Y)/(Z1`*Y)/(Z2`*Y);
C=INV(LHS);
BU=C*RHS;
print BU ;
finish main;
run;
quit;
```

“BLUP Common year random.sas”

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# Lecture 9: $G \times E$ : Genotype-environment interaction

Bruce Walsh lecture notes  
SISG -Mixed Model Course  
Seattle, 16 - 18 July 2014

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## $G \times E$

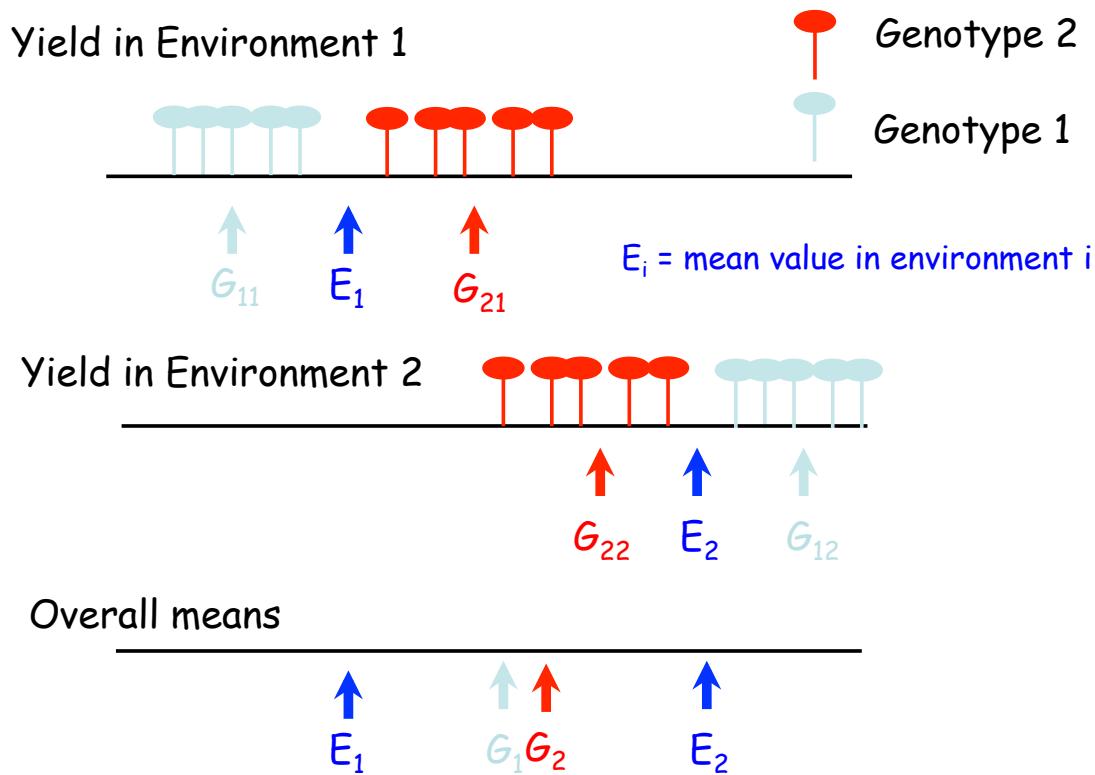
- Introduction to  $G \times E$ 
  - Basics of  $G \times E$
  - Some suggested rules
  - Treating  $G \times E$  as a correlated-trait problem
- Estimation of  $G \times E$  terms
  - Finlay-Wilkinson regressions
- SVD-based methods
  - The singular value decomposition (SVD)
  - AMMI models
- Factorial regressions
- Mixed-Model approaches
  - BLUP
  - Structured covariance models

2

# Genotypes vs. individuals

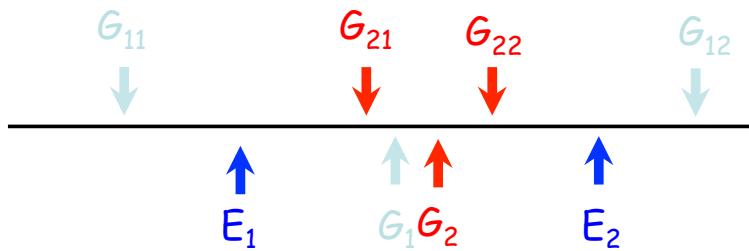
- Much of the  $G \times E$  theory is developed for plant breeders who are using pure (= fully inbred) lines, so that every individual has the same genotype
- The same basic approaches can be used by taking family members as the replicates for outbred species. Here the "genotype" over the family members is some composite value (the mean breeding value of the family).

3



4

$G_{ij}$  = mean of genotype i in environment j

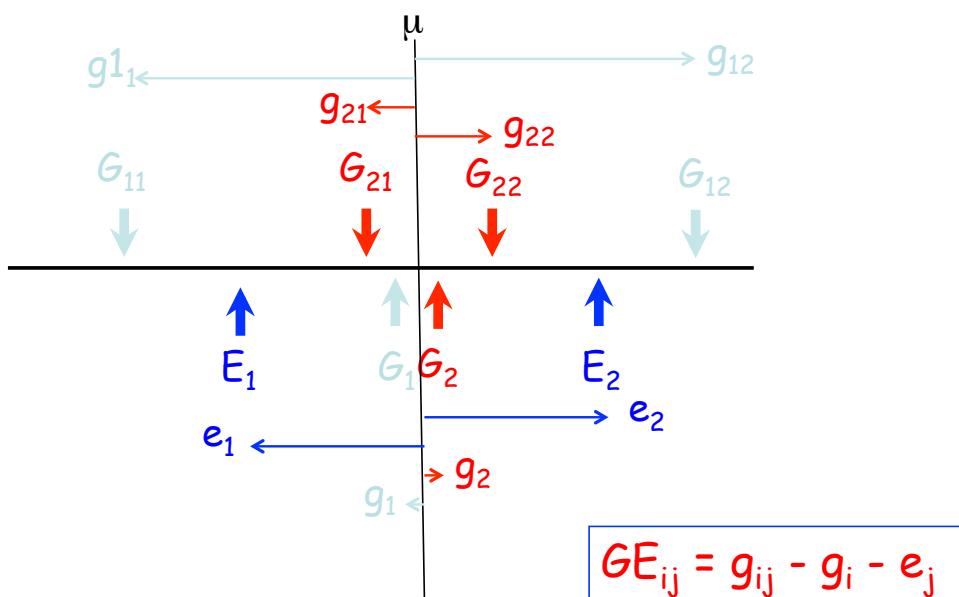


Under base model of Quantitative Genetics,

$$G_{ij} = \mu + G_i + E_j$$

When  $G \times E$  present, there is an interaction between a particular genotype and a particular environment so that  $G_{ij}$  is no longer additive,  $G_{ij} = \mu + G_i + E_i + GE_{ij}$

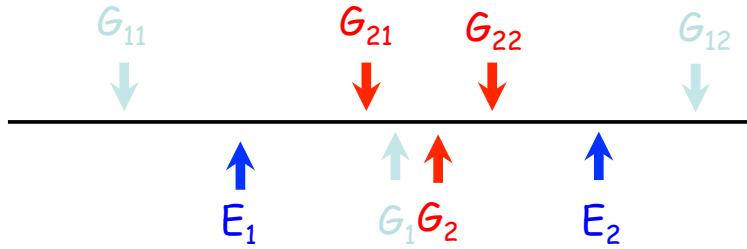
5



Components measured as deviations  
from the mean  $\mu$

6

# Which genotype is the best?



Depends: If the genotypes are grown in both environments,  $G_2$  has a higher mean

If the genotypes are only grown in environment 1,  $G_2$  has a higher mean

If the genotypes are only grown in environment 2,  $G_1$  has a higher mean

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## $G \times E$ : Both a problem and an opportunity

- A line with little  $G \times E$  has **stability across environments**.
- However, a line with high  $G \times E$  may **outperform all others in specific environments**.
- $G \times E$  implies the **opportunity to fine-tune specific lines to specific environments**
- High  $\sigma^2(GE)$  implies high  $G \times E$  in at least some lines in the sample.

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		Mean Performance	
		High	Low
Amount of G × E	High	Potential for locally-adapted lines	Potential for locally-adapted lines
	Low	Ideal. Potential for widely adaptive lines	Undesirable

Ideal: high mean performance, low  $G \times E$

Low  $G \times E$  = widely adaptive lines/genotypes

High  $G \times E$  = locally adaptive lines/genotypes

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## Major vs. minor environments

- An identical genotype will display slightly different traits values even over apparently identical environments due to micro-environmental variation and developmental noise
- However, **macro-environments** (such as different locations or different years <such as a wet vs. a dry year>) can show substantial variation, and genotypes (pure lines) may differentially perform over such macro-environments ( $G \times E$ ).
- Problem: The **mean environment of a location** may be **somewhat predictable** (e.g., corn in the tropics vs. temperate North American), but **year-to-year variation** at the same location is **essentially unpredictable**.
- Decompose  $G \times E$  into components
  - $G \times E_{\text{locations}} + G \times E_{\text{years}} + G \times E_{\text{years} \times \text{locations}}$
  - Ideal: **strong  $G \times E$  over locations, high stability over years.**

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### Components of $\sigma_{G \times E}^2$ : Variance Heterogeneity and Lack of Correlations

It is useful to remind the reader that there are two different sources for  $G \times E$  — differences in the genetic variances across environments (**genetic heterogeneity**, often referred to as **scale effects**) and lack of perfect correlation among breeding values across environments (LW Chapter 22). For two environments, Robertson (1959) showed that the  $G \times E$  interaction variance can be partitioned into these two sources,

$$\sigma_{G \times E}^2 = \frac{(\sigma_{A_1} - \sigma_{A_2})^2}{2} + \sigma_{A_1} \sigma_{A_2} (1 - r_A) \quad (38.1a)$$

where  $\sigma_{A_i}^2$  is the additive variance in environment  $i$  and  $r_A$  is the additive genetic correlation across environments. Cockerham (1963) and Itoh and Yamada (1990) extended Robertson's decomposition to  $n_e$  environments,

$$\sigma_{G \times E}^2 = \frac{1}{n_e - 1} \sum_j^{n_e} (\sigma_{A_j} - \bar{\sigma}_A)^2 + \frac{2}{n_e(n_e - 1)} \sum_{i < j}^{n_e} \sigma_{A_i} \sigma_{A_j} [1 - r_A(i, j)] \quad (38.1b)$$

**Key:** **differences in scale** and **lack of perfect correlation** over environments both generate  $G \times E$

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## Falconer: $G \times E$

- The modern treatment of  $G \times E$  starts with Falconer (1952)
  - Measures of the same trait in different environments are correlated traits
  - Hence, if measured in  $k$  environments, it's a  $k$ -dimensional trait
  - Thus results from direct and correlated responses apply to selection on  $G \times E$
- If selection in environment  $i$ , expected change in environment  $j$  is
  - $CR_j = i_i h_i h_j r_A \sigma_p(j)$

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# Hammond's Conjecture

- Hammond (1947) suggested that selection be undertaken in a more favorable environment to maximize progress in a less favorable one.
- Idea: perhaps more genetic variation, and hence greater discrimination between genotypes.
- Downside: don't know if  $\text{Var}(G)$  greater in "better" environments. Even if it is, between-environment correlation can be small.

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**Example 38.2.** Falconer and Latyszewski (1952) and Falconer (1960) selected for growth rate in mice in two nutritional environments (this work was also discussed in Example 30.7). In one environment, mice were housed individually and food was restricted to around 75% of normal intake, while in the other, mice were housed in groups of four to six and given unlimited food. Selection for increased weight gain was effective in both environments, although heritability was higher (0.29 to 0.20) in the restricted diet environment (although this difference was not significant). The higher heritability value arose because while the additive genetic variance was reduced in the poorer environment (by around 45%), the environmental variance was reduced even more (around 66%). Falconer suggested that this reduction in  $\sigma_e^2$  may be, in part, due to rearing single versus multiple individuals.

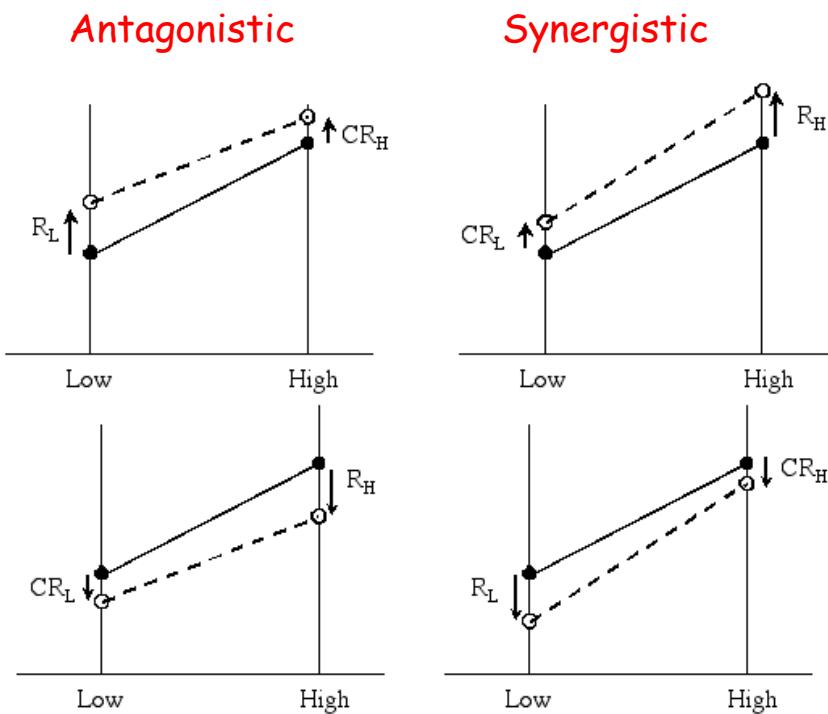
When the restricted-diet selected individuals were grown in the unrestricted environment, they showed a significant weight gain, but when the unrestricted-selected individuals were reared in the restricted diet environment, they did not. These results are a direct contradiction to Hammond's conjecture, in that selection in the *poorer* environment gave the larger response in the target population. Further, there were other significant differences. The high-feed selected lines contained around 24% more body fat than the restricted-diet lines when both were grown in the high-feed environment. Thus, selection in the restricted diet also resulted in leaner mice, which (in many cases) would also be economically favored in a selection program.

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# Jinks-Connolly rule

- Stability of the genotypic value over environments is a measure of  $G \times E$  sensitivity.
  - High stability = low sensitivity
- **Antagonistic  $G \times E$  selection**
  - Up-selecting in the bad environment
- **Synergistic  $G \times E$  selection**
  - Up-selecting in the good environment
- **Jinks-Connolly rule:**
  - Antagonistic selection improves stability (decreases environmental sensitivity), while synergistic selection decreases stability

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Slope = measure of sensitivity. Reducing the slope increases stability 16

While Jinks-Connolly suggests a general trend and is expected to hold more often than not, Falconer (1990) noted that a modification of this rule held in all 24 experimental cases he examined, namely that the *sensitivity is less after antagonistic selection than after synergistic selection*. Since the sensitivity is a slope, this means that the change in the numerator of Equation 38.5 is greater under antagonistic selection than under synergistic selection. When selecting to decrease a trait, this requires

$$(R_H - CR_L) - (CR_H - R_L) > 0 \quad (38.6a)$$

which rearranges to recover

$$R_H + R_L > CR_H + CR_L \quad (38.6b)$$

with this same condition holding for selection to increase a trait. Hence, for Falconer's modification to hold, the less restrictive assumption that the sum of the direct responses is greater than the sum of correlated responses must hold.

What about Falconer's (1989) suggestion that *mean performance* over the two environments is best improved by antagonistic selection? If the mean change is equally weighted in both environments, then when selecting to increase a trait, under antagonistic selection direct response occurs in the low environment, while under synergistic selection direct response occurs in the high environment. Thus, Falconer's (1989) suggestion holds when the average of the direct response in low and the correlated response in high exceeds the direct response in high and the correlated response in low,

$$R_L + CR_H > R_H + CR_L \quad (38.7a)$$

Assuming equal selection in both environments, then from Equation 38.3a, this reduces to

$$h_L (\sigma_{A_L} + r_A \sigma_{A_H}) > h_H (\sigma_{A_H} + r_A \sigma_{A_L}) \quad (38.7b)$$

Conversely, when selecting to decrease trait value, this condition becomes

$$R_H + CR_L > R_L + CR_H \quad (38.7c)$$

Note that Equations 38.7a and 38.7c are mutually exclusive, so that if antagonistic selection is better in one direction, it will be worse in the opposite direction. Thus, as Falconer (1990) pointed out, there is little theoretical justification for his earlier (1989) suggestion.

### The Cost to Response from $G \times E$

As a benchmark for selection when  $G \times E$  is present, if environmental structure is ignored and simple mass selection used (choosing the best performing individuals based solely on their phenotypic values), then the expected response becomes

$$R = \bar{t}\sigma_z h_z^2 = \bar{t} \frac{\sigma_A^2}{\sigma_z} = \bar{t} \frac{\sigma_A^2}{\sqrt{\sigma_G^2 + \sigma_{G \times E}^2 + \sigma_E^2}} \quad (38.9a)$$

where  $\sigma_G^2$  and  $\sigma_E^2$  are the genetic and environmental variances. When  $\sigma_{G \times E}^2$  is large relative to  $\sigma_A^2$ , the heritability is low and selection very inefficient, as an individual's phenotypic value in one environment is a poor predictor of their average breeding value over all environments. If we are selecting among clones (or pure lines) then  $\sigma_G^2$  replaces  $\sigma_A^2$ . Setting  $\sigma_{G \times E}^2$  to zero, Matheson and Cotterill (1990) note that the "cost" (loss of potential gain) of genotype-environment interaction when using standard mass selection is

$$1 - \sqrt{\frac{\sigma_G^2 + \sigma_E^2}{\sigma_G^2 + \sigma_{G \times E}^2 + \sigma_E^2}} \quad (38.9b)$$

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### Replication over environments can reduce effect of $G \times E$ in selection response

If members of the same genotype/line are replicated over  $n_e$  random environments, response to selection based on line (or family) means is

$$R = \bar{t} \frac{\sigma_G^2}{\sigma_z} = \bar{t} \frac{\sigma_G^2}{\sqrt{\sigma_G^2 + (\sigma_E^2 + \sigma_{G \times E}^2)/n_e + \sigma_e^2/(n_r n_e)}}$$

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# Estimating the GE term

- While GE can be estimated directly from the mean in a cell (i.e.,  $G_i$  in  $E_j$ ) we can usually get more information (and a better estimate) by considering the entire design and exploiting structure in the GE terms
- This approach also allows us to potentially predict the GE terms in specific environments
- Basic idea: replace  $GE_{ij}$  by  $\alpha_i\gamma_j$  or more generally by  $\sum_k \alpha_{ki}\gamma_{kj}$ . These are called biadditive or bilinear models. This (at first sight) seems more complicated. Why do this?
- With  $n_G$  genotypes and  $n_E$  environments, we have
  - $n_G n_E$  GE terms (assuming no missing values)
  - $n_G + n_E$   $\alpha_i$  and  $\gamma_j$  unique terms
  - $K(n_G + n_E)$  unique terms in  $\sum_k \alpha_{ki}\gamma_{kj}$ .
- Suppose 50 genotypes in 10 environments
  - 500 GE<sub>ij</sub> terms, 60 unique  $\alpha_i$  and  $\gamma_j$  terms, and (for k=3), 180 unique  $\alpha_{ki}$  and  $\gamma_{kj}$  terms.

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# Finlay-Wilkinson Regression

Also called a joint regression or regression on an environmental index.

Let  $\mu + G_i$  be the mean of the  $i$ th genotype over all environments, and  $\mu + E_j$  be the average yield of all genotypes in environment  $j$

$$\mu_{ij} = \mu + G_i + E_j(1 + \beta_i) + \delta_{ij}$$

The FW regression estimates  $GE_{ij}$  by the regression  $GE_{ij} = \beta_i E_j + \delta_{ij}$ . The regression coefficient is obtained for each genotype from the slope of the regression of the  $G_{ij}$  over the  $E_j$ .  $\delta_{ij}$  is the residual (lack of fit). If  $\sigma^2(GE) \gg \sigma^2(\delta)$ , then the regression accounted for most of the variation in GE.

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# Slope a stability measure

$$\mu_{ij} = \mu + G_i + E_j(1 + \beta_i) + \delta_{ij}$$

If  $\beta_i = -1$ , strong  $G \times E$ , with genotype  $i$  having identical performance over all environments (good and bad).

If  $\beta_i = 0$ , no  $G \times E$ .

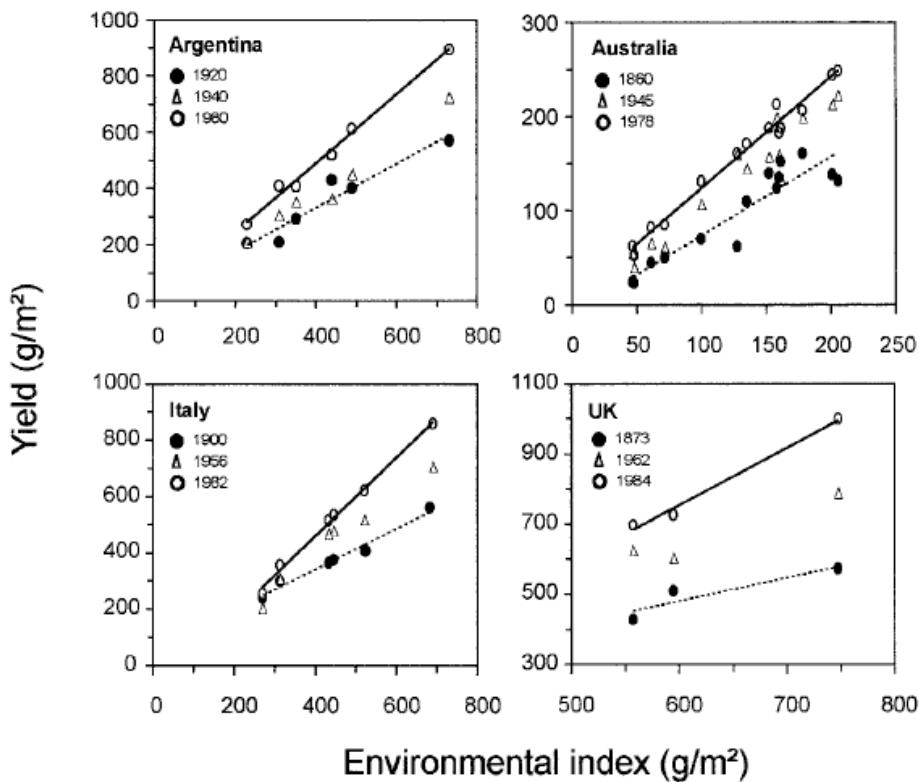
If  $\beta_i > 0$ ,  $G \times E$ , magnifying the effect of the environment. Over-performs in good environments, under-performs in bad environments.

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## Application

- Yield in lines of wheat over different environments was examined by Calderini and Slafer (1999). The lines examined were from different eras of breeding (for four different countries)
- Newer lines had larger values, but also had higher slopes (large  $\beta_i$  values), indicating less stability over mean environmental conditions than seen in older lines

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Regression slope for each genotype is  $\beta_i$

## SVD approaches

- In Finlay-Wilkinson, the  $GE_{ij}$  term was estimated by  $\beta_i E_j$ , where  $E_j$  was observed. We could also have used  $\gamma_j G_i$ , where  $\gamma_j$  is the regression of genotype values over the  $j$ -th environment. Again  $G_i$  is observable.
- Singular-value decomposition (SVD) approaches consider a more general approach, approximating  $GE_{ij}$  by  $\sum_k \alpha_{ki} \gamma_{kj}$  where the  $\alpha_{ki}$  and  $\gamma_{kj}$  are determined by the first  $k$  terms in the SVD of the matrix of GE terms.
- The SVD is a way to obtain the best approximation of a full matrix by some matrix of lower dimension.

### The Singular-Value Decomposition (SVD)

An  $n \times p$  matrix  $\mathbf{A}$  can always be decomposed as the product of three matrices: an  $n \times p$  diagonal matrix  $\mathbf{A}$  and two unitary matrices,  $\mathbf{U}$  which is  $n \times n$  and  $\mathbf{V}$  which is  $p \times p$ . The resulting **singular value decomposition (SVD)** of  $\mathbf{A}$  is given by

$$\mathbf{A}_{n \times p} = \mathbf{U}_{n \times n} \mathbf{A}_{n \times p} \mathbf{V}_{p \times p}^T \quad (39.16a)$$

We have indicated the dimensionality of each matrix to allow the reader to verify that each matrix multiplication conforms. The diagonal elements  $\lambda_1, \dots, \lambda_s$  of  $\mathbf{A}$  correspond to the **singular values** of  $\mathbf{A}$  and are ordered by decreasing magnitude. Returning to the unitary matrices  $\mathbf{U}$  and  $\mathbf{V}$ , we can write each as a row vector of column vectors,

$$\mathbf{U} = (\mathbf{u}_1, \dots, \mathbf{u}_i, \dots, \mathbf{u}_n), \quad \mathbf{V} = (\mathbf{v}_1, \dots, \mathbf{v}_i, \dots, \mathbf{v}_p) \quad (39.16b)$$

where  $\mathbf{u}_i$  and  $\mathbf{v}_i$  are  $n$  and  $p$ -dimensional column vectors (often called the **left** and **right singular vectors**, respectively). Since both  $\mathbf{U}$  and  $\mathbf{V}$  are unitary, by definition (Appendix 4) each column vector has length one and are mutually orthogonal (i.e., if  $i \neq j$ ,  $\mathbf{u}_i \mathbf{u}_j^T = \mathbf{v}_i \mathbf{v}_j^T = 0$ ). Since  $\mathbf{A}$  is diagonal, it immediately follows from matrix multiplication that we can write any element in  $\mathbf{A}$  as

$$A_{ij} = \sum_{k=1}^s \lambda_k u_{ik} v_{kj} \quad (39.16c)$$

where  $\lambda_k$  is the  $k$ th singular value and  $s \leq \min(p, n)$  is the number of non-zero singular values.

The importance of the singular value decomposition in the analysis of G  $\times$  E arises from the **Eckart-Young theorem** (1938), which relates the best approximation of a matrix by some lower-rank (say  $m$ ) matrix with the SVD. Define as our measure of goodness of fit between a matrix  $\mathbf{A}$  and a lower rank approximation  $\hat{\mathbf{A}}$  as the sum of squared differences over all elements,

$$\sum_{ij} (A_{ij} - \hat{A}_{ij})^2$$

Eckart and Young show that the best fitting approximation  $\hat{\mathbf{A}}$  of rank  $m < s$  is given from the first  $m$  terms of the singular value decomposition (the **rank-m SVD**),

$$\hat{A}_{ij} = \sum_{k=1}^m \lambda_k u_{ik} v_{kj} \quad (39.17a)$$

For example, the best rank-2 approximation for the G  $\times$  E interaction is given by

$$GE_{ij} \simeq \lambda_1 u_{i1} v_{j1} + \lambda_2 u_{i2} v_{j2} \quad (39.17b)$$

where  $\lambda_i$  is the  $i$ th singular value of the GE matrix,  $\mathbf{u}$  and  $\mathbf{v}$  are the associated singular vectors (see Example 39.3). The fraction of total variation of a matrix accounted for by taking the first  $m$  terms in its SVD is

$$\sum_{k=1}^m \lambda_k^2 / \sum_{ij} A_{ij}^2 = \frac{\lambda_1^2 + \dots + \lambda_m^2}{\lambda_1^2 + \dots + \lambda_s^2}$$

A data set for soybeans grown in New York (Gauch 1992) gives the GE matrix as

$$GE = \begin{pmatrix} 57 & 176 & -233 \\ -36 & -196 & 233 \\ -45 & -324 & 369 \\ -66 & 178 & -112 \\ 89 & 165 & -254 \end{pmatrix} \quad \text{Where } GE_{ij} = \text{value for Genotype } i \text{ in envir. } j$$

In R, the compact SVD (Equation 39.16d) of a matrix X is given by `svd(x)`, returning the SVD of GE as

$$\begin{pmatrix} 0.40 & 0.21 & 0.18 \\ -0.41 & 0.00 & 0.91 \\ -0.66 & 0.12 & -0.30 \\ 0.26 & -0.83 & 0.11 \\ 0.41 & 0.50 & 0.19 \end{pmatrix} \begin{pmatrix} 746.10 & 0 & 0 \\ 0 & 131.36 & 0 \\ 0 & 0 & 0.53 \end{pmatrix} \begin{pmatrix} 0.12 & 0.64 & -0.76 \\ 0.81 & -0.51 & -0.30 \\ 0.58 & 0.58 & 0.58 \end{pmatrix}$$

The first singular value accounts for  $746.10^2 / (746.10^2 + 131.36^2 + 0.53^2) = 97.0\%$  of the total variation of GE, while the second singular value accounts for 3.0%, so that together they account for essentially all of the total variation. The rank-1 SVD approximation of GE is given by setting all of the diagonal elements of A except the first entry to zero,

$$GE_1 = \begin{pmatrix} 0.40 & 0.21 & 0.18 \\ -0.41 & 0.00 & 0.91 \\ -0.66 & 0.12 & -0.30 \\ 0.26 & -0.83 & 0.11 \\ 0.41 & 0.50 & 0.19 \end{pmatrix} \begin{pmatrix} 746.10 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \begin{pmatrix} 0.12 & 0.64 & -0.76 \\ 0.81 & -0.51 & -0.30 \\ 0.58 & 0.58 & 0.58 \end{pmatrix}$$

Similarly, the rank-2 SVD is given by setting all but the first two singular values to zero,

$$GE_2 = \begin{pmatrix} 0.40 & 0.21 & 0.18 \\ -0.41 & 0.00 & 0.91 \\ -0.66 & 0.12 & -0.30 \\ 0.26 & -0.83 & 0.11 \\ 0.41 & 0.50 & 0.19 \end{pmatrix} \begin{pmatrix} 746.10 & 0 & 0 \\ 0 & 131.36 & 0 \\ 0 & 0 & 0 \end{pmatrix} \begin{pmatrix} 0.12 & 0.64 & -0.76 \\ 0.81 & -0.51 & -0.30 \\ 0.58 & 0.58 & 0.58 \end{pmatrix}$$

For example, the rank-1 SVD approximation for  $GE_{32}$  is  $g_{31}\lambda_1 e_{12} = 746.10 * (-0.66) * 0.64 = -315$

The rank-2 SVD approximation is  $g_{31}\lambda_1 e_{12} + g_{32}\lambda_2 e_{22} = 746.10 * (-0.66) * 0.64 + 131.36 * 0.12 * (-0.51) = -323$

Actual value is -324

Generally, the rank-2 SVD approximation for  $GE_{ij}$  is  $g_{i1}\lambda_1 e_{1j} + g_{i2}\lambda_2 e_{2j}$

# AMMI models

Additive main effects, multiplicative interaction (AMMI) models use the first m terms in the SVD of GE:

$$GE_{ij} = \sum_{k=1}^m \lambda_k \gamma_{ki} \eta_{kj} + \delta_{ij}$$

Giving

$$\mu_{ij} = \mu + G_i + E_j + \sum_{k=1}^m \lambda_k \gamma_{ki} \eta_{kj} + \delta_{ij}$$

AMMI is actually a **family** of models, with **AMMI<sub>m</sub>** denoting AMMI with the first m SVD terms.

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# AMMI models

$$\mu_{ij} = \mu + G_i + E_j + \sum_{k=1}^m \lambda_k \gamma_{ki} \eta_{kj} + \delta_{ij}$$

↑  
Fit main effects

Fit principal components

to the interaction term

(SVD is a generalization  
of PC methods)

$$GE_{ij} = \sum_{k=1}^m \lambda_k \gamma_{ki} \eta_{kj} + \delta_{ij}$$

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# Factorial Regressions

- While AMMI models attempt to extract information about how  $G \times E$  interactions are related across sets of genotypes and environments, factorial regressions incorporate **direct measures of environmental factors** in an attempt to account for the observed pattern of  $G \times E$ .
- The power of this approach is that if we can **determine which genotypes are more (or less) sensitive to which environmental features**, the breeder may be able to more finely tailor a line to a particular environment without necessarily requiring trials in the target environment.

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Suppose we have a series of  $m$  measured values from the environments of interest (such as average rainfall, maximum temperature, etc.) Let  $x_{kj}$  denote the value of the  $k$ -th environmental variable in environment  $j$

Factorial regressions model the GE term as the **sensitivity  $\zeta_{ki}$  of environmental value  $k$  to genotype  $i$** , (this is a regression slope to be estimated from the data)

$$GE_{ij} = \sum_{k=1}^m \zeta_{ki} x_{kj} + \delta_{ij}$$

Note that the Finlay-Wilkinson regression is a special case where  $m = 1$  and  $x_j$  is the mean trait value (over all genotypes) in that environment.

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Model	Interpretation
<b>Finlay-Wilkinson</b> $GE_{ij} = \beta_i(E_j - \mu) + \delta_{ij}$	$\beta_i$ = sensitivity of genotype $i$ to the average effect $E_j$ of the environment.
<b>AMMI</b> $GE_{ij} = \sum_{k=1}^m \lambda_k \gamma_{ki} \eta_{kj} + \delta_{ij}$	First $m$ terms of the SVD of the <b>GE</b> matrix $\lambda_k^2$ is the amount of variation explained by axis $k$ $\gamma_{ki}$ = sensitivity of genotype $i$ to environmental axis $k$ $\eta_{kj}$ = value of environment $j$ on the $k$ th environmental axis
<b>Factorial Regression</b> $GE_{ij} = \sum_{k=1}^m \zeta_{ki} x_{kj} + \delta_{ij}$	Modeling $G \times E$ using $m$ measured environmental factors $x_{kj}$ = value of $k$ th environmental factor in environment $j$ $\zeta_{ki}$ = sensitivity of genotype $i$ to $k$ th environmental factor
<b>Reduced rank Factorial Regression</b> $GE_{ij} = \sum_{k=1}^m \zeta_{ki} (\sum_p c_{kp} x_{pj}) + \delta_{ij}$	Modeling $G \times E$ based on a reduced dimensional set of the observed environmental factors by constructing $m$ combinations (axes) of these effects. $c_{kp}$ = loading of $p$ th environmental factor on axis $k$ . $\zeta_{ki}$ = sensitivity of genotype $i$ to $k$ th environmental combination (axis)
<b>AMMI using Reduced rank Factorial Regression</b> $GE_{ij} = \sum_k \lambda_k \gamma_{ki} (\sum_p c_{kp} x_{pj}) + \delta_{ij}$	The environmental axes $\eta_{kj}$ under AMMI are replaced by the environmental axes generated by linear combinations of measured environmental factors generated by a reduced rank factorial regression, with $\eta_{kj} = \sum_p c_{kp} x_{pj}$ .

## Mixed model analysis of $G \times E$

- Thus far, our discussion of estimating GE has been set in terms of fixed effects.
- Mixed models are a powerful alternative, as they easily handle missing data (i.e., not all combinations of  $G$  and  $E$  explored).
- As with all mixed models, key is the assumed covariance structure
  - Structured covariance models
    - Compound symmetry
    - Finlay-Wilkinson
    - **Factor-analytic** models (closely related to AMMI)

# Basic GxE Mixed model

- Typically, we assume either G or E is fixed, and the other random (making GE random)
- Taking E as fixed, basic model becomes
- $\mathbf{z} = \mathbf{X}\beta + \mathbf{Z}_1\mathbf{g} + \mathbf{Z}_2\mathbf{ge} + \mathbf{e}$ 
  - The vector  $\beta$  of fixed effects includes estimates of the  $E_j$ . The vector  $\mathbf{g}$  contains estimates of the  $G_i$  values, while the vector  $\mathbf{ge}$  contains estimates of all the  $GE_{ij}$ .
  - Typically we assume  $\mathbf{e} \sim \mathbf{0}, \sigma_e^2 \mathbf{I}$ , and independent of  $\mathbf{g}$  and  $\mathbf{ge}$ .
  - Models significantly differ on the variance/covariance structure of  $\mathbf{g}$  and  $\mathbf{ge}$ .

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## Example

We have two genotypes and three environments. Let  $z_{ijk}$  denote the k-th replicate of genotype i in environment j. Suppose we have single replicates of genotype 1 in all three environments, two replicates of genotype 2 in environment 1, and one in environment 3

$$\mathbf{z} = \begin{pmatrix} z_{111} \\ z_{121} \\ z_{131} \\ z_{211} \\ z_{212} \\ z_{231} \end{pmatrix}, \quad \beta = \begin{pmatrix} E_1^* \\ E_2^* \\ E_3^* \end{pmatrix}, \quad \mathbf{g} = \begin{pmatrix} G_1 \\ G_2 \end{pmatrix}, \quad \mathbf{ge} = \begin{pmatrix} GE_{11} \\ GE_{12} \\ GE_{13} \\ GE_{21} \\ GE_{22} \\ GE_{23} \end{pmatrix}, \quad \mathbf{e} = \begin{pmatrix} \epsilon_{111} \\ \epsilon_{121} \\ \epsilon_{131} \\ \epsilon_{211} \\ \epsilon_{212} \\ \epsilon_{231} \end{pmatrix}$$

Here  $E_i^* = \mu + E_i$ , with the  $E_i$  constrained to sum to zero. The resulting design matrices are

$$\mathbf{X} = \begin{pmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \\ 1 & 0 & 0 \\ 1 & 0 & 0 \\ 0 & 0 & 1 \end{pmatrix}, \quad \mathbf{Z}_1 = \begin{pmatrix} 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \end{pmatrix}, \quad \mathbf{Z}_2 = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{pmatrix}$$

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# Compound Symmetry assumption

- To proceed further on the analysis of the mixed model, we need covariance assumptions on  $\mathbf{g}$  and  $\mathbf{ge}$ .
- The compound symmetry assumption is
  - $\sigma^2(G_i) = \sigma_G^2$ ,  $\sigma^2(GE_{ij}) = \sigma_{GE}^2$
  - Under this assumption, the covariance of any genotype across any two (different) environments is the same.
  - Likewise, the genetic variance within any environment is constant across environments
  - Net result, the genetic covariance is the same between any two environments

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Under the compound symmetry assumption, the genetic variance and covariances become as follows:

Expected genetic variance within a given environment

$$\begin{aligned}\sigma(z_{ijk}, z_{ij\ell}) &= \sigma(G_i + GE_{ij}, G_i + GE_{ij}) \\ &= \sigma(G_i, G_i) + \sigma(GE_{ij}, GE_{ij}) \\ &= \sigma_G^2 + \sigma_{GE}^2\end{aligned}$$

Genetic covariance of the same genotype across environments

$$\sigma(z_{ij}, z_{ik}) = \sigma(G_i + GE_{ij}, G_i + GE_{ik}) = \sigma(G_i, G_i)$$

Genetic correlation across environments is constant

$$\rho_G = \frac{\sigma_G^2}{\sigma_G^2 + \sigma_{GE}^2}$$

For our example, the resulting covariance matrix becomes

$$\mathbf{V}_Z = \mathbf{Z}_1 \mathbf{V}_g \mathbf{Z}_1^T + \mathbf{Z}_2 \mathbf{V}_{ge} \mathbf{Z}_2^T + \mathbf{V}_e$$

$$\mathbf{V}_g = \sigma_G^2 \mathbf{I}_{2 \times 2}, \quad \mathbf{V}_{ge} = \sigma_{G \times E}^2 \mathbf{I}_{6 \times 6}, \quad \mathbf{V}_e = \sigma_e^2 \mathbf{I}_{6 \times 6} \quad 40$$

Mixed-model allows for missing values.

Under fixed-effect model, estimate of  $\mu_{ij} = \bar{z}_{ij}$ .

**BLUP estimates under mixed-model (E fixed, G random)**

Assuming equal number of replicates for each  $ij$  combination, the predicted yield  $\mu_{ij}$  given an observed mean of  $z_{ij}$  is given by

$$\begin{aligned}\text{BLUP}(\mu_{ij}) &= \bar{z}_{\cdot j} + h_G^2(\bar{z}_{i\cdot} - \bar{z}_{\cdot\cdot}) + h_{GE}^2(z_{ij} - \bar{z}_{\cdot j} - \bar{z}_{i\cdot} + \bar{z}_{\cdot\cdot}) \\ &= \hat{\mu} + \hat{E}_j + h_G^2 \hat{G}_i + h_{GE}^2 \hat{GE}_{ij}\end{aligned}$$

where for  $n_e$  environments, the repeatability of genetic effects and interactions, are respectively,

$$h_G^2 = \frac{\sigma_{GE}^2 + n_e \sigma_G^2}{\sigma_{GE}^2 + n_e \sigma_G^2 + \sigma_e^2}, \quad h_{GE}^2 = \frac{\sigma_{GE}^2}{\sigma_{GE}^2 + \sigma_e^2}$$

Contrasting the estimated cell mean under LS (given by the observed sample mean  $z_{ij}$ ) with the predicted cell means under BLUP shows how BLUP shrinks the contributions from the two random effects ( $G_i$ ,  $GE_{ij}$ ).

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**BLUP shrinks (regresses) the BLUE estimate back towards zero**

$$h_G^2 = \frac{\sigma_{GE}^2 + n_e \sigma_G^2}{\sigma_{GE}^2 + n_e \sigma_G^2 + \sigma_e^2}, \quad h_{GE}^2 = \frac{\sigma_{GE}^2}{\sigma_{GE}^2 + \sigma_e^2}$$

In particular, the BLUP contribution of the genotypic effect is  $h_G^2 \hat{G}_i$ , which is a shrinkage of the BLUE estimate  $\hat{G}_i$  back to its mean (zero). The same is true for the  $G \times E$  effect. The amount of shrinkage is proportional to the lack of repeatability of these two contributions. If  $h^2$  is near one, there is very little shrinkage, while if  $h^2$  is near zero, its contribution is shrunk back towards nearly zero. An informal (but helpful) way of thinking about shrinkage is that the coefficient of shrinkage is the ratio of signal over signal plus noise, and is a measure of the “borrowing strength” from correlated observations. If there is little such information, there is much more noise than signal, and the resulting shrinkage is considerable, while if there is a strong signal, there is little shrinkage.

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# Modification of the residual covariance

Under compound symmetry, all the covariance matrices are a variance component times an identity matrix. More realistic models replace these simple matrices with more complex ones. We could allow residual variances to vary over lines [ $\sigma^2(\epsilon_{ijk}) = \sigma^2_{e_4}$ ] or environments [ $\sigma^2(\epsilon_{ijk}) = \sigma^2_{e_j}$ ], in which case  $\mathbf{V}_e$  becomes a diagonal matrix with the diagonal the appropriate residual variance component (e.g., Cullis et al. 1996). For our hypothetical design, if residual variances are genotype-dependent,

$$\mathbf{V}_e = \text{diagonal}(\sigma^2_{e_1}, \sigma^2_{e_1}, \sigma^2_{e_1}, \sigma^2_{e_2}, \sigma^2_{e_2}, \sigma^2_{e_2})$$

while if they are environment-dependent

$$\mathbf{V}_e = \text{diagonal}(\sigma^2_{e_1}, \sigma^2_{e_2}, \sigma^2_{e_3}, \sigma^2_{e_1}, \sigma^2_{e_1}, \sigma^2_{e_3})$$

Again, these can be estimated via REML. Another modification is when pedigree information exists on the genotypes, in which case  $\mathbf{V}_g$  may have off-diagonal elements reflecting relationships among genotypes (Crossa et al. 2006, Oakey et al. 2007, Piepho et al. 2008). Finally, one can allow for differential correlations among genotype-environment interactions by suitably modifying  $\mathbf{V}_{ge}$ , a point we develop in detail shortly.

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# Extending genetic covariances

- **Shukla's model:** starts with the compound symmetry model, but allows for different  $G \times E$  variances over genotypes,
  - $GE_{ij} \sim N(0, \sigma^2_{G_iE})$
  - $G_i \sim N(0, \sigma_G^2)$
  - $\text{Cov}(ge) = \text{Diagonal}(\sigma^2_{G_1E}, \dots, \sigma^2_{G_nE})$
  - The covariance of a genotype across environments is still  $\sigma_G^2$
- **Structured covariance models** allow more complicated (and more general) covariance matrices

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# Covariances based on Finlay-Wilkinson

$$z_{ijk} = \mu + G_i + (1 + \beta_i)E_j + \delta_{ij} + \epsilon_{ijk}$$

Previously we analyzed this model assuming a fixed-effects framework. Digby (1979) showed that one could use an iterative least-squares approach to accommodate missing data (certain genotype-environment combinations are missing). This is reasonable, as one can borrow information from other observations in an attempt to predict the missing observation. Suppose that line five was not measured in environment three. Data from the other genotypes can be used to estimate  $E_3$  while observations on genotype five from other environments can be used to estimate  $\beta_5$ , with  $GE_{53}$  being estimated by  $(1 + \beta_5)E_3$ . This shows how information can be borrowed from other observations under this model by using correlations between observations. In a mixed-model framework, such information borrowing occurs through the covariance matrix associated with the vector of random effects.

We treat  $G_i$  and  $\beta_i$  as fixed effects,  $\delta_{ij}$  and  $\epsilon_{ijk}$  as random (fixed genetic effects, random environmental effects)

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Assume that the environmental effect, regression deviation, and residual error are all independent random effects and have constant variances,

$$E_j \sim N(0, \sigma_E^2), \quad \delta_{ij} \sim N(0, \sigma_\delta^2), \quad \epsilon_{ijk} \sim N(0, \sigma_\epsilon^2)$$

Hence,

$$\sigma(E_j, E_\ell) = \begin{cases} 0 & j \neq \ell \\ \sigma_E^2 & j = \ell \end{cases}, \quad \sigma(\delta_{ij}, \delta_{k\ell}) = \begin{cases} 0 & ij \neq k\ell \\ \sigma_\delta^2 & ij = k\ell \end{cases}$$

The variance of the trait value from an individual from line  $i$  randomly drawn across environments is

$$\sigma^2(z_{ijk}) = (1 + \beta_i)^2 \sigma_E^2 + \sigma_\delta^2 + \sigma_\epsilon^2$$

Peipho (1997a) notes that the regression residual and normal residual variances (if both homoscedastic) cannot be separately estimated and hence can be combined into a single general residual variance. The covariance between two different genotypes ( $i$  and  $k$ ) in the same environment ( $j$ ) similarly becomes

$$\begin{aligned} \sigma^2(z_{ij}, z_{kj}) &= \sigma[(1 + \beta_i)E_j + \delta_{ij}, (1 + \beta_k)E_j + \delta_{kj}] \\ &= (1 + \beta_i)(1 + \beta_k)\sigma_E^2 \end{aligned}$$

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Let  $\mathbf{z}_j$  be a vector of observations of the line means within environment  $j$  (for simplification we assume a single observation, but multiple, and unequal, replication is easily accommodated by modification of  $\mathbf{V}_e$ ). In matrix form, the covariance matrix for  $\mathbf{z}_j$  is

$$\mathbf{V}_{\mathbf{z}_j} = \sigma_E^2 \boldsymbol{\lambda} \boldsymbol{\lambda}^T + (\sigma_\delta^2 + \sigma_e^2) \mathbf{I}, \quad \text{where } \boldsymbol{\lambda} = \begin{pmatrix} 1 + \beta_1 \\ \vdots \\ 1 + \beta_{n_g} \end{pmatrix}$$

Observe that the assumed structure of the Finlay-Wilkinson model translates underlying independent random effects ( $E$ ,  $\delta$ ) into correlated effects across the vector  $\mathbf{z}$  of observations. This is a simple example of a **factor-analytic covariance structure** where the covariance structure is determined by a small number of interacting factors.

**Factor-analytic covariance structures** allow one to consider more general covariance structures informed by the data, rather than assumed by the investigator.

Piepho (1997a) and Denis et al. (1997) showed how this general framework can be extended to cases (e.g., Shulka 1972) where the lines have different variances,

$$\mathbf{V}_{\mathbf{z}_j} = \sigma_E^2 \boldsymbol{\lambda} \boldsymbol{\lambda}^T + \text{diag}(\sigma_{\delta_1}^2, \dots, \sigma_{\delta_{n_g}}^2) + \sigma_e^2 \mathbf{I}$$

Likewise much more general covariance structures for the residuals can be incorporated,

$$\mathbf{V}_{\mathbf{z}_j} = \sigma_E^2 \boldsymbol{\lambda} \boldsymbol{\lambda}^T + \text{diag}(\sigma_{\delta_1}^2, \dots, \sigma_{\delta_{n_g}}^2) + \mathbf{V}_e$$

## AMMI-based structured covariance models

The same logic used to generate a mixed-model Finlay-Wilkinson regression easily extends to other biadditive models, such as AMMI. The AMMI<sub>m</sub> model is given by

$$\begin{aligned} z_{ij\ell} &= \mu + G_i + E_j + \sum_{k=1}^m \lambda_k \gamma_{ki} \eta_{kj} + \delta_{ij} + \epsilon_{ij\ell} \\ &= \mu + G_i + E_j + \sum_{k=1}^m w_{ki} v_{kj} + \epsilon_{ij\ell}^* \end{aligned}$$

The second line simplifies the AMMI model (to allow for estimability) in two ways. First, the singular value  $\lambda_k$  is absorbed into the genotype sensitivity ( $w_{ki}$ ) and environmental ( $v_{kj}$ ) coefficients. Second, the error in predicting GE from the AMMI approximation ( $\delta_{ij}$ ) and the model residual ( $\epsilon_{ij\ell}$ ) are combined into a single residual  $\epsilon_{ij\ell}^*$ . Assume genotypes are random and environments are fixed, so that  $E_j$  and  $v_{kj}$  are fixed, while  $G_i$  and  $w_{ki}$  are random (as is, of course,  $\epsilon_{ij\ell}^*$ ). Assume these underlying components are independent and homoscedastic,

$$G_i \sim N(0, \sigma_G^2), \quad w_{ki} \sim N(0, \sigma_k^2), \quad \epsilon_{ijk}^* \sim N(0, \sigma_e^2 + \sigma_\delta^2)$$

The resulting variance for the trait value of a random individual drawn from environment  $j$  becomes

$$\sigma^2(z_{ijk}) = \sigma_G^2 + \sum_{k=1}^m \sigma_k^2 v_{kj}^2 + \sigma_\delta^2 + \sigma_e^2 c$$

Hence, the resulting genetic variance in environment  $j$  is just

$$\sigma^2(z_{ij}) = \sigma_G^2 + \sum_{k=1}^m \sigma_k^2 v_{kj}^2 + \sigma_\delta^2$$

Likewise, the covariance between the same random genotype over different environments ( $j$  and  $\ell$ ) becomes

$$\begin{aligned}\sigma^2(z_{ij}, z_{i\ell}) &= \sigma \left( G_i + \sum_{k=1}^m w_{ki} v_{kj}, G_i + \sum_{k=1}^m w_{ki} v_{k\ell} \right) \\ &= \sigma_G^2 + \sum_{k=1}^m \sigma(w_{ki} v_{kj}, w_{ki} v_{k\ell}) = \sigma_G^2 + \sum_{k=1}^m v_{kj} v_{k\ell} \sigma(w_{ki}, w_{ki}) \\ &= \sigma_G^2 + \sum_{k=1}^m \sigma_k^2 v_{kj} v_{k\ell}\end{aligned}$$

The resulting covariance matrix for the vector  $\mathbf{z}_i$  of observations of genotypes over the  $n_e$  environments can be written in the form

$$\mathbf{V}_{\mathbf{z}_i} = \sigma_G^2 \mathbf{J} + \lambda \boldsymbol{\lambda}^T + \sigma_e^2 \mathbf{I}$$

where  $\mathbf{J}$  is a matrix of ones, and  $\boldsymbol{\lambda}$  is the  $n_e \times m$  matrix,

$$\boldsymbol{\lambda} = (\lambda_1 \quad \cdots \quad \lambda_m), \quad \text{where } \lambda_k = \sigma_k^2 \begin{pmatrix} v_{k1} \\ \vdots \\ v_{kn_e} \end{pmatrix} = \begin{pmatrix} \lambda_{k1} \\ \vdots \\ \lambda_{kn_e} \end{pmatrix}$$

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## Summary: Structured Covariance models

	$G$ random, $E$ Fixed		$E$ random, $G$ Fixed	
$\sigma^2(z_{ij})$	$\sigma(z_{ij}, z_{ik})$		$\sigma^2(z_{ij})$	$\sigma(z_{ij}, z_{kj})$
Index range	$1 \leq j \leq n_e$	$1 \leq k, j \leq n_e$	$1 \leq i \leq n_g$	$1 \leq i, k \leq n_g$
C	$\sigma_G^2 + \sigma_{GE}^2$	$\sigma_G^2$	$\sigma_E^2 + \sigma_{GE}^2$	$\sigma_E^2$
S	$\sigma_G^2 + \sigma_{GE_j}^2$	$\sigma_G^2$	$\sigma_E^2 + \sigma_{G_E}^2$	$\sigma_E^2$
FW	$\sigma_G^2 + E_j^2 \sigma_\beta^2 + \sigma_{\delta_j}^2$	$\sigma_G^2 + E_j E_k \sigma_\beta^2$	$\alpha_i^2 \sigma_E^2 + \sigma_{\delta_i}^2$	$\alpha_i \alpha_k \sigma_E^2$
FA(m)	$\sigma_G^2 + \sum_\ell^m \lambda_{\ell j}^2$	$\sigma_G^2 + \sum_\ell^m \lambda_{\ell j} \lambda_{\ell k}$	$\sigma_E^2 + \sum_\ell^m \lambda_{\ell i}^2$	$\sigma_E^2 + \sum_\ell^m \lambda_{\ell i} \lambda_{\ell k}$
U	$\sigma_j^2$	$\sigma_{jk}$	$\sigma_i^2$	$\sigma_{ik}$

Summary the covariance structures for various mixed-models for  $G \times E$ . When  $G$  is taken as random with  $E$  fixed,  $\sigma^2(z_{ij})$  is genetic variance in environment  $j$ , while  $\sigma(z_{ij}, z_{ik})$  is the covariance between a random genotype ( $i$ ) measured in environments  $j$  and  $k$ . When  $E$  taken as random,  $\sigma^2(z_{ij})$  corresponds to the variance for an individual from genotype  $i$  drawn from a random environment, while  $\sigma(z_{ij}, z_{kj})$  is the covariance between genotypes  $i$  and  $k$  when measured in across a random environment ( $j$ ). C corresponds to the Compound Symmetry model, S is Shukla's extension, FW is Finlay-Wilkinson where  $\alpha_i = 1 + \beta_i$ , FA(m) is factor-analytic model (i.e., a mixed AMMI-type model) with  $m$  factors, U is the completely Unstructured model.

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## Indirect Genetic Effects

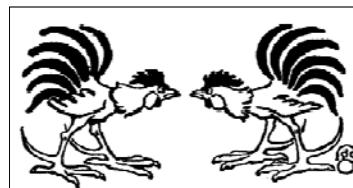
- Inherited Genetic effect of one animals measured another
- Examples
  - Mothering ability
    - Maternal Care
    - Maternal Nutrition
  - Social interactions
    - Competition
    - Mutualism
    - Pack behavior



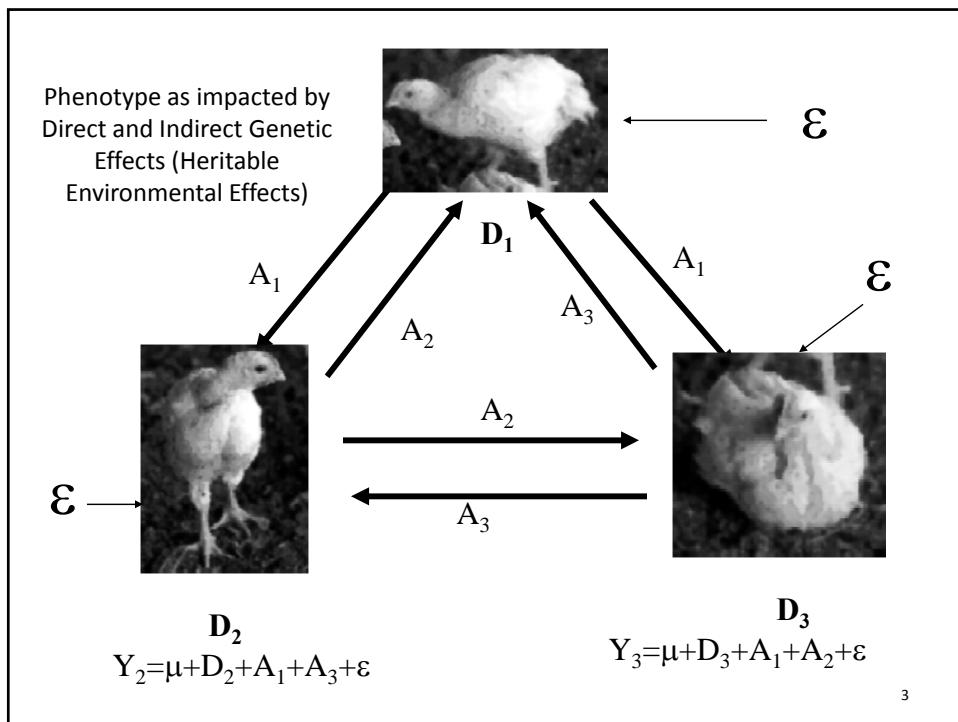
1

## Social Effects Interacting Genotypes

Animals



2



## Mixed Model Equations

$$\mathbf{Y} = \mathbf{X}\beta + \mathbf{Z}_d\boldsymbol{\mu}_d + \mathbf{Z}_a\boldsymbol{\mu}_a + \varepsilon$$

Muir and Schinckel (2002)

$$\mathbf{Y} = \mathbf{X}\beta + \mathbf{Z}_d\boldsymbol{\mu}_d + \mathbf{Z}_a\boldsymbol{\mu}_a + \varepsilon$$

Include correlated residual in R matrix

$$\mathbf{Y} = \mathbf{X}\beta + \mathbf{Z}_d\boldsymbol{\mu}_d + \mathbf{Z}_a\boldsymbol{\mu}_a + \mathbf{Z}_c\boldsymbol{\mu}_c + e$$

Random effect for shared group

Bijma, P., Muir, W. M., Ellen, E. D., Wolf, J. B., & Van Arendonk, J. A. M. 2007

## Variances

$$\mathbf{K} = \begin{bmatrix} k_1 & k_2 \\ k_2 & k_3 \end{bmatrix} = \sigma_e^2 \begin{bmatrix} \sigma_d^2 & \sigma_{ad} \\ \sigma_{ad} & \sigma_a^2 \end{bmatrix}^{-1}$$

$\sigma_d^2$  Additive Direct Effects

$\sigma_a^2$  Additive Associate Effects

$\sigma_{ad}$  Covariance Between Additive Direct and Additive Associate Effects

$\sigma_E^2$  Environmental

```

graph TD
    sigmaE2[σ_E²] --> sigmaC2[σ_c²]
    sigmaE2 --> sigmaE2[σ_e²]
    sigmaC2 --- BG[Between Group]
    sigmaE2 --- WG[Within Group]
  
```

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## MME with correlated residuals

$$\begin{bmatrix} X'R^{-1}X & X'R^{-1}Z_d & X'R^{-1}Z_a \\ Z_d R^{-1}X' & Z_d R^{-1}Z_d + s_1 A^{-1} & Z_d R^{-1}Z_a + s_2 A^{-1} \\ Z_a R^{-1}X' & Z_a R^{-1}Z_d + s_2 A^{-1} & Z_a R^{-1}Z_a + s_3 A^{-1} \end{bmatrix} \begin{bmatrix} \beta \\ \mu_d \\ \mu_a \end{bmatrix} = \begin{bmatrix} X'R^{-1}X \\ X'R^{-1}Z_d \\ X'R^{-1}Z_a \end{bmatrix}$$

$$\mathbf{R} = (\sigma_c^2 + \sigma_e^2) \begin{bmatrix} 1 & \rho & \rho & \cdots & 0 & 0 & 0 \\ \rho & 1 & \rho & \cdots & 0 & 0 & 0 \\ \rho & \rho & 1 & \cdots & 0 & 0 & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots & \vdots \\ 0 & 0 & 0 & \cdots & 1 & \rho & \rho \\ 0 & 0 & 0 & \cdots & \rho & 1 & \rho \\ 0 & 0 & 0 & \cdots & \rho & \rho & 1 \end{bmatrix} \begin{bmatrix} S_1 & S_2 \\ S_2 & S_3 \end{bmatrix} = \begin{bmatrix} \sigma_d^2 & \sigma_{ad} \\ \sigma_{ad} & \sigma_a^2 \end{bmatrix}^{-1}$$

$\rho$  = intra-class environmental correlation

$$\rho = \frac{\sigma_c^2}{\sigma_c^2 + \sigma_e^2}$$

Note if  $\rho < 0$ , then then

$$\sigma_c^2 < 0$$

6

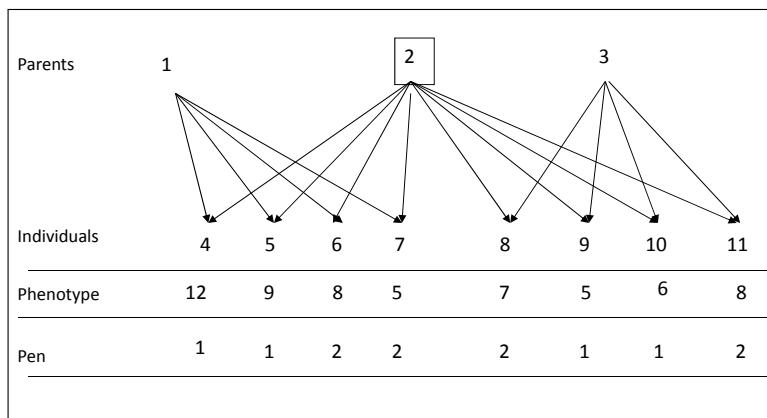
## MME with random effect for shared environmental effect

$$\begin{bmatrix} \mathbf{X}'\mathbf{X} & \mathbf{X}'\mathbf{Z}_D & \mathbf{X}'\mathbf{Z}_A & \mathbf{X}'\mathbf{Z}_c \\ \mathbf{Z}_D'\mathbf{X} & \mathbf{Z}_D'\mathbf{Z}_D + \mathbf{A}^{-1}\mathbf{k}_{11} & \mathbf{Z}_D'\mathbf{Z}_A + \mathbf{A}^{-1}\mathbf{k}_{12} & \mathbf{Z}_D'\mathbf{Z}_c \\ \mathbf{Z}_A'\mathbf{X} & \mathbf{Z}_A'\mathbf{Z}_D + \mathbf{A}^{-1}\mathbf{k}_{21} & \mathbf{Z}_A'\mathbf{Z}_A + \mathbf{A}^{-1}\mathbf{k}_{22} & \mathbf{Z}_A'\mathbf{Z}_c \\ \mathbf{Z}_c'\mathbf{X} & \mathbf{Z}_c'\mathbf{Z}_D & \mathbf{Z}_c'\mathbf{Z}_A & \mathbf{Z}_c'\mathbf{Z}_c + \mathbf{I}k_{33} \end{bmatrix} \begin{bmatrix} \hat{\mathbf{b}} \\ \boldsymbol{\mu}_d \\ \boldsymbol{\mu}_a^s \\ \boldsymbol{\mu}_a^e \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{y} \\ \mathbf{Z}_D'\mathbf{y} \\ \mathbf{Z}_A'\mathbf{y} \\ \mathbf{Z}_c'\mathbf{y} \end{bmatrix}$$

$$\mathbf{K} = \begin{bmatrix} k_1 & k_2 \\ k_2 & k_3 \end{bmatrix} = \sigma_\varepsilon^2 \begin{bmatrix} \sigma_D^2 & \sigma_{ad} \\ \sigma_{ad} & \sigma_a^2 \end{bmatrix}^{-1} \quad k_{33} = \sigma_\varepsilon^2 / \sigma_c^2$$

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## Example



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Associative Genetic Matrix

Sir	Da	Anim	Pen	Y
2	1	4	1	12
2	1	5	1	9
2	1	6	2	8
2	1	7	2	5
2	3	8	2	7
2	3	9	1	5
2	3	10	1	6
2	3	11	2	8

Animal

$$Z_a = \begin{bmatrix} 1 & 2 & 3 & \xrightarrow{4} & 5 & 6 & 7 & 8 & 9 & 10 & 11 \\ 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 1 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 1 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 & 1 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & 1 & 1 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & 1 & 1 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 1 & 0 & 0 & 0 \end{bmatrix}$$

Who was in the same pen as animal 4

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## Genetic Parameters

$$\sigma_e^2 \begin{bmatrix} \sigma_d^2 & \sigma_{ad}^2 \\ \sigma_d^2 & \sigma_a^2 \end{bmatrix} = 60 \begin{bmatrix} 30 & -4 \\ -4 & 10 \end{bmatrix}$$

$$\sigma_c^2 = 6$$

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## R code Example 10

```

Y=matrix(c( 12,      X=matrix(c(
1,      1,
9,      1,
8,      1,
5,      1,
7,      1,
5,      1,
6,      1,
8),8,1)           1,      1,
                           0, 1, 0, .5, .5, .5, .5, 0, 0, 0, 0,
                           0, 0, 1, 0, 0, 0, 0, 0, .5, .5, .5, .5,
                           .5, .5, 0, 1, .5, .5, .5, .25, .25, .25, .25,
                           .5, .5, 0, .5, 1, .5, .5, .25, .25, .25, .25,
                           .5, .5, 0, .5, .5, 1, .5, .25, .25, .25, .25,
                           .5, .5, 0, .5, .5, 1, .25, .25, .25, .25,
                           0, .5, .5, .25, .25, .25, .25, 1, .5, .5, .5,
                           0, .5, .5, .25, .25, .25, .25, .5, .5, 1, .5,
                           0, .5, .5, .25, .25, .25, .25, .5, .5, 1, 11,11)
A=matrix(c(
1, 0, 0, .5, .5, .5, .5, 0, 0, 0, 0,
0, 1, 0, .5, .5, .5, .5, .5, .5, .5, .5,
0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0,
.5, .5, 0, 1, .5, .5, .5, .25, .25, .25, .25,
.5, .5, 0, .5, 1, .5, .5, .25, .25, .25, .25,
.5, .5, 0, .5, .5, 1, .25, .25, .25, .25,
0, .5, .5, .25, .25, .25, .25, 1, .5, .5, .5,
0, .5, .5, .25, .25, .25, .25, .5, .5, 1, .5,
0, .5, .5, .25, .25, .25, .25, .5, .5, 1, 11,11)
ZD=matrix(c(
0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0,
0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0,
0, 0, 0, 0, 1, 0, 0, 0, 0, 0,
0, 0, 0, 0, 0, 1, 0, 0, 0, 0,
0, 0, 0, 0, 0, 0, 1, 0, 0, 0,
0, 0, 0, 0, 0, 0, 0, 1, 0, 0,
0, 0, 0, 0, 0, 0, 0, 0, 1, 0,
0, 0, 0, 0, 0, 0, 0, 0, 0, 1,
0, 0, 0, 0, 0, 0, 0, 0, 0, 0,
,8,11,byrow=TRUE)           ZA=matrix(c(
0, 0, 0, 0, 1, 0, 0, 0, 1, 1, 0,
0, 0, 0, 1, 0, 0, 0, 0, 1, 1, 0,
0, 0, 0, 0, 0, 1, 1, 0, 0, 1,
0, 0, 0, 0, 1, 0, 1, 0, 0, 1,
0, 0, 0, 0, 1, 1, 0, 0, 0, 1,
0, 0, 0, 1, 1, 0, 0, 0, 1, 0,
0, 0, 0, 1, 1, 0, 0, 0, 0, 1,
0, 0, 0, 0, 1, 1, 0, 0, 0, 0,
,8,11,byrow=TRUE)           ZC=matrix(c(
1, 0,
1, 0,
0, 1,
0, 1,
0, 1,
0, 1,
0, 1,
0, 1,
,8,2,byrow=TRUE)

```

11

```

Sig_d=30
Sig_a=10
Sig_ad=-4
Sig_e=60
Sig_c=6
N=8
P=matrix(c(Sig_d, Sig_ad,
           Sig_ad, Sig_a),2,2)
K=solve(P)*Sig_e
AINV=solve(A)
I2=matrix(c(1,0,
           0,1),2,2)
K33=Sig_e/Sig_c
LHS= rbind(
cbind(t(X)%*%X, t(X)%*%ZD, t(X)%*%ZA, t(X)%*%ZC),
cbind(t(ZD)%*%X, t(ZD)%*%ZD+AINV*K[1,1],t(ZD)%*%ZA+AINV*K[1,2], t(ZD)%*%ZC),
cbind(t(ZA)%*%X, t(ZA)%*%ZD+AINV*K[2,1], t(ZA)%*%ZA+AINV*K[2,2], t(ZA)%*%ZC),
cbind(t(ZC)%*%X, t(ZC)%*%ZD, t(ZC)%*%ZA, t(ZC)%*%ZC+I2*K33))

```

12

```

RHS=matrix(rbind(
  t(X) %*% Y,
  t(ZD) %*% Y,
  t(ZA) %*% Y,
  t(ZC) %*% Y))
C=solve(LHS)
BU=C %*% RHS
RMSE=(t(Y) %*% Y-t(BU)%*% RHS)*(1/(N-2))
BU
[1,] 7.500000e+00
[2,] 5.151515e-01
[3,] -6.085976e-15
[4,] -5.151515e-01
[5,] 1.027597e+00
[6,] 4.204545e-01
[7,] 3.522727e-01
[8,] -2.548701e-01
[9,] -2.180736e-01
[10,] -7.570346e-01
[11,] -5.546537e-01
[12,] -1.569264e-02
[13,] -2.121212e-01
[14,] 5.988626e-015
[15,] 2.121212e-01
[16,] -3.598485e-01
[17,] -1.098485e-01
[18,] -2.083333e-01
[19,] 4.166667e-02
[20,] 2.651515e-02
[21,] 3.750000e-01
[22,] 2.916667e-01
[23,] -5.681818e-02
[24,] 9.090909e-02
[25,] -9.090909e-02

```

13

## Estimates

$$\hat{\mathbf{u}} = 7.5$$

Individual	Direct Genetic ( $u_d$ )	Indirect Genetic ( $u_a$ )	Cage Effect
1	0.515152	-0.21212	0.090909
2	-2.40E-15	3.37E-15	-0.09091
3	-0.51515	0.212121	
4	1.027597	-0.35985	
5	0.420455	-0.10985	
6	0.352273	-0.20833	
7	-0.25487	0.041667	
8	-0.21807	0.026515	
9	-0.75704	0.375	
10	-0.55465	0.291667	
11	-0.01569	-0.05682	

Note animal with best  
direct effect has worst  
associative effect

14

## Index Selection

$$I = b_1 \hat{\mu}_d + b_2 \hat{\mu}_a$$

The total breeding value (TBV) is the sum  
of the direct and all IGE effects

$$TBV = \hat{\mu}_d + (n - 1) \hat{\mu}_a$$

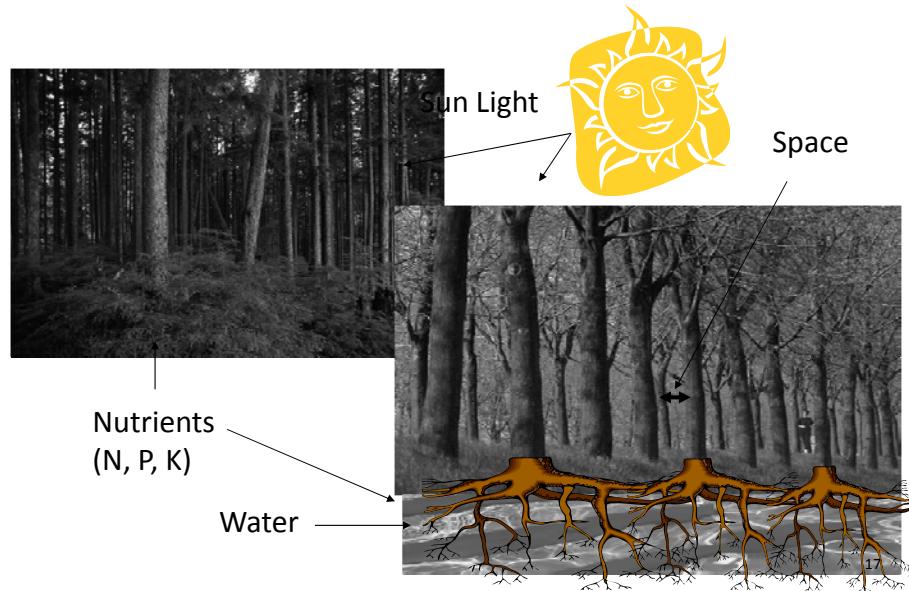
15

## Competitive Effects in Tree Breeding Programs Competition by Distance

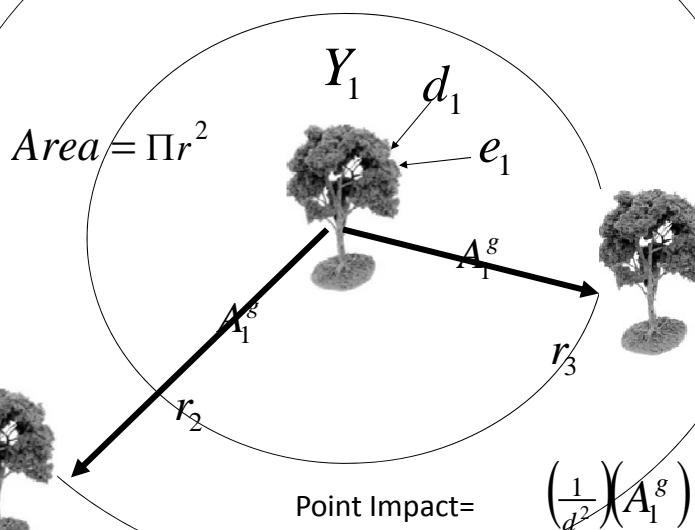


16

## Trees Compete For Limited Resources

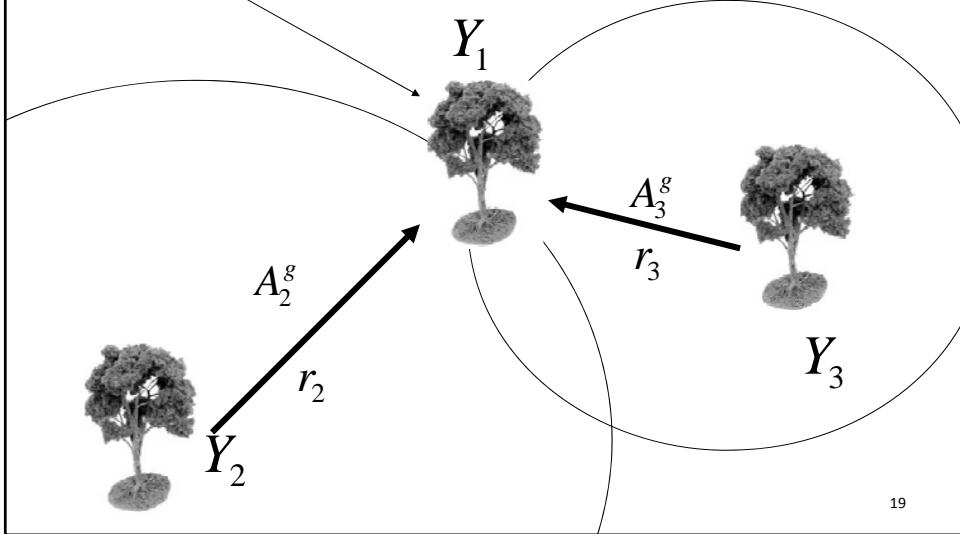


## Circle of Influence



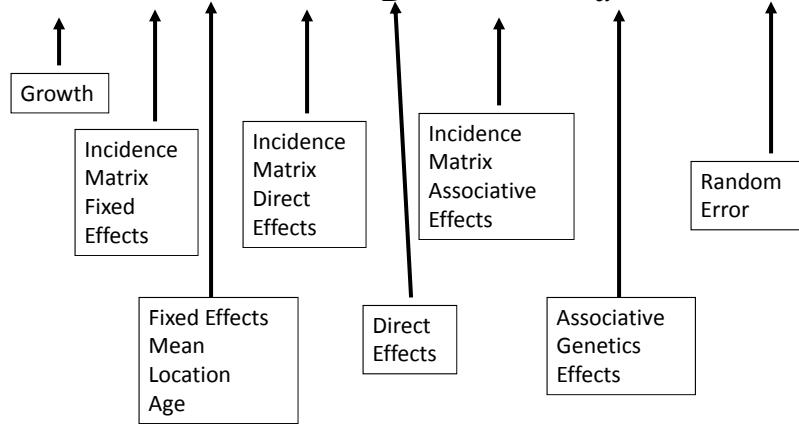
### Interacting Genotype Model

$$Y_1 = \mu + D_1 + \left( \frac{1}{d_2^2} \right) A_2^g + \left( \frac{1}{d_3^2} \right) A_3^g + \varepsilon$$



### Mixed Model Equations

$$\mathbf{Y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}_D D + \mathbf{Z}_a a + \varepsilon$$



## Associative Effects Incidence Matrix

$$\mathbf{Z}_{A^g} = \begin{bmatrix} 0 & \frac{1}{d_2^2} & \frac{1}{d_3^2} \\ \frac{1}{d_2^2} & 0 & \frac{1}{d_4^2} \\ \frac{1}{d_3^2} & \frac{1}{d_4^2} & 0 \end{bmatrix}$$

21

## MME Competition

$$\begin{bmatrix} X'R^{-1}X & X'R^{-1}Z_d & X'R^{-1}Z_a \\ Z_d'R^{-1}X & Z_d'R^{-1}Z_d + s_1 A^{-1} & Z_d'R^{-1}Z_a + s_2 A^{-1} \\ Z_a'R^{-1}X & Z_a'R^{-1}Z_d + s_2 A^{-1} & Z_a'R^{-1}Z_a + s_3 A^{-1} \end{bmatrix} \begin{bmatrix} \beta \\ \mu_d \\ \mu_a \end{bmatrix} = \begin{bmatrix} X'R^{-1}X \\ X'R^{-1}Z_d \\ X'R^{-1}Z_a \end{bmatrix}$$

$\mathbf{A}^{-1}$       Inverse of Additive  
Relationship Matrix

$$\begin{bmatrix} s_1 & s_2 \\ s_2 & s_3 \end{bmatrix} = \begin{bmatrix} \sigma_d^2 & \sigma_{ad} \\ \sigma_{ad} & \sigma_a^2 \end{bmatrix}^{-1}$$

22

# Appendix A

- SAS IML code

23

```
proc iml;
start main;
y={12,      X={1,
9,        1,
8,        1,
5,        1,
7,        1,
5,        1,
6,        1,
8};      1};
A={1  0  0  .5  .5  .5  .5  0  0  0  0  0,
   0  1  0  .5  .5  .5  .5  .5  .5  .5  .5  .5,
   0  0  1  0  0  0  0  .5  .5  .5  .5  .5,
   .5  .5  0  1  .5  .5  .5  .25 .25 .25 .25,
   .5  .5  0  .5  1  .5  .5  .25 .25 .25 .25,
   .5  .5  0  .5  .5  1  .5  .25 .25 .25 .25,
   .5  .5  0  .5  .5  .5  1  .25 .25 .25 .25,
   0  .5  .5  .25 .25 .25 .25 1  .5  .5  .5,
   0  .5  .5  .25 .25 .25 .25 .5  1  .5  .5,
   0  .5  .5  .25 .25 .25 .25 .5  .5  1  .5,
   0  .5  .5  .25 .25 .25 .25 .5  .5  .5  1};

Z_d={0 0 0 1 0 0 0 0 0 0 0 0,
      0 0 0 1 0 0 0 0 0 0 0 0,
      0 0 0 0 0 1 0 0 0 0 0 0,
      0 0 0 0 0 0 1 0 0 0 0 0,
      0 0 0 0 0 0 0 1 0 0 0 0,
      0 0 0 0 0 0 0 0 1 0 0 0,
      0 0 0 0 0 0 0 0 0 1 0 0,
      0 0 0 0 0 0 0 0 0 0 1 0};

Z_a={0 0 0 0 1 0 0 0 1 1 0,
      0 0 0 1 0 0 0 0 1 1 0,
      0 0 0 0 0 0 1 1 0 0 1,
      0 0 0 0 0 0 1 0 1 0 0 1,
      0 0 0 0 0 0 1 1 0 0 0 1,
      0 0 0 1 1 0 0 0 0 1 0,
      0 0 0 1 1 0 0 0 1 0 0,
      0 0 0 0 0 1 1 1 0 0 0};

Z_c={1 0,
      1 0,
      0 1,
      0 1,
      0 1,
      1 0,
      1 0,
      0 1};
```

24

```

I2=I(2); *IDENTITY MATRIX;
P={30 -4,
   -4 10};
K=inv(P)#60;
K33=(60/6);

LHS=((X`*X) ||(X`*Z1) ||(X`*Z2) ||(X`*Z3))
//((Z1`*X)|| (Z1`*Z1+AINV#K[1,1])||(Z1`*Z2+AINV#K[1,2])||(Z1`*Z3))
//((Z2`*X)|| (Z2`*Z1+AINV#K[2,1])||(Z2`*Z2+AINV#K[2,2])||(Z2`*Z3))
//((Z3`*X)|| (Z3`*Z1) ||(Z3`*Z2) ||(Z3`*Z3)+I2#K33);

RHS=(X`*Y)//(Z1`*Y)//(Z2`*Y)//(Z3`*Y);
C=INV(LHS);
BU=C*RHS;
RMSE=(Y`*Y-BU`*RHS)#{1/6};
print BU ;
finish main;
run;
quit;

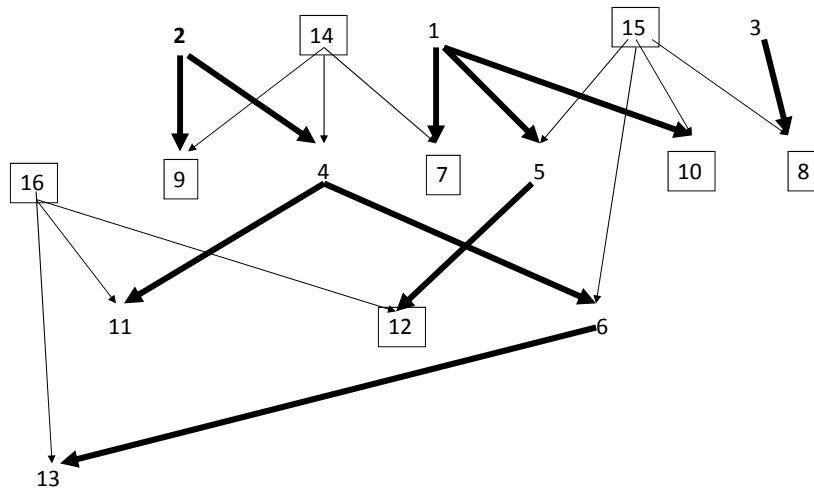
```

## Cytoplasmic Effects

Nuclear Environmental Effect  
Follows Maternal Lines Only

1

Pedigree



2

## Model Cytoplasmic Effects

$$y_{ijkmn} = (HY)_i + S_j + D_k + M_n + e_{ijkmn}$$

Herd Year      Sex      Direct Genetic      Cytoplasmic      Random error  
 ↓                  ↓                  ↓                  ↓                  ↓  
 Fixed Effects      Random Effects

3

## Cytoplasmic Effects Mixed Model

$$\mathbf{y} = \mathbf{X}\mathbf{b} + \mathbf{Z}_1\mathbf{d} + \mathbf{Z}_2\mathbf{c} + \mathbf{e}$$

Direct effect      Cytoplasmic

$$V \begin{bmatrix} \mathbf{d} \\ \mathbf{c} \\ \mathbf{e} \end{bmatrix} = \begin{bmatrix} \mathbf{A}\sigma_d^2 & 0 & 0 \\ 0 & \mathbf{I}\sigma_c^2 & 0 \\ 0 & 0 & \mathbf{I}\sigma_e^2 \end{bmatrix}$$

Assumes no  
 cytoplasmic –  
 nuclear gene  
 interaction

4

Year      sex  
86 87 88 m

$$\mathbf{X} = \begin{bmatrix} 1 & 0 & 0 & 1 \\ 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 1 \\ 0 & 1 & 0 & 0 \\ 0 & 1 & 0 & 1 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 1 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 1 & 1 \\ 0 & 0 & 1 & 0 \end{bmatrix}$$

$$\mathbf{B} = \begin{bmatrix} b_1 \\ b_2 \\ b_3 \\ b_4 \end{bmatrix} \quad \begin{array}{c} \text{Herd} \\ \text{Year} \\ \text{Sex} \end{array}$$

$$\mathbf{Y} = \begin{bmatrix} 400 \\ 380 \\ 410 \\ 350 \\ 420 \\ 360 \\ 390 \\ 390 \\ 430 \\ 370 \end{bmatrix}$$

5

### Direct effect: Animal

An	Sire	Dam
7	14	1
4	14	2
8	15	3
5	15	1
9	14	2
6	15	4
10	15	1
11	16	4
12	16	5
13	16	6

$$\mathbf{Z}_1 = \begin{bmatrix} 14 & 1 & 2 & 15 & 3 & 16 \rightarrow 7 & 4 & 8 & 5 & 9 & 6 & 10 & 11 & 12 & 13 \end{bmatrix}$$

$$\begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \end{bmatrix}$$

6

### Cytoplasmic

Animal 1 was the mother lineage of animals 7, 5, 10, 12

An	Sire	Dam
7	14	1
4	14	2
8	15	3
5	15	1
9	14	2
6	15	4
10	15	1
11	16	4
12	16	5
13	16	6

$$\mathbf{Z}_2 = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \\ 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 1 & 0 \\ 1 & 0 & 0 \\ 0 & 1 & 0 \\ 1 & 0 & 0 \\ 0 & 1 & 0 \end{bmatrix} \quad \text{Maternal Lineages}$$

7

### MME

$$\begin{bmatrix} \mathbf{X}'\mathbf{X} & \mathbf{X}'\mathbf{Z}_1 & \mathbf{X}'\mathbf{Z}_2 \\ \mathbf{Z}_1'\mathbf{X} & \mathbf{Z}_1'\mathbf{Z}_1 + \mathbf{A}^{-1}k_{11} & \mathbf{Z}_1'\mathbf{Z}_2 \\ \mathbf{Z}_2'\mathbf{X} & \mathbf{Z}_2'\mathbf{Z}_1 & \mathbf{Z}_2'\mathbf{Z}_2 + \mathbf{I}k_{22} \end{bmatrix} \begin{bmatrix} \hat{\mathbf{b}} \\ \hat{\mathbf{a}} \\ \hat{\mathbf{c}} \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{y} \\ \mathbf{Z}_1'\mathbf{y} \\ \mathbf{Z}_2'\mathbf{y} \end{bmatrix}$$

$$\begin{bmatrix} k_{11} & k_{12} \\ k_{21} & k_{22} \end{bmatrix} = \begin{bmatrix} \sigma_d^2 & 0 \\ 0 & \sigma_e^2 \end{bmatrix}^{-1} \sigma_c^2 \quad I = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

$$\begin{bmatrix} k_{11} & k_{12} \\ k_{21} & k_{22} \end{bmatrix} = \begin{bmatrix} 2000 & 0 \\ 0 & 1200 \end{bmatrix}^{-1} 6500 = \begin{bmatrix} 3.25 & 0 \\ 0 & 5.42 \end{bmatrix}$$

8

```

proc iml;
start main;
y={400,
380,
410,
350,
420,
360,
390,
390,
430,
370};
Z1={0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0,
      0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0,
      0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0,
      0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0,
      0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0,
      0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0,
      0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0,
      0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0,
      0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0,
      0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0,
      0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0,
      0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0,
      0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1};

Z2={ 1 0 0,
      0 1 0,
      0 0 1,
      1 0 0,
      0 1 0,
      0 0 1,
      0 0 0,
      1 0 0,
      0 0 0,
      0 0 0,
      0 0 0,
      0 0 0};

X={1 0 0 1,
  1 0 0 0,
  1 0 0 1,
  0 1 0 0,
  0 1 0 1,
  0 1 0 0,
  0 0 1 1,
  0 0 1 0,
  0 0 1 1,
  0 0 1 0};

l={1 0 0,
   0 1 0,
   0 0 1};

```

9

```

Ainv={2.5 .5 1 0 0 0 -1 -1 0 0 -1 0 0 0 0 0 0,
      .5 2.5 0 1 0 0 -1 0 0 -1 0 0 -1 0 0 0 0 0,
      1 0 2 0 0 0 0 -1 0 0 -1 0 0 0 0 0 0 0,
      0 1 0 3 .5 0 0 .5 -1 -1 0 -1 -1 0 0 0,
      0 0 0 .5 1.5 0 0 0 -1 0 0 0 0 0 0 0 0,
      0 0 0 0 0 2.5 0 .5 0 .5 0 .5 0 -1 -1 -1,
      -1 -1 0 0 0 0 2 0 0 0 0 0 0 0 0 0 0 0,
      -1 0 -1 .5 0 .5 0 3 0 0 0 -1 0 -1 0 0,
      0 0 0 -1 -1 0 0 0 2 0 0 0 0 0 0 0 0 0,
      0 -1 0 -1 0 .5 0 0 0 2.5 0 0 0 0 -1 0,
      -1 0 -1 0 0 0 0 0 0 0 2 0 0 0 0 0 0 0,
      0 0 0 -1 0 .5 0 -1 0 0 0 2.5 0 0 0 -1,
      0 -1 0 -1 0 0 0 0 0 0 0 0 2 0 0 0 0,
      0 0 0 0 0 -1 0 -1 0 0 0 0 0 0 2 0 0 0,
      0 0 0 0 0 -1 0 0 0 -1 0 0 0 0 0 2 0 0,
      0 0 0 0 0 -1 0 0 0 0 -1 0 0 0 0 0 2 0 0,
      0 0 0 0 0 -1 0 0 0 0 0 -1 0 0 0 0 0 2 0};

```

10

```

P={2000 0,
  0 1200};

K=inv(P)#6500;

LHS=((X`*X)|| (X`*Z1)|| (X`*Z2))
//((Z1`*X)|| (Z1`*Z1+AINV#K[1,1])|| (Z1`*Z2))
//((Z2`*X)|| (Z2`*Z1)|| (Z2`*Z2+l#K[2,2]));

RHS=(X`*Y)/(Z1`*Y)/(Z2`*Y);
C=INV(LHS);
BU=C*RHS;
RMSE=(Y`*Y-BU`*RHS)#{(1/6);
print BU RMSE;
finish main;run;quit;

```

"BLUP cytoplasmic Genetic.sas"

11

<b>B</b>	$\hat{a}$	Animal	$\hat{c}$	Animal
368.15	1.55	14	-2.81	1
361.75	-3.45	1	2.73	2
373.55	2.53	2	0.08	3
42.94	-3.40			
	0.06			
	2.70			
	-1.92			
	3.17			
	-1.60			
	-3.20			
	3.44			
	-1.10			
	6.12			
	4.37			
	1.95			
	-0.14			
		1 2 3 4 5 6 7 8 9 10 11 12 13		

12

## Indirect Genetic Effects

- Inherited Genetic effect of one animals measured another
- Examples
  - Mothering ability
    - Maternal Care
    - Maternal Nutrition
  - Social interactions
    - Competition
    - Mutualism
    - Pack behavior



1

## IGEs of the Dam

Previous Example we considered maternal effects that were not inherited, this resulted in a correlated residual or environmental effect

Here we are considering a maternal effect that is inherited, this results in a correlated genetic effect between the effects of the dam and the offspring.

The model from the previous example is the same but the co(variance) structure is different

$$y_{ijkmn} = (HY)_i + S_j + G_k + M_n + e_{ijkmn}$$

↑      ↑      ↑      ↑      ↘  
Herd Year   Sex   Additive   Maternal   Random  
↓      ↓      ↓      ↓      ↙  
Fixed Effects      Random Effects

2

## Maternal IGEs

$$\mathbf{y} = \mathbf{X}\mathbf{b} + \mathbf{Z}_1\mathbf{G} + \mathbf{Z}_2\mathbf{m}_g + \mathbf{e}$$

Additive Genetic effect      Maternal Genetic

$$V \begin{bmatrix} \mathbf{G} \\ \mathbf{m} \\ \mathbf{e} \end{bmatrix} = \begin{bmatrix} \mathbf{A}\sigma_d^2 & \mathbf{A}\sigma_{G,m_g} & 0 \\ \mathbf{A}\sigma_{G,m_g} & \mathbf{A}\sigma_{m_g}^2 & 0 \\ 0 & 0 & \mathbf{I}\sigma_e^2 \end{bmatrix}$$

There is a genetic correlation between the animals direct and maternal genetic effect

The are inherited and determined by additive effects in the mother

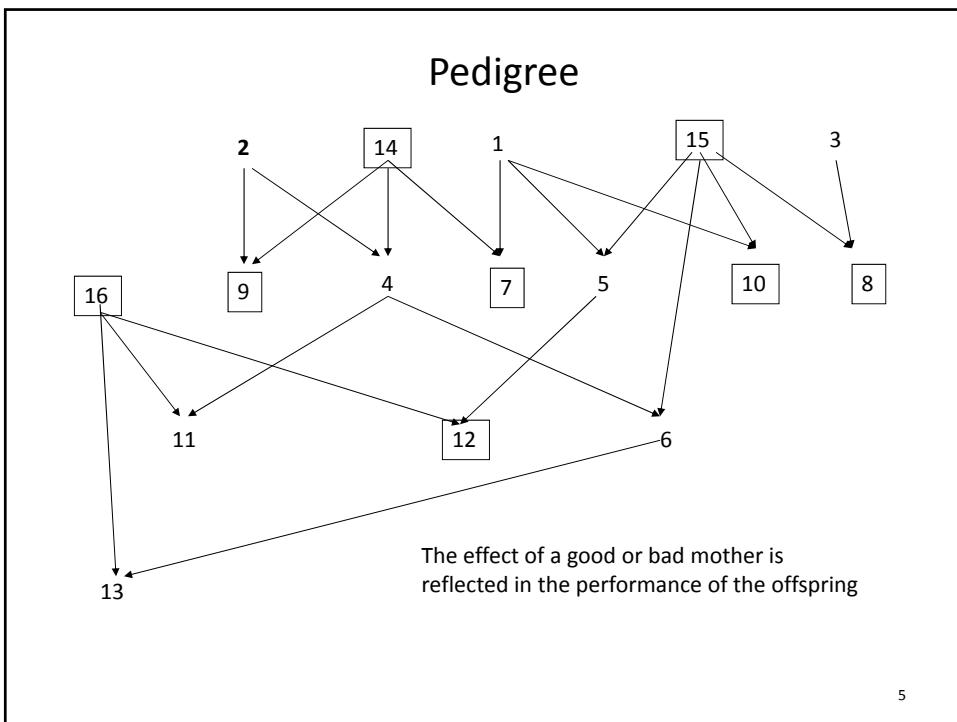
No environmental correlations

3

## Maternal Effects Example

Animal	Sire	Dam	Year	Sex	Wean Wt
7	14	1	86	M	400
4	14	2	86	F	380
8	15	3	86	M	410
5	15	1	87	F	350
9	14	2	87	M	420
6	15	4	87	F	360
10	15	1	88	M	390
11	16	4	88	F	390
12	16	5	88	M	430
13	16	6	88	F	370

4



Year	sex	
86	87	88 m
1	0	0 1
1	0	0 0
1	0	0 1
0	1	0 0
0	1	0 1
0	1	0 0
0	0	1 1
0	0	1 0
0	0	1 1
0	0	1 0

$$\mathbf{X} = \begin{bmatrix} 1 & 0 & 0 & 1 \\ 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 1 \\ 0 & 1 & 0 & 0 \\ 0 & 1 & 0 & 1 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 1 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 1 & 1 \\ 0 & 0 & 1 & 0 \end{bmatrix}$$
  

$$\mathbf{B} = \begin{bmatrix} b_1 \\ b_2 \\ b_3 \\ b_4 \end{bmatrix}$$

Herd
Year

←
Sex

$$\mathbf{Y} = \begin{bmatrix} 400 \\ 380 \\ 410 \\ 350 \\ 420 \\ 360 \\ 390 \\ 390 \\ 430 \\ 370 \end{bmatrix}$$

6

Animal Direct Genetic Effect

Note that sires and dams did not have records and are missing

**An**    **Sire**    **Dam**

An	Sire	Dam
7	14	1
4	14	2
8	15	3
5	15	1
9	14	2
6	15	4
10	15	1
11	16	4
12	16	5
13	16	6

$Z_1 =$

$$\begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \end{bmatrix}$$

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Maternal Genetic Effect-identify the mothers of the animal

Animal 1 was the mother of animals 7, 5, 10

**An**    **Sire**    **Dam**

An	Sire	Dam
7	14	1
4	14	2
8	15	3
5	15	1
9	14	2
6	15	4
10	15	1
11	16	4
12	16	5
13	16	6

$Z_2 =$

$$\begin{bmatrix} 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \end{bmatrix}$$

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## MME

$$\begin{bmatrix} \mathbf{X}'\mathbf{X} & \mathbf{X}'\mathbf{Z}_1 & \mathbf{X}'\mathbf{Z}_2 \\ \mathbf{Z}_1'\mathbf{X} & \mathbf{Z}_1'\mathbf{Z}_1 + \mathbf{A}^{-1}\mathbf{k}_{11} & \mathbf{Z}_1'\mathbf{Z}_2 + \mathbf{A}^{-1}\mathbf{k}_{12} \\ \mathbf{Z}_2'\mathbf{X} & \mathbf{Z}_2'\mathbf{Z}_1 + \mathbf{A}^{-1}\mathbf{k}_{21} & \mathbf{Z}_2'\mathbf{Z}_2 + \mathbf{A}^{-1}\mathbf{k}_{22} \end{bmatrix} \begin{bmatrix} \hat{\mathbf{b}} \\ \hat{\mathbf{G}} \\ \hat{\mathbf{m}}_g \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{y} \\ \mathbf{Z}_1'\mathbf{y} \\ \mathbf{Z}_2'\mathbf{y} \end{bmatrix}$$

$$\begin{bmatrix} k_{11} & k_{12} \\ k_{21} & k_{22} \end{bmatrix} = \begin{bmatrix} \sigma_G^2 & \sigma_{G,m_g} \\ \sigma_{G,m_g} & \sigma_{m_g}^2 \end{bmatrix}^{-1} \sigma_e^2$$

$$\begin{bmatrix} k_{11} & k_{12} \\ k_{21} & k_{22} \end{bmatrix} = \begin{bmatrix} 2000 & -300 \\ -300 & 1200 \end{bmatrix}^{-1} 6500 = \begin{bmatrix} 3.3766 & .8441 \\ .8441 & 5.6288 \end{bmatrix}$$

9

```

proc iml;
start main;
y={400,
  380,
  410,
  350,
  420,
  360,
  390,
  390,
  430,
  370};
Z1={0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0,
      0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0,
      0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0,
      0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0,
      0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0,
      0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0,
      0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0,
      0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0,
      0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0,
      0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0,
      0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0,
      0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1};

X={1 0 0 1,
  1 0 0 0,
  1 0 0 1,
  0 1 0 0,
  0 1 0 1,
  0 1 0 0,
  0 0 1 1,
  0 0 1 0,
  0 0 1 1,
  0 0 1 0};

Z2={ 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0,
      0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0,
      0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0,
      0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0,
      0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0,
      0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0,
      0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0,
      0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0,
      0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0,
      0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0};

```

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```

Ainv={2.5 .5 1 0 0 0 -1 -1 0 0 -1 0 0 0 0 0,
      .5 2.5 0 1 0 0 -1 0 0 -1 0 0 -1 0 0 0 0,
      1 0 2 0 0 0 0 -1 0 0 -1 0 0 0 0 0 0,
      0 1 0 3 .5 0 0.5 -1 -1 0 -1 -1 0 0 0 0 0,
      0 0 0 .5 1.5 0 0 0 -1 0 0 0 0 0 0 0 0 0,
      0 0 0 0 0 2.5 0 .5 0 .5 0 .5 0 -1 -1,
      -1 -1 0 0 0 0 2 0 0 0 0 0 0 0 0 0 0 0,
      -1 0 -1 .5 0 .5 0 3 0 0 0 -1 0 -1 0 0,
      0 0 0 -1 -1 0 0 0 2 0 0 0 0 0 0 0 0 0 0,
      0 -1 0 -1 0 .5 0 0 0 2.5 0 0 0 0 -1 0,
      -1 0 -1 0 0 0 0 0 0 0 2 0 0 0 0 0 0 0,
      0 0 0 -1 0 .5 0 -1 0 0 0 2.5 0 0 0 -1,
      0 -1 0 -1 0 0 0 0 0 0 0 2 0 0 0 0 0 0,
      0 0 0 0 -1 0 -1 0 0 0 0 0 0 2 0 0 0 0,
      0 0 0 0 0 -1 0 0 0 0 0 -1 0 0 0 0 2 0,
      0 0 0 0 0 -1 0 0 0 0 0 -1 0 0 0 0 2 0};

```

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```

P={2000 -300,
   -300 1200};

K=inv(P)#6500;
LHS=((X`*X)|| (X`*Z1)|| (X`*Z2))
//((Z1`*X)|| (Z1`*Z1+AINV#K[1,1])|| (Z1`*Z2+AINV#K[1,2]))
//((Z2`*X)|| (Z2`*Z1+AINV#K[2,1])|| (Z2`*Z2+AINV#K[2,2]));
RHS=(X`*Y)/(Z1`*Y)/(Z2`*Y);
C=INV(LHS);
BU=C*RHS;
print BU ;
finish main;
run;
quit;

```

“BLUP Maternal Genetic.sas”

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<b>B</b>	$\hat{d}$	Animal	$\hat{m}_g$	Animal
369.40		1.567	0.09	14
363.10	Year	-2.43	-3.65	1
374.56		1.79	2.68	2
41.48	← Sex	-3.57	1.16	15
		0.07	0.10	3
		2.58	-0.38	16
		-1.34	-1.64	7
		2.67	1.55	4
		-1.65	0.61	8
		-3.28	-0.09	5
		3.15	1.16	9
		-1.26	1.00	6
		-5.59	-0.85	10
		4.13	0.36	11
		1.56	-0.52	12
		-0.16	0.43	13

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## What to do with the estimates in a breeding program

- Selection Index Give a weight to each effect and combine in an index

$$I_i = w_1 \hat{G}_i + w_2 \hat{m}_i$$

For total breeding value, the weights are  $w_1=1$  and  $w_2=n-1$  because there are  $n-1$  IGEs in a litter of size  $n$

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## Incorporation of both Maternal Genetic and Maternal Environment

Add another random effect for common maternal environment

$$\mathbf{y} = \mathbf{X}\mathbf{b} + \mathbf{Z}_1\mathbf{G} + \mathbf{Z}_2\mathbf{m}_g + \mathbf{Z}_3\mathbf{m}_e + \mathbf{e}$$

$$V \begin{bmatrix} \mathbf{d} \\ \mathbf{m} \\ \mathbf{p} \\ \mathbf{e} \end{bmatrix} = \begin{bmatrix} \mathbf{A}\sigma_d^2 & \mathbf{A}\sigma_{d,m_g} & 0 & 0 \\ \mathbf{A}\sigma_{d,m_g} & \mathbf{A}\sigma_{m_g}^2 & 0 & 0 \\ 0 & 0 & \mathbf{I}\sigma_{m_e}^2 & 0 \\ 0 & 0 & 0 & \mathbf{I}\sigma_e^2 \end{bmatrix}$$

Question: what is an alternative approach?

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## MME

$$\begin{bmatrix} \mathbf{X}'\mathbf{X} & \mathbf{X}'\mathbf{Z}_1 & \mathbf{X}'\mathbf{Z}_2 & \mathbf{X}'\mathbf{Z}_3 \\ \mathbf{Z}_1'\mathbf{X} & \mathbf{Z}_1'\mathbf{Z}_1 + \mathbf{A}^{-1}\mathbf{k}_{11} & \mathbf{Z}_1'\mathbf{Z}_2 + \mathbf{A}^{-1}\mathbf{k}_{12} & \mathbf{Z}_1'\mathbf{Z}_3 \\ \mathbf{Z}_2'\mathbf{X} & \mathbf{Z}_2'\mathbf{Z}_1 + \mathbf{A}^{-1}\mathbf{k}_{21} & \mathbf{Z}_2'\mathbf{Z}_2 + \mathbf{A}^{-1}\mathbf{k}_{22} & \mathbf{Z}_2'\mathbf{Z}_3 \\ \mathbf{Z}_3'\mathbf{X} & \mathbf{Z}_3'\mathbf{Z}_1 & \mathbf{Z}_3'\mathbf{Z}_2 & \mathbf{Z}_3'\mathbf{Z}_3 + \mathbf{I}k_{33} \end{bmatrix} \begin{bmatrix} \hat{\mathbf{b}} \\ \hat{\mathbf{d}} \\ \hat{\mathbf{m}}_g \\ \hat{\mathbf{m}}_e \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{y} \\ \mathbf{Z}_1'\mathbf{y} \\ \mathbf{Z}_2'\mathbf{y} \\ \mathbf{Z}_3'\mathbf{y} \end{bmatrix}$$

$$\begin{bmatrix} k_{11} & k_{12} \\ k_{21} & k_{22} \end{bmatrix} = \begin{bmatrix} \sigma_G^2 & \sigma_{G,m_g} \\ \sigma_{G,m_g} & \sigma_{m_g}^2 \end{bmatrix}^{-1} \sigma_e^2 \quad k_{33} = \frac{\sigma_e^2}{\sigma_{m_e}^2} = \frac{6500}{130} = 50$$

$$\begin{bmatrix} k_{11} & k_{12} \\ k_{21} & k_{22} \end{bmatrix} = \begin{bmatrix} 2000 & -300 \\ -300 & 1200 \end{bmatrix}^{-1} 6500 = \begin{bmatrix} 3.3766 & .8441 \\ .8441 & 5.6288 \end{bmatrix}$$

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For this example, all other matrices as previously defined

$$\mathbf{Z}_3 = \begin{bmatrix} 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{bmatrix}$$

$$\mathbf{I} = \begin{bmatrix} 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{bmatrix}$$

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#### SAS Program Changes

```
I6=I(6); *IDENTITY MATRIX;
P={2000 -300,
   -300 1200};
K=inv(P)#6500;
K33=(6500/130);
LHS=((X*X) ||(X*Z1)      ||(X*Z2)      ||(X*Z3))
  //((Z1*X)|| (Z1*Z1+GINV#K[1,1])||(Z1*Z2+GINV#K[1,2])||(Z1*Z3))
  //((Z2*X)|| (Z2*Z1+GINV#K[2,1])||(Z2*Z2+GINV#K[2,2])||(Z2*Z3))
  //((Z3*X)|| (Z3*Z1)      ||(Z3*Z2)      ||(Z3*Z3)+I6#K33);
RHS=(X*Y)/(Z1*X)/(Z2*Y)/(Z3*Y);
C=INV(LHS);
BU=C*RHS;
RMSE=(Y*Y-BU*RHS)^(1/6);
print BU ;
```

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$\hat{d}$	Animal	$\hat{m}_g$	$\hat{m}_e$
1.5428319	14	0.0801625	-0.559916
-2.359447	12	-3.53917	0.2879317
1.7392423	15	2.6088634	0.0115168
-3.527759	3	1.1385914	0.1232801
0.0620136	16	0.0930204	0.2434657
2.5431176	7	-0.381468	-0.106279
-1.269176	4	-1.600374	
2.6021552	8	1.5119326	
-1.644282	5	0.6025173	
-3.191177	9	-0.081604	
3.083619	6	1.1281257	369.48125
-1.288459	10	0.9769888	363.16015
-5.48672	11	-0.818822	374.63341
4.0604681	12	0.3420577	41.482657
1.5487832	13	-0.512458	
-0.190198		0.4203896	