ASReml workshop

2.1 A matrix refresher

Arthur Gilmour

NSW DEPARTMENT OF
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Some vectors

- A *vector* is a column of numbers
  $\boldsymbol{y}$ is the response variable
  $\hat{\boldsymbol{\tau}}$ is the fixed effects
  $\tilde{\boldsymbol{u}}$ is the random effects
  $\tilde{\boldsymbol{\epsilon}}$ is the residuals

Some matrices

- A *matrix* is a rectangular array of numbers
  $\boldsymbol{X}$ is the design matrix for fixed effects
  $\boldsymbol{Z}$ is the design matrix for random effects
  $\boldsymbol{W} = [\boldsymbol{X}\ \boldsymbol{Z}]$ is the whole design matrix
  $\boldsymbol{G} =$var$(\boldsymbol{u})$
  $\boldsymbol{R} =$var$(\boldsymbol{\epsilon})$
  $\boldsymbol{A}$ is a relationship matrix

Matrix operations

- Transpose

$$[a\ b\ c]' = \begin{pmatrix} a \\ b \\ c \end{pmatrix}$$

- Addition - matrices of the same order are added element by element

$$[1\ \ 2] + [3\ \ 4] = [4\ \ 6]$$

- Multiplication by scalar

$$3[1\ \ 2] = [3\ \ 6]$$

Matrix operations

- Matrix multiplication – must be conformable

$$\begin{pmatrix} a & b & c \\ d & e & f \end{pmatrix} \begin{pmatrix} A \\ B \\ C \end{pmatrix} = \begin{pmatrix} aA + bB + cC \\ dA + eB + fC \end{pmatrix}$$

- Direct product

$$\begin{pmatrix} a \\ b \end{pmatrix} \otimes [A\ B\ C] = \begin{pmatrix} aA & aB & aC \\ bA & bB & bC \end{pmatrix}$$

Mixed model equations

- Mixed model

$$\boldsymbol{y} = \boldsymbol{X}\boldsymbol{\tau} + \boldsymbol{Z}\boldsymbol{u} + \boldsymbol{\epsilon}$$

$$\begin{pmatrix} \boldsymbol{X}'\boldsymbol{R}^{-1}\boldsymbol{X} & \boldsymbol{X}'\boldsymbol{R}^{-1}\boldsymbol{Z} \\ \boldsymbol{Z}'\boldsymbol{R}^{-1}\boldsymbol{X} & \boldsymbol{Z}'\boldsymbol{R}^{-1}\boldsymbol{Z} + \boldsymbol{G}^{-1} \end{pmatrix} \begin{pmatrix} \boldsymbol{\tau} \\ \boldsymbol{u} \end{pmatrix} = \begin{pmatrix} \boldsymbol{X}'\boldsymbol{R}^{-1}\boldsymbol{y} \\ \boldsymbol{Z}'\boldsymbol{R}^{-1}\boldsymbol{y} \end{pmatrix}$$

REML

- Let $\boldsymbol{C} = \begin{pmatrix} \boldsymbol{X}'\boldsymbol{R}^{-1}\boldsymbol{X} & \boldsymbol{X}'\boldsymbol{R}^{-1}\boldsymbol{Z} \\ \boldsymbol{Z}'\boldsymbol{R}^{-1}\boldsymbol{X} & \boldsymbol{Z}'\boldsymbol{R}^{-1}\boldsymbol{Z} + \boldsymbol{G}^{-1} \end{pmatrix}$

$$\boldsymbol{P} = \boldsymbol{R}^{-1} - \boldsymbol{R}^{-1}\boldsymbol{W}\boldsymbol{C}^{-1}\boldsymbol{W}'\boldsymbol{R}^{-1}$$

$$l_R = -(\log|\boldsymbol{C}| + \log|\boldsymbol{R}| + \log|\boldsymbol{G}| + \nu\log\sigma^2 + \boldsymbol{y}'\boldsymbol{P}\boldsymbol{y}/\sigma^2)/2$$

Two forms

- $\boldsymbol{V} = \sigma^2(\boldsymbol{R} + \boldsymbol{ZGZ}')$
  default for univariate single site analyse.
  $\boldsymbol{R}$ defined as a correlation matrix
  $\boldsymbol{G}$ defined as a variance ratio
- $\boldsymbol{V} = \boldsymbol{R} + \boldsymbol{ZGZ}'$
  used for multivariate and multisite analyses.

Differentiation

- $l_R = -(\log|\boldsymbol{C}| + \log|\boldsymbol{R}| + \log|\boldsymbol{G}| + \nu \log\sigma^2 + \boldsymbol{y}'\boldsymbol{P}\boldsymbol{y}/\sigma^2)/2$
- $\partial l_R/\partial\phi_i = -(-\boldsymbol{C}_i\boldsymbol{C}^{Z'Z} + 0 + \mathrm{tr}(\boldsymbol{G}_i\boldsymbol{G}^{-1}) + 0 - \boldsymbol{y}'\boldsymbol{P}\boldsymbol{y}_i/\sigma^2)/2$
  $\boldsymbol{y}_i = \boldsymbol{Z}\boldsymbol{G}_i\boldsymbol{G}^{-1}\tilde{u}$
- $\partial l_R/\partial\kappa_j = -(-\boldsymbol{C}_j\boldsymbol{C}^{-1} + \mathrm{tr}(\boldsymbol{R}_j\boldsymbol{R}^{-1}) + 0 + 0 - \boldsymbol{y}'\boldsymbol{P}\boldsymbol{y}_j/\sigma^2)/2$
  $\boldsymbol{y}_j = \boldsymbol{R}_j\boldsymbol{R}^{-1}e\tilde{t}a$

The challenge

- to define $\boldsymbol{X}$ $\boldsymbol{Z}$ $\boldsymbol{R}$ and $\boldsymbol{G}$ to obtain the desired analysis.
- Often several ways of writing equivalent models.

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2.2 Sire and Animal model

Arthur Gilmour

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Harvey.dat

- animal sire dam
  line DamAge ADG Age WT

```
101 1 0 1 3 192 390 224 1
102 1 0 1 3 154 403 265 1
103 1 0 1 4 185 432 241 1
104 1 0 1 4 183 457 225 1
105 1 0 1 5 186 483 258 1
106 1 0 1 5 177 469 267 1
```

Harvey.dat summary

- 9 sires representing 3 sire lines
  (1 2 3) (4 5) (6 7 8 9)
  8 8 5 8 7 6 8 7 8 records (65)
- Data set originally distributed with Harvey's program

2.2 Sire model

- Harvey Test data - Sire Model

```
animal sire 9 dam line 3
DamAge ADG Age WT
harvey.dat
ADG ~ mu line DamAge !r sire
```

Summary

Model term	Size	#mv	#00	MinNon0	Mean	MaxNon
1 ID		0	0	101.0	133.0	165.
2 Sire	9	0	0	1	5.0154	
3 Dam		0	65	0.000	0.000	0.00
4 Line	3	0	0	1	2.1231	
5 DamAge		0	0	3.000	4.385	5.00
6 ADG Variate		0	0	144.0	176.6	206.
7 Age		0	0	337.0	416.8	498.
8 InitialWT		0	0	144.0	241.1	300.

Fixed Design

- $\boldsymbol{X}$ has 5 columns
  `mu` is a column of ones
  `line-1` has 21 1's, 15 0's, 29 0's
  `line-2` has 21 0's, 15 1's, 29 0's
  `line-3` has 21 0's, 15 0's, 29 1's
  `DamAge` (covariate) has vector of dam ages
- This design has 1 singularity because the three `line` columns sum to give the `mu` column.
- ASReml will set $\tau_2 = 0$

Random design

- $\boldsymbol{Z}$ has 9 columns being zeros except for 8 8 5 8 7 6 8 7 8 1's respectively indicating which sire
- The variance model is $\sigma_e^2(I + \gamma \boldsymbol{Z}\boldsymbol{Z}')$ where $\sigma_s^2 = \gamma\sigma_e^2$
- The genetic model
  $\sigma_A^2 = 4\sigma_s^2;\ \sigma_s^2 = 0.25\sigma_A^2$
  $\sigma_E^2 = \sigma_e^2 - 3\sigma_s^2;\ \sigma_e^2 = \sigma_E^2 + 0.75\sigma_A^2$

Components

- 5 LogL=-188.777 S2= 132.76 61 df 0.2176 1.000

Source	terms	Gamma	Component	Comp/SE	% C
Sire	9	9	0.217651	28.8946	1.04	0 P
Variance	65	61	1.00000	132.756	5.25	0 P

- Notice $\gamma = 0.21765$, $\sigma_e^2 = 132.756$, $\sigma_s^2 = \gamma\sigma_e^2 = 28.8946$.

Genetic components

- Create a PIN file (harvey.pin)

```
#                    1 is Sire component
#                    2 is Residual
F PhenVar 1 2     #3 is Sire + Residual
F GenVar 1*4.     #4 is Sire x 4.0
H 4 3             #Heritability is GenVar/Phe
```

- Run using `ASReml -p harvey`
  This extracts the variance components from the .asr file and their variances from the .vvp file and computes the requested quantities

Genetic parameters

```
   3 PhenVar  1      161.7     35.07
   4 GenVar   1      115.6     110.8
Heritability = GenVar 4/PhenVar 3
             =      0.7150   0.5877
Notice: The parameter estimates are
        followed by their
        approximate standard errors
```

Sire BLUPS

- from the .sln file – sum to zero within lines

```
Sire    1     -0.5386E-01    4.137
Sire    2       3.591        4.142
Sire    3      -3.538        4.269
Sire    4      -5.112        4.468
Sire    5       5.112        4.468
Sire    6     0.6051E-01     4.055
Sire    7       3.420        3.914
Sire    8      0.4042        3.990
Sire    9      -3.885        3.914
```

ANOVA

- Degrees of Freedom and Stratum Variances

```
      5.93    341.034          7.2      1.0
     55.07    132.756          0.0      1.0

ANOVA          NumDF    DenDF    F-incr      Prob
  9 mu             1      5.9   5906.95     <.001
  4 Line           2      5.9      6.19     0.035
  5 DamAge         1     57.8      0.62     0.435
WARNING: The DenDF values are calculated ig
         fixed/boundary/singular variance p
         and may change with the order of f
```

- Damage is NS; Line is significant tested against Sire variance

Fixed effects

Term	Level	Effect	SE
DamAge	1	-1.478	1.881
Line	1	0.000	0.000
Line	2	-14.41	6.286
Line	3	6.466	5.293
mu	1	183.5	9.319

- Notes:
  Terms are in reverse order (ASReml solves from bottom)
  Line-1 effect is singular.

Predict

- predict Line

```
Predicted values of ADG
DamAge evaluated at average value 4.
Sire   is ignored in the prediction

Line  Predicted_Value Stand_Error Ec
 1.0000       177.0109       4.0193 E
 2.0000       162.5983       4.8301 E
 3.0000       183.4766       3.4415 E
Overall Stnd Error of Diff 5.851
```

Line+Sire

- predict Sire !present Sire Line

```
Line is average of combinations present
DamAge  is evaluated at    4.3846

 Sire    Pred_Value Stand_Error Ecode
 1.0000   176.9570      3.5634 E
 2.0000   180.6023      3.5962 E
 3.0000   173.4734      4.1885 E
 4.0000   157.4867      3.6989 E
 5.0000   167.7099      3.8875 E
 6.0000   183.5371      3.8512 E
```

Line+Sire

- predict Sire !present Sire Line

```
   3.0000    173.4734        4.1885 E
   4.0000    157.4867        3.6989 E
   5.0000    167.7099        3.8875 E
   6.0000    183.5371        3.8512 E
   7.0000    186.8966        3.4811 E
   8.0000    183.8807        3.6774 E
   9.0000    179.5918        3.4811 E
 Overall Stnd Error of Diff 5.146
```

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2.3 Animal model

Arthur Gilmour

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Relationship Matrix

- The diagonal of the relationship matrix ($a_{i,i}$) is $1 + f$ where $f = a_{s,d}/2$ is the inbreeding coefficient.
- The relationship of an animal with other animals is the average of its parental values.
- When parents are listed before progeny, this gives a straight forward way to calculate relationships.
- However, the inverse relationship matrix is in fact easier to calculate and more sparse.

reducing to

- $\boldsymbol{A}_i^{-1} = \begin{pmatrix} \boldsymbol{A}^{-1} + \boldsymbol{p}q\boldsymbol{p}' & \boldsymbol{p}q \\ q\boldsymbol{p}' & q \end{pmatrix}$ where $\boldsymbol{p}$ is zero except for two $\frac{1}{2}$'s in parental rows, $q = (1 + f_i - \boldsymbol{p}'\boldsymbol{A}\boldsymbol{p})^{-1} = (1 - (a_{s,s} + a_{d,d})/4)^{-1}$ so that it just requires keeping diag($\boldsymbol{A}$).
- For the case of a sire model (dams unknown, sires not inbred),

$$\boldsymbol{A} = \begin{pmatrix} \boldsymbol{I}_9 & 0.5\boldsymbol{Z}_s' \\ 0.5\boldsymbol{Z}_s & 0.25\boldsymbol{Z}_s\boldsymbol{Z}_s' + 0.75\boldsymbol{I}_{65} \end{pmatrix}$$

Variance model

- Fitting an animal model for the harvey data
  $\boldsymbol{V} = \sigma^2_E \boldsymbol{I}_{65} + \sigma^2_A \boldsymbol{Z} \boldsymbol{A} \boldsymbol{Z}'$
  where $\boldsymbol{Z} = (\boldsymbol{0}_{65\times 9}\ \boldsymbol{I}_{65})$
  Thus $\boldsymbol{V}$ simplifies to
  $\sigma^2_E + \sigma^2_A(0.25\boldsymbol{Z}_s\boldsymbol{Z}'_s + 0.75\boldsymbol{I}_{65})$
  $= (\sigma^2_E + 0.75\sigma^2_A)\boldsymbol{I}_{65} + 0.25\sigma^2_A\boldsymbol{Z}_s\boldsymbol{Z}'_s$ which is exactly the same as under the sire variance model.

Running the model in ASReml

```
!REDO !ARG !? 1=Sire 2=Animal
Harvey Test data - Sire and Animal M
 animal !P sire 9 dam line 3 # Added
 DamAge ADG Age WT
harvey.dat     # Pedigree file line a
harvey.dat     !DOPART $1 # Data
!PART 1
 ADG ~ mu line DamAge !r sire
!PART 2
 ADG ~ mu line DamAge !r animal
```

Results - components

```
5 LogL=-188.781 S2=54.092 61df 1.957
6 LogL=-188.777 S2=47.314 61df 2.411
7 LogL=-188.777 S2=46.100 61df 2.506
Final parameter values          2.508

Source    terms  Gamma Component C/SE
animal     74 74 2.5086  115.578 1.04
Variance   65 61 1.0000  46.0723 0.51
```

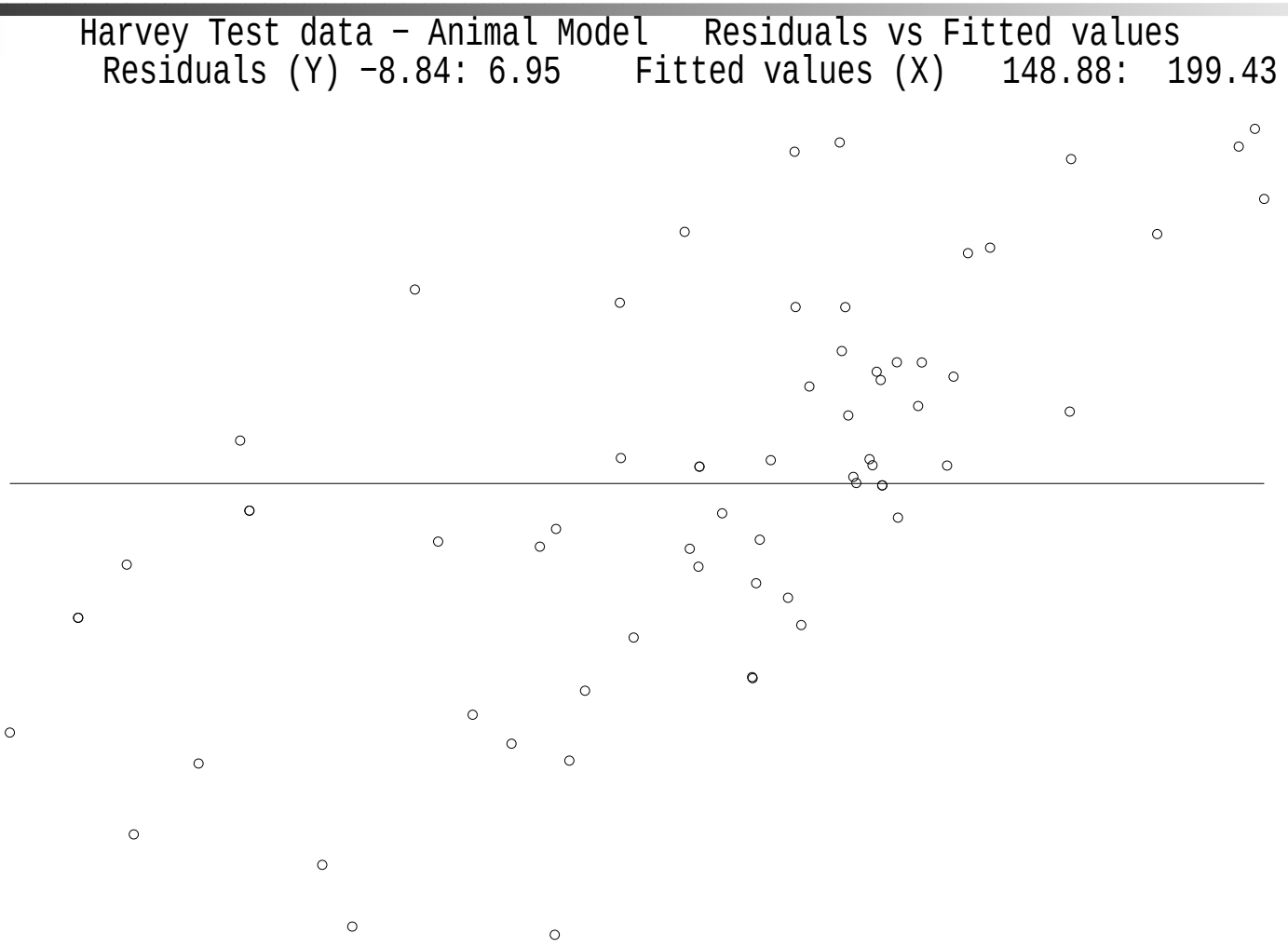
Results - ANOVA

- ANOVA NumDF DenDF F-incr Prob
  9 mu 1 5.9 5906.95 <.001
  4 line 2 5.9 6.19 0.035
  5 DamAge 1 57.8 0.62 0.435
  is the same as the Sire model

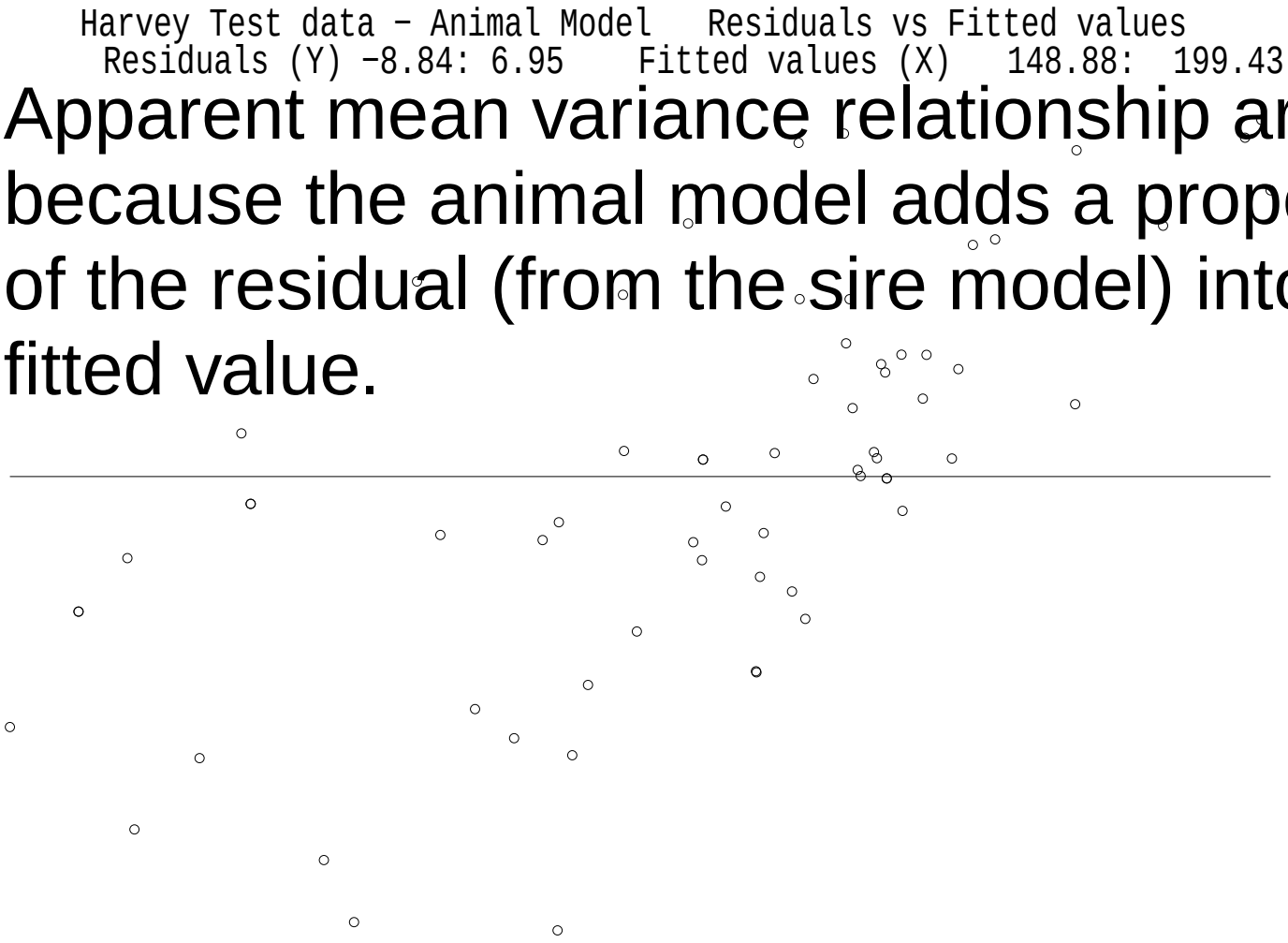
Results - Effects

		Estimate	StandErr	T-val
5 DamAge	1	-1.47752	1.88080	-0.79
4 line	2	-14.4126	6.28603	-2.29
	3	6.46567	5.29341	1.22
9 mu	1	183.489	9.31871	19.69
1 animal		74 effects fitted		

Plot of Residuals



Plot of Residuals



- Apparent mean variance relationship arises because the animal model adds a proportion of the residual (from the sire model) into the fitted value.

Other genetic components

- Genetic maternal definition `DAM !P` and include DAM in the model
- Permanent environment effect Use `ide(animal)`
- Maternal environment effect Use `ide(DAM)`

Estimability of Components

- Hendersons method III equated the Sire Mean Square (SMS) to its expectation $\sigma_e^2 + k\sigma_s^2$
- While SMS ≥ 0, $\sigma_s^2 =$ (SMS-EMS)$/k$ is $\geq$ -EMS$/k$
- In REML, often constrain components to be positive (equivalent to estimating σ_e^2 after dropping `sire` from the model).

Sire model $\rightarrow$ Animal model

- Solving the model in terms of genetic components can lead to further problems. $\sigma^2_E = \sigma^2_e - 3\sigma^2_s$ may be negative and not estimable (ASReml requires a positive residual variance)
- $h^2 = 4\sigma^2_s/(\sigma^2_e + \sigma^2_s)$ is ≤ 4 but if the genetic model is correct, should be less than 1.
- I.e. Our model may not adequately represent the variation in the data leading to unacceptable genetic parameter estimates.

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2.4 Bivariate Analysis

Arthur Gilmour

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Bivariate Analysis

- With Harvey data, could analyse ADG and WT - to get two sets of sire effects and two sets of residuals.
- Consider sire effects ($\boldsymbol{U}$) in a 9×2 table. Rows are independent: $\Sigma_R = \boldsymbol{I}_9$ Columns are correlated but have different variances: $\Sigma_C = \begin{pmatrix} S_{11} & S_{12} \\ S_{21} & S_{22} \end{pmatrix}$

Bivariate continued

- Now stack WT effects below ADG effects:
  $\boldsymbol{u} = \text{vec}(\boldsymbol{U})$
  $\text{var}(\boldsymbol{u}) = \Sigma_C \otimes \Sigma_R$
- Essential to get order correct: second term is nested within first.
- Adding part 3 to the Harvey job: the model

```
!PART 3
ADG WT ~ Trait Tr.line,
         at(Tr,2).Age !r Tr.sire
```

Variance header line

```
ADG WT ~ Trait Tr.line,
         at(Tr,2).Age !r Tr.sire
1 2 1                  # <============
0    # 65 records
Trait 0 US
3*0
Tr.sire 2
Tr 0 US
3*0
sire 0 ID
```

1 R structure

- ```
  ADG WT ~ Trait Tr.line,
           at(Tr,2).Age !r Tr.sire
  1 2 1
  0    # 65 records # <============
  Trait 0 US         # <============
  3*0                # <============
  Tr.sire 2
  Tr 0 US
  3*0
  sire 0 ID
  ```
  ```

1 G Structure

- ADG WT ~ Trait Tr.line,
  at(Tr,2).Age !r Tr.sire

```
1 2 1
0    # 65 records
Trait 0 US
3*0
Tr.sire 2          # <============
Tr 0 US            # <============
3*0                # <============
sire 0 ID          # <============
```

Notes

- R structure is 65×2 because data is ordered traits within records
- G structure is 2×9 because `Tr.sire` means the effects are ordered sires within traits
- Initial values must be supplied but are often difficult to guess. Specifying them as zeros (`3*0`) tells ASReml to work out some values from the data.

Missing data

- Multivariate analysis, with US error variance matrix, ASReml will automatically handle missing values in the traits.

Output:convergence

- ```
  1 LogL=-466.835 S2=1.0000 123 df
  2 LogL=-451.914 S2=1.0000 123 df
  3 LogL=-437.150 S2=1.0000 123 df
  4 LogL=-428.395 S2=1.0000 123 df
  5 LogL=-427.247 S2=1.0000 123 df
  6 LogL=-427.201 S2=1.0000 123 df
  7 LogL=-427.201 S2=1.0000 123 df
  ```
- Analysis on Variance scale
  $\boldsymbol{V} = \sigma^2(\boldsymbol{R} + \boldsymbol{ZGZ}')$ with $\sigma^2 = 1$.
  ```

Output:components

Source	Model	terms	Gamma	Component	C/SE	%	C
Residual	UnStru	1 1	132.370	132.370	5.29	0	U
Residual	UnStru	2 1	-98.0288	-98.0288	-2.27	0	U
Residual	UnStru	2 2	659.005	659.005	5.19	0	U
Tr.sire	UnStru	1 1	27.2002	27.2002	1.02	0	U
Tr.sire	UnStru	2 1	-12.1986	-12.1986	-0.30	0	U
Tr.sire	UnStru	2 2	98.7165	98.7165	0.88	0	U

Output:structures

- ```
  Covar/Var/Corr UnStructured
   132.4     -0.3319
  -98.03       659.0
  Covar/Var/Corr  UnStructured
   27.20     -0.2354
  -12.20       98.72
  ```
  ```

Output:ANOVA

- ANOVA NumDF DenDF F-incr Pro
  9 Trait 2 4.9 5019.79 <.00
  10 Tr.line 4 5.3 2.65 0.15
  12 at(Tr,2).Age 1 58.5 6.33 0.01

Usual process

- Univariate analysis of each trait.
  - Identify an appropriate fixed model
  - Check for outliers and problems with data structure
  - Sort out fixed model appropriate for each trait
  - Ensure there is variance at each level: if there is no sire variance in a univariate model, ASReml will not be able to estimate it in a multivariate model

Multivariate analysis

- Modelling becomes more difficult as number of traits increases - there may be variance but the matrix may not be positive definite (covariances too big).
  - Maybe do bivariate pairs first
  - !GP constrain positive definite - will use EM updates if AI updates generate NPD matrix
  - try FA or CHOL reduced parameterization
  - try Singular XFA or CHOL paramaterization

Exercises

- Coopworth data set - see Reference manual
- Five traits with varying amounts of data.
- No depth of pedigree (dams not linked to sires)
- Do univariate analyses
- Do bivariate analyses.
- Use COOP data set and attempt multivariate models.