Quantitative genetics of skin wrinkle in sheep

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Contents

1 Introduction

The purpose of this investigation is to take a close look at the quantitative genetics of wrinkle score in Merino sheep. Recent advances in our understanding of wrinkle formation (Watts personal communication) suggest that there may be maternal effects, with temperature regulation in the mother affecting skin development in the foetus. A close look at modes of inheritance of wrinkle, other than by simple additive genes, is also warranted. There is a summary of what is known about additive genetics of wrinkle score in Jackson and Watts(2017) [4].

2 Sheep population studied

Data from CSIRO sheep breeding experiments (AB1, AB20, and AB32 in CSIRO jargon) is utilised. These are all medium and fine wool Merino sheep. The AB1 experiment is documented in Turner etal(1968) [22], the AB20 experiment in Watson, Jackson, and Whiteley(1977) [20], and the AB32 experiment in Jackson(2017) [3].

Pedigree information was available on all sheep.

3 Traits measured

Wrinkle scores on all of the above flocks were made according to the photographic standards of Turner etal(1953) [23]. These photo standards are reproduced here (Figures 1 , 2 and 3).

Breech wrinkle scores were not used because the sheep were mulesed. Neck wrinkle scores range from 1 to 6, body wrinkle scores range from 1 to 5, the higher number meaning more wrinkled. All scores were made at the hogget stage, approximately 12 to 15 months of age, immediately after hogget shearing. Animals were held in a standing position for scoring. Analyses were also made of an overall wrinkle score which was the total of separate neck and body scores and therefore had a range of 2 to 11.

All other measurements were as described in Jackson(2017) [3], or in the original papers describing each experiment. The measurements of particular interest in relation to their correlation with wrinkle score are detailed in Table 1

Figure 1: Photographic standards for sheep neck wrinkle scores from Turner etal(1953) [23]

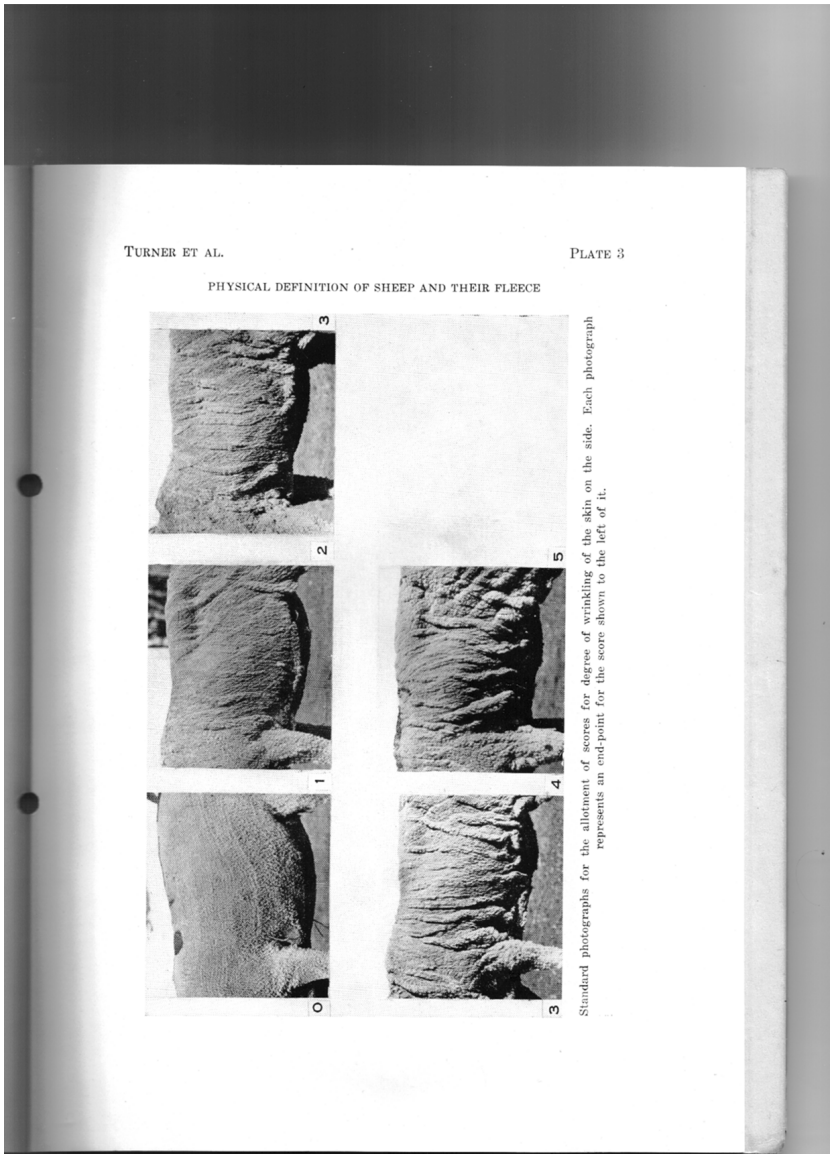

Figure 2: Photographic standards for sheep body wrinkle scores from Turner etal(1953) [23]

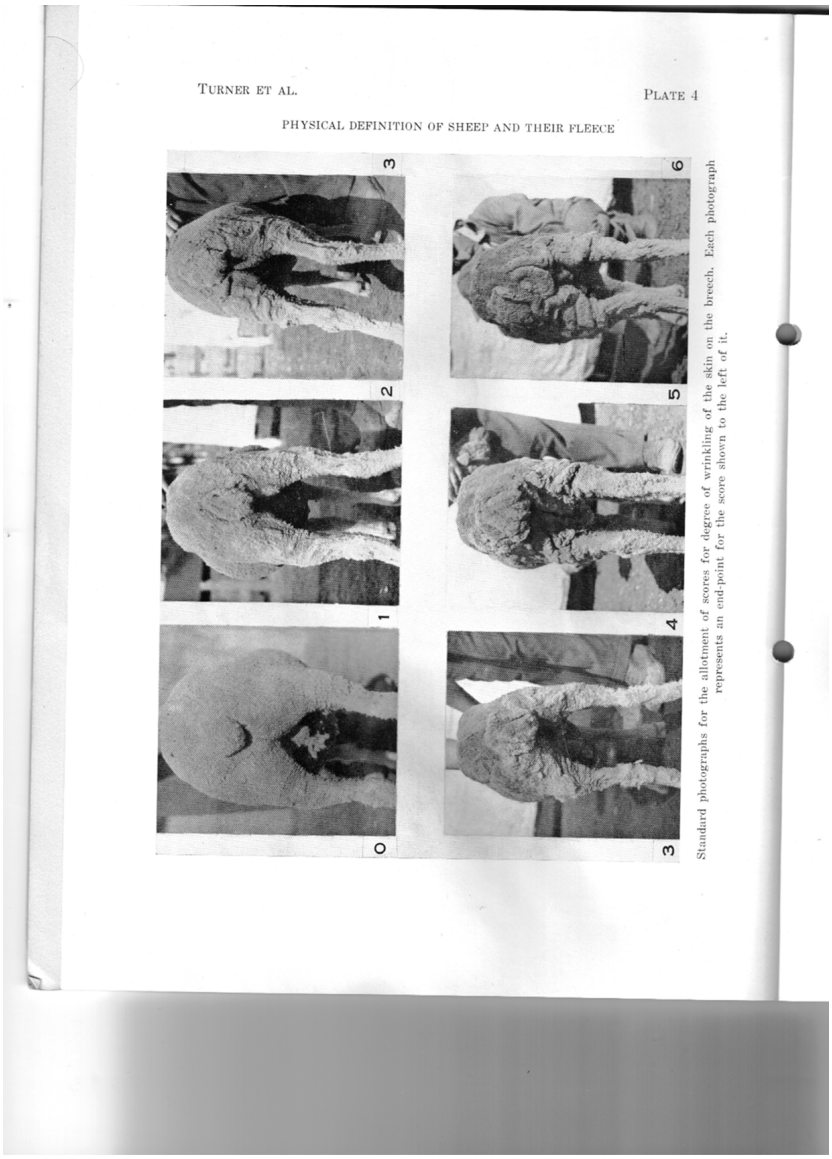

Figure 3: Photographic standards for sheep breech wrinkle scores from Turner etal(1953) [23]

Table 1: Definition of traits measured

Trait name	Abbreviation	Units	Age measured	Description
Staple length	Stal	mm	14 months	Length of wool staple 10 months growth
Crimp frequency	Crimp	no per 2.5cm	14 months	Staple crimp frequency
Fibre diameter	Diam	microns	14 months	Mean fibre diameter by airflow technique
Greasy Fleece Weight	Gfw	Kg	14 months	Weight of fleece in shearing shed
Yield	Yld	percentage	14 months	Percent of clean wool in fleece at 16% regain
Clean wool weight	Cww	Kg	14 months	Weight of clean fibre at 16% regain
Bodyweight	Bwt	Kg	14 months	Live weight of animal
Neck wrinkle	WrN	score 0-6 (0=plain,6=wrinkled)	14 months	Score for skin wrinkle on neck region
Body wrinkle	WrB	score 0-5 (0=plain,5=wrinkled)	14 months	Score for skin wrinkle on body region
Total wrinkle	WrT	sum of WrN and WrB	14 months	Sum of neck and body wrinkle scores
Face cover	Face	score 1-7 (1=open, 7=muffled)	14 months	Score for wool cover on the face
Follicle number per unit area	Fnua	no per mm_2	14 months	No of primary and secondary follicles per mm_2 from skin biopsy
Follicle S/P ratio	Fr	no units	14 months	Ratio of no of primary to no of secondary follicles from skin biopsy
Follicle depth	Fd	mm	14 months	Average follicle depth from skin biopsy and vertical section
Follicle curvature	Fc	score 1-7 (1=straight, 7=curved)	14 months	Follicle curvature score from skin biopsy and vertical section
Follicle unevenness	Fu	score 1-5 (1=even, 5=uneven)	14 months	Score for unevenness of follicle depth from skin biopsy and vertical section

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Table 1 – *Continued from previous page*

Trait name	Abbreviation	Units	Age measured	Description
Birth weight	Birwt	Kg	day of birth	Weight of lamb on day of birth
Birthcoat score side	Bcts	score 1-6 (1=no halo hairs on side, 6=fully covered)	day of birth	Score for pattern of halo hairs on side of lamb at day of birth
Birthcoat score back	Bctb	score 1-6 (1=no halo hairs on mid backline, 6=dense halo hairs)	day of birth	Score for density of halo hairs on mid backline on day of birth
Weaning weight	Weanwt	Kg	approx 4 months	Weight of lamb on day of weaning
Mean diameter of primaries	Dp	microns	14 months	Mean diameter of primary fibres from biopsy and horizontal section
Mean diameter of secondaries	Ds	microns	14 months	Mean diameter of secondary fibres from biopsy and horizontal section
Mean diameter of primaries and secondaries	Dps	microns	14 months	Mean diameter of primary and secondary fibres from biopsy and horizontal section
Primary to secondary diameter ratio	DpovDs	no units	14 months	Ratio of mean diameter of primary fibres to mean diameter of secondary fibres

4 Statistical techniques

The initial step in analysing these data was to fit a mixed model which adjusted for appropriate fixed effects and estimated additive genetic, environmental, and phenotypic variance components for wrinkle scores.

In subsequent steps various nonadditive genetic effects were added to the mixed model and their contributions to phenotypic variance estimated. The reason for doing this sequentially is that nonadditive genetic effects are often strongly correlated with additive genetic and environmental effects, so one needs to be cautious of introducing confounding into the fitted model.

After finding which effects were important for wrinkle scores, the relationship between wrinkle and some other traits was examined ina multivariate model.

4.1 Mixed model fitting

The software used for mixed model fitting and estimation of variance components and genetic parameters is known as *dmm*. *dmm* is free software available under the GPL licence from the CRAN repository. *dmm* runs as a package under the R statistical language [17]. *dmm* has a comprehensive user's guide (Jackson(2015) [8]) which covers the statistical theory used for estimation and a set of worked examples.

Variance component estimation is one of the most difficult areas of statistics. It is comprehensively documented by Searle et al (1992) [18]. The procedure which current wisdom seems to consider most appropriate is called REML. The procedures used by *dmm* are MINQUE and bias-corrected-ML. In most cases where data are not extremely unbalanced, there is very little difference between procedures. For the current task, *dmm* is most suited, because it handles multiple traits with unequal replication, because it estimates both variance/covariance components and genetic parameters arising therefrom, because it allows estimation of maternal as well as individual genetic and environmental variance components and the covariances between them. *dmm* makes extensive use of procedures developed by Wolak(2014) [21] for computing additive and non-additive relationship matrices .

The procedure followed by *dmm* is heirarchical. We first fit a model for fixed effects modelling observations on individual sheep as follows

$$Y_{ijk} = \mu + Sex_i + YearbixLine_j + r_{ijk} \tag{1}$$

where

Y_{ijk} is an observation on the kth individual of the ith Sex and the jth Year of birth x Line combination

μ is an overall mean of the observations

Sex_i is an effect due to the ith Sex

$YearbixLine_j$ is an effect due to the jth combination of Year of birth and Line

r_{ijk} is a residual deviation for the kth individual of the ith Sex and the jth Year of birth x Line combination

Equation 1 is stated as a univariate model for simplicity. It can, of course be fitted to each of a set of traits. The residual deviations from model 1 represent the observations *adjusted for* the fixed effect.

The next step is to fit a dyadic model to the residuals from model 1. A dyad is a pair of individuals. A dyadic model is a model for the covariances between the residuals for pairs of individuals. The dyadic model attempts to fit various genetic and environmental variance/covariance components to the covariances between the residuals for each dyad. In the present case we first attempt an elementary partitioning of the dyadic covariances into additive genetic and environmental variance/covariance components. The dyadic model for this simple case can be written

$$Cov(r_k, r_{k'}) = A_{kk'} VarG(Ia) + E_{kk'} VarE(I) + \Delta_{kk'} \tag{2}$$

where

$Cov(r_k, r_{k'})$ is the covariance of the kth and k'th residuals from the fitting of model 1

$A_{kk'}$ is the kk'th element of the additive genetic relationship matrix, that is the relationship coefficient between the kth and k'th individuals

$VarG(Ia)$ is the individual additive genetic variance

$E_{kk'}$ is the kk'th element of the environmental relationship matrix which is usually assumed to be an identity matrix

$VarE(I)$ is the individual environmental variance

$\Delta_{kk'}$ is the k'th residual for the dyadic model 2

Again, equation 2 is stated as a univariate model for simplicity, and only the most elementary partitioning into $VarG(Ia)$ and $VarE(I)$ is presented. There is a full exposition in Jackson(2015) [8].

The dyadic model 2 represents a set of equations which can be solved by ordinary least squares regression techniques to yield estimates of $VarG(Ia)$ and $VarE(I)$. This yields MINQUE estimates for the two variance components. Given these estimates we can then go back to the monadic model 1 and obtain GLS estimates of the fixed effects and residuals. If we then use the GLS residuals in the dyadic model 2 we obtain bias-corrected-ML estimates for the two variance components. There is a full presentation of variance component estimation in Jackson(2015) [8].

Given variance component estimates we can readily transform each component to a heritability (if it is univariate) or to a genetic(or environmental) correlation (if it is a between trait covariance component). These transforms, and the accompanying standard error estimates, are fully covered in Jackson(2015) [8]

4.2 Genetic models

The simple partitioning of phenotypic (co)variances into additive genetic and environmental (co)variances given in equation 2 is almost always the starting point for quantitative genetic analysis. It should be noted that just beacuse a considerable proportion of the phenotypic (co)variancees come out as additive genetic does not mean that most of the gene effects have to be additive. Dominance and epistatic gene effects also generate some additive genetic variance. This simple analysis leads to estimates of the following components of variance

VarG(Ia) variance genetic individual additive

VarE(I) variance environmental individual

VarP(I) variance phenotypic individual

In these analyses $VarE(I)$ is simply the variance not accounted for by additive genetic effects. It is the *convention* to call it *environmental*. It is actually just the residual unexplained variance, most likely due to random environmental differences between individuals, and measurement or appraisal errors, but could also include variation due to other components not fitted in this model.

After fitting the above additive model, the following nonadditive and maternal effects were investigated by adding stepwise to the model

VarG(Ma) variance genetic maternal additive

VarE(M) variance environmental maternal

VarG(Ia:a) variance genetic individual additive x additive epistatic

VarGs(Ia) variance sexlinked individual additive

VarGs(Ma) variance sexlinked maternal additive

CovG(Ia,Ma) covariance genetic individual additive x maternal additive

CovG(Ma,Ia) covariance genetic maternal additive x individual additive

VarG(Id) variance genetic individual dominance

VarG(Md) variance genetic maternal dominance

VarGlm(I) variance genetic maternal lines (cytoplasmic inheritance)

VarGlp(I) variance genetic paternal lines (Y chromosomal inheritance)

5 Results

5.1 Wrinkle scores partitioning of variance

We start with data from AB32 and AB20, and with all three wrinkle scores (WrN, WrB, WrT). The result of fitting the basic model with just additive genetic variance is given in Table 2

Table 2: Estimates of proportion of phenotypic variance (VarP(I)) due to VarE(I) and VarG(Ia), with standard errors and confidence limits, for neck, body, and total wrinkle scores

Trait	Component	Estimate	StdErr	CI95lo	CI95hi
WrN	VarE(I)	0.599	0.013	0.574	0.623
WrN	VarG(Ia)	0.401	0.013	0.377	0.426
WrN	VarP(I)	1.000	0.000	1.000	1.000
WrB	VarE(I)	0.604	0.013	0.580	0.629
WrB	VarG(Ia)	0.396	0.013	0.371	0.421
WrB	VarP(I)	1.000	0.000	1.000	1.000
WrT	VarE(I)	0.553	0.013	0.528	0.579
WrT	VarG(Ia)	0.447	0.013	0.421	0.472
WrT	VarP(I)	1.000	0.000	1.000	1.000

The three wrinkle scores are similar in this respect - if this simple model is appropriate, around 40 percent of the phenotypic variance is additive genetic. When we speak about phenotypic variance, we mean variance among individuals within a cohort. A cohort is a group of animals reared under common conditions, such as a drop of lambs all born within a short periond and grazed together. To get phenotypic variance we remove systematic effects by including fixed effects for Sex and Year x Line in the model. The result from fitting these fixed effects is given in Table 5.1

	Df	Pillai	approx F	num Df	den Df	Pr(>F)
(Intercept)	1	0.92	13662.10	3	3580	0.0000
Sex	1	0.03	41.69	3	3580	0.0000
YbxLi	39	0.26	8.69	117	10746	0.0000
Residuals	3582					

We see that both Sex and combinations of Year of birth and Line have significant effects. It is the residual variance from this analysis of variance which is called phenotypic variance, and it is this residual variance which we partition into random effects VarE(I) and VarG(Ia) in Table 2.

We can also partition the residual or phenotypic covariances between the three wrinkle scores. We do this in Table 3 not as covariances, but as correlations.

Table 3: Estimates of correlation among wrinkle scores for each component of variance

Traits	Component	Estimate	StdErr	CI95lo	CI95hi
WrN:WrB	VarE(I)	0.527	0.022	0.483	0.570

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Table 3 – *Continued from previous page*

Traits	Component	Estimate	StdErr	CI95lo	CI95hi
WrN:WrB	VarG(Ia)	0.949	0.017	0.916	0.981
WrN:WrB	VarP(I)	0.695	0.010	0.675	0.715
WrN:WrT	VarE(I)	0.851	0.011	0.828	0.981
WrN:WrT	VarG(Ia)	0.986	0.009	0.970	1.002
WrN:WrT	VarP(I)	0.907	0.005	0.897	0.917
WrB:WrT	VarE(I)	0.854	0.011	0.831	0.876
WrB:WrT	VarG(Ia)	0.988	0.008	0.972	1.004
WrB:WrT	VarP(I)	0.909	0.005	0.899	0.919

We see that the three wrinkle scores have very high genetic correlations , but the environmental correlations are not so high. A correlation of 0.527 between WrB and WrN means only 27 percent of the variance in WrN is correlated with WrB, at the environmental level. This is probably because the VarE(I) component includes measurement or scoring errors, and these might be uncorrelated.

We are not going to go through all the tedious steps of testing adding various types of nonadditive or maternal variance components to the model. What we do is present the final model containing all random effects found to be significant and of important magnitude. We simply note those components which were either too confounded to be estimable or too small or insignificant to be included.

The random effects found to be important are shown, with their estimated proportions of variance, in Table 4

Table 4: Estimates of proportion of phenotypic variance (VarP(I)) due to all components found to be significant, with standard errors and confidence limits, for neck, body, and total wrinkle scores

Trait	Component	Estimate	StdErr	CI95lo	CI95hi
WrN	VarE(I)	0.368	0.045	0.279	0.456
WrN	VarG(Ia)	0.277	0.022	0.233	0.322
WrN	VarG(Ia:a)	0.213	0.062	0.091	0.334
WrN	VarG(Ma)	0.141	0.031	0.079	0.203
WrN	VarE(M)	0.002	0.017	-0.031	0.035
WrN	VarGs(Ia)	0.006	0.008	-0.009	0.022
WrN	VarGs(Ma)	0.004	0.017	-0.030	0.022
WrN	CovG(Ia,Ma)	-0.006	0.018	-0.041	0.029
WrN	CovG(Ma,Ia)	-0.006	0.018	-0.041	0.029
WrN	VarP(I)	1.000	0.000	1.000	1.000
WrB	VarE(I)	0.250	0.047	0.158	0.343
WrB	VarG(Ia)	0.236	0.023	0.191	0.282
WrB	VarG(Ia:a)	0.372	0.064	0.245	0.498

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Table 4 – *Continued from previous page*

Trait	Component	Estimate	StdErr	CI95lo	CI95hi
WrB	VarG(Ma)	0.237	0.033	0.171	0.303
WrB	VarE(M)	0.001	0.017	-0.033	0.035
WrB	VarGs(Ia)	0.050	0.008	0.033	0.067
WrB	VarGs(Ma)	0.006	0.018	-0.029	0.042
WrB	CovG(Ia,Ma)	-0.077	0.018	-0.115	-0.040
WrB	CovG(Ma,Ia)	-0.077	0.018	-0.115	-0.040
WrB	VarP(I)	1.000	0.000	1.000	1.000
WrT	VarE(I)	0.251	0.045	0.161	0.340
WrT	VarG(Ia)	0.285	0.022	0.241	0.329
WrT	VarG(Ia:a)	0.301	0.062	0.179	0.422
WrT	VarG(Ma)	0.224	0.032	0.160	0.287
WrT	VarE(M)	0.000	0.001	-0.001	0.001
WrT	VarGs(Ia)	0.024	0.008	0.007	0.040
WrT	VarGs(Ma)	0.000	0.015	-0.030	0.031
WrT	CovG(Ia,Ma)	-0.043	0.017	-0.078	-0.007
WrT	CovG(Ma,Ia)	-0.043	0.017	-0.078	-0.007
WrT	VarP(I)	1.000	0.000	1.000	1.000

The dominance variance components VarG(Id) and VarG(Md) were found to be very highly correlated, in this dataset, with the environmental variance components VarE(I) and VarE(M) respectively. The actual correlations were 0.985 and 0.998 respectively. This means that is these data, dominance variance is inseparable from environmental variance. We therefore had to omit VarG(Id) and VarG(Md) from the fitted model. There may be dominance effects, but we could not separate them from environmental effects with these data. That is not unusual in pedigrees with a low level of inbreeding.

Also omitted were the maternal epistatic component VarG(Ma:a), and the variances between male and female founder lines, VarGlm(I) and VarGlp(I). These were omitted because the estimates were extremely small (less than 10^{-5}). There was therefore no evidence of maternal additive x additive epistatic effects. and no evidence of either cytoplasmic inheritance (VarGlm(I)) or paternal Y chromosomal inheritance (VarGlm(I)).

Because the dominance effects were confounded , we were also unable to look at epistatic variance components involving dominance (VarG(Ia:d), VarG(Id:d) and their maternal equivalents).

That leaves us with the effects listed in Table 4. A number of these are also quite small proportions of the phenotypic variance. We could omit VarE(M), VarGs(Ia), VarGs(Ma), CovG(Ia,Ma), and CovG(Ma,Ia) and we would be ignoring only about 10 percent of phenotypic variance. Thus there is little evidence for sexlinked genetic effects, either individual or maternal, and only a tiny (negative) covariance of individual and maternal additive genetic effects.

We are left with VarE(I), VarG(Ia), VarG(Ia:a), and VarG(Ma), and these each account for roughly 1/4 each of the phenotypic variance. Thus there is evidence for additive genetic variance (VarG(Ia)), additive x additive epistatic interaction variance (VarG(Ia:a)), and maternal additive genetic variance (VarG(Ma)).

As a final check we ran the model fit once more, with just the above 4 components of variance included. This is shown in Table 5

Table 5: Estimates of proportion of phenotypic variance (VarP(I)) due to the four most significant components, with standard errors and confidence limits, for neck, body, and total wrinkle scores

Trait	Component	Estimate	StdErr	CI95lo	CI95hi
WrN	VarE(I)	0.400	0.050	0.301	0.498
WrN	VarG(Ia)	0.313	0.024	0.266	0.360
WrN	VarG(Ia:a)	0.262	0.069	0.125	0.398
WrN	VarG(Ma)	0.025	0.010	0.005	0.045
WrB	VarE(I)	0.278	0.050	0.179	0.378
WrB	VarG(Ia)	0.252	0.024	0.205	0.300
WrB	VarG(Ia:a)	0.439	0.070	0.302	0.578
WrB	VarG(Ma)	0.029	0.010	0.008	0.049
WrT	VarE(I)	0.273	0.051	0.173	0.373
WrT	VarG(Ia)	0.318	0.024	0.271	0.366
WrT	VarG(Ia:a)	0.374	0.070	0.237	0.512
WrT	VarG(Ma)	0.033	0.010	0.012	0.053

We see that the proportions of variance attributed to VarE(I), VarG(Ia), and VarG(Ia:a) have remained similar, but the proportion of variance attributed to VarG(Ma) is less. So we confirm the epistatic component but there is some doubt attached to the size of the maternal genetic component. This sort of shifting around often happens when small but correrlated components are removed from a model. Notice that the standard errors in Table 5 are larger than in Table 4; there is more unexplained variation. The most reliable estimates are those of Table 4 with all significant components fitted.

We started this investigation expecting to find some maternal effects on wrinkle, and we have found some, but they are small in terms of proportion of variance. Some genes carried by the mother affect the development of the wrinkle phenotype of the offspring.

What we did not expect was such a large epistatic component. There are some pairs genes at separate loci which combine to produce a greater effect on wrinkle than would be expected by adding the effects of the two genes alone. This sort of gene action accounts for 21 percent of phenotypic variance in neck wrinkle (WrN) and 37 percent of phenotypic variance in body wrinkle (WrB).

There are consequences for breeding and selection. Gains made by selecting epistatic combinations of genes are not permanent, they disappear when the genes segregate.

We have conducted a number of further checks on this analysis. These are presented in Appendix B. In particular we wanted to see if the estimate of VarG(Ia:a), the epistatic component, had been biased in some way. We found nothing. We have to conclude that the epistatic variance for wrinkle score is real and large.

6 Discussion

Maternal genetic effects on wrinkle have a ready made explanation, but the details of proof are not yet at hand. Mothers with a genetically high wrinkle score are deficient in temperature regulation . Poor temperature regulation may affect foetal skin development (there is evidence of adverse effects on neural system and developmental disorders in mice, and evidence of adverse effects on lamb mortality in sheep). So 14 percent of phenotypic variance for neck wrinkle, and 24 percent for body wrinkle, being additive genetic maternal is not unexpected. It supports the above explanation, but we have a long way to go finding all the biological evidence.

Epistatic genetic effects on wrinkle are another matter. We did not expect this, but we should have, because it strongly supports our current theory about the way that wrinkles are formed. The supporting evidence is still being assembled, but briefly, wrinkles form because there are two layers in the skin of the developing lamb foetus which expand at different rates. These are the papillary layer containing the wool follicles, and the layer of dermis immediately below the follicle bulbs which can contain varying amounts of collagen fibril development. When a lot of follicles initiate they expand the upper dermis considerably (Jackson and Watts (2018) [11]). When a lot of collagen fibrils form in the dermis below follicle bulbs, it binds the dermis against expansion and may even shrink it (Watts personal communication). The conflict between these two tensions causes the epidermis and dermis to fold, just like a bimetal strip bending. Only sheep with both a high follicle number and a high collagen develop wrinkle. That is where the interaction or epistatic effect is coming from. The genes for follicle number interact with the genes for collagen development. That is what causes epistatic effects - two sets of genes interacting.

The other issue that complicates this interpretation is that not all epistatic gene effects appear as epistatic variance when we do a partitioning of phenotypic variation. Some of them do, and some appear in the additive genetic variance. So the 27 percent of additive genetic variance for neck wrinkle (and 24 percent for body wrinkle) may also be at least in part a reflection of epistatic gene action. Our wrinkle theory actually says that all the variation in wrinkle is controlled by interaction between follicle number and collagen amount, so it is possible that all the variance analysed as additive genetic is actually due to interaction, as well as all that actually analysed as epistatic, and in that case

we are looking at 50 percent of the phenotypic variance supporting our theory. That is a phenomenally successful result.

We tried to show, using a covariance analysis, that some traits which we regarded as indicators of the two interacting components of wrinkle , could 'explain' some of the epistatic variance. This was only partly successful. It is shown in Appendix A. There were too many analysis difficulties for it to be definitive.

We conclude with a quotation from Lynch and Walsh(1997) [12]

> Because of the heirarchical way in which genetic effects are defined, we might expect the magnitude of genetic variance components to become progressively smaller at higher stages in the heirarchy. Indeed, it is common for quantitative geneticists to use this argument as a rationalization for ignoring epistasis altogether. Unfortunately, such logic does not always hold up – as pointed out in the previous chapter, unless information on gene frequencies is available, variance components provide limited insight into the physiological mode of gene action.

That says it all.

A Appendix - can covariance analyses confirm the epistasis explanation?

We have asserted that the reason why wrinkle score has a large epistatic variance component is that wrinkle is determined by two interacting components. We have tentatively identified these components as

dermal expansion due to follicle development in particular the development of large numbers of secondary derived follicles at around day 100 of gestation results in an expansion of the upper dermis relative to other skin layers

dermal binding or contraction due to collagen development in particular the development of a layer of non reticular collagen below the follicle bulbs in the dermis prevents dermal expansion and may even lead to contraction

We suggest it is the tension between these two components which leads to skin folding.

One way of checking this explanation of epistasis is to find some measures of the two components of wrinkle, to remove their effect on wrinkle using covariance analysis, and to see if the variance of 'covariance adjusted wrinkle score' is still epistatic. For the follicle development factor we really need a measure of the number of secondary derived or branching follicles. We do not have these data. The best we can do is S/P ratio (Fr) or diameter of primary follicles (Dp). For collagen development we have no direct measure at all. We do know , however,

that one strong side effect of collagen development is follicle curvature (Fc), so we propose to use Fc, and its wool effect crimp frequency (Crimp).

We did these covariance analyses one trait at a time. So we have one analysis of WrN unadjusted, one analysis of WrN/Fr (wrinkle adjusted for Fr), one analysis of WrN/Dp, one analysis of WrN/Crimp, and one analysis of WrN/Fc. The result is shown in Figure 4

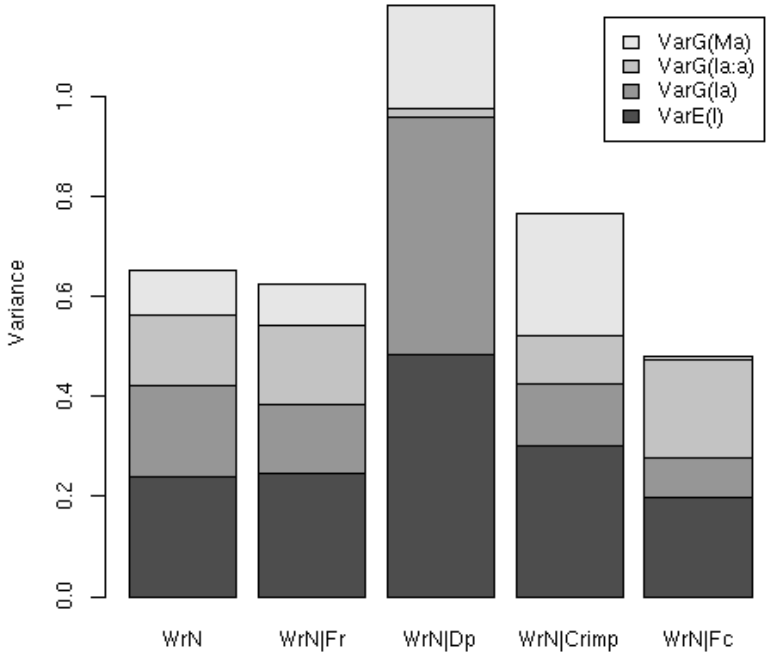

Figure 4: Variance component analyses of neck wrinkle scores (WrN) unadjusted and adjusted for each of the four component indicators (Fr, Dp, Crimp, Fc) in turn

Then we repeat the whole thing for WrB, with result shown in Figure 5

We see that for both WrN and WrB, the only adjustment that substantially reduced the epistatic variance was Dp. For body wrinkle Fr, Crimp and Fc adjustment also reduced epistatic variance slightly. For neck wrinkle, epistatic variance was not as large unadjusted, and only Dp adjustment led to further reduction.

There were a number of difficulties with these covariance analyses. The numbers of degrees of freedom changed substantially when the covariance ad-

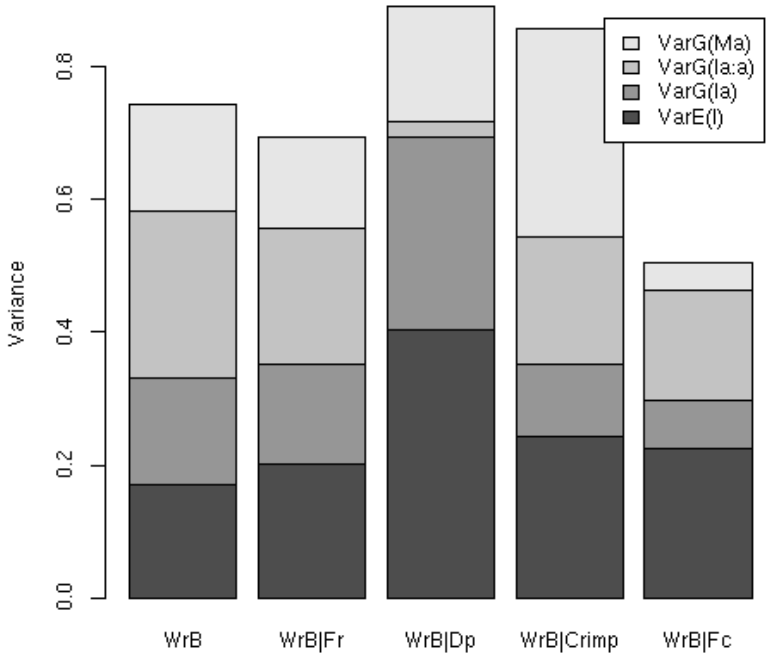

Figure 5: Variance component analyses of body wrinkle scores (WrB) unadjusted and adjusted for each of the four component indicators (Fr, Dp, Crimp, Fc) in turn

justments were added, due to missing data for the covariates. We have only shown the four most significant components in Figures 4 and 5, the remaining five components also varied with adjustment. The total phenotypic variance tended to increase with adjustment in some cases, this being a reflection of added measurement errors. One would expect, that everything else being equal, the phenotypic variance would be less for an adjusted variable, than for unadjusted.

So what can we conclude from this exercise? For body wrinkle there is some evidence that covariance adjustment removes some of the epistasis. For neck wrinkle it is less clear, and the epistatic component was smaller anyway for neck wrinkle. It may be that neck folds have an additional component that we have not identified.

Why was the adjustment using Dp succesful in removing epistatic variance? Well Dp is a powerful indicator of ability to develop masses of secondary derived follicles. The other 3 indicators are less direct. In particular, Fc and Crimp are

side effects of collagen development, and not all the variation in Fc and Crimp is due to collagen, some being due to intrinsic curvature of the fibre. Fr includes So follicles as well as Sd, so it is also influenced by extraneous factors. We simply do not have direct accurate measures of branching follicle development or of collagen development.

B Appendix - checks on the variance component analyses

B.1 Omitted variable bias

Variance component analyses are not straightforward. In a mixed model, when partitioning the phenotypic variance into components, one needs to be extremely careful that one does not omit some component that is both large and significant. To do so would bias the estimates for all components. One can see this by comparing Tables 2 and 5 from the Results section. When only VarE(I) and VarG(Ia) are partitioned, these account for about 60 percent and 40 percent of the phenotypic variance. When VarG(Ia:a) and VarG(Ma) are also fitted, the four components each account for about 25 percent of the phenotypic variance. So the heritability has 'shrunk' from 40 percent top 25 percent. The 40 percent estimate is substantially wrong. It is biased because not all important components were fitted.

So we need to be sure that our 4 component partitioning has not ignored some other effect that is large and significant. In the Results section we note that there were some components (VarG(Id) and VarG(Md)) which were too highly correlated with other components to be separately estimable. We also noted that VarG(Ma:a), VarGlm(I) and VarG(lp(I) were absolutely tiny and could be safely omitted. THen there were 5 components (VarE(M), VarGs(Ia), VarGs(Ma), CovG(Ia,Ma), and CovG(Ma,Ia)) which were quite small but not zero, and could also be omitted.

What we have not checked is environmental cross-effect covariances. In particular CovE(I,M) and CovE(M,I) need to be examined. We ran another analysis partitioning the phenotypic variance into 9 components (VarE(I), VarG(Ia) , VarG(Ia:a), VarE(M), VarG(Ma), CovG(Ia,Ma), CovG(Ma,Ia), CovE(I,M), CovE(M,I)), so that all possible cross effect covariances were included). The estimates for CovE(I,M) and CovE(M,I) were tiny, and the other components did not shift around significantly. We conclude that cross effect covariances are not an issue, and can be ignored.

B.2 Maximum likelihood estimates

Another way of checking is to use a different estimation technique. The package *dmm* can also do bias-corrected maximum likelihood estimates. This is an iterative procedure in which the fixed effects are iterated towards GLS estimates, using successively improved estimates of the variance components.

The results of a bias-corrected ML iteration are given in Table 6

Table 6: Bias-corrected maximum likelihood estimates of proportion of phenotypic variance (VarP(I)) due to the four most significant components, with standard errors and confidence limits, for neck, body, and total wrinkle scores

Trait	Component	ML Estimate	StdErr	CI95lo	CI95hi
WrN	VarE(I)	0.343	0.028	0.268	0.399
WrN	VarG(Ia)	0.269	0.013	0.242	0.295
WrN	VarG(Ia:a)	0.351	0.039	0.274	0.429
WrN	VarG(Ma)	0.035	0.005	0.024	0.046
WrB	VarE(I)	0.228	0.029	0.169	0.286
WrB	VarG(Ia)	0.195	0.013	0.168	0.221
WrB	VarG(Ia:a)	0.530	0.040	0.450	0.609
WrB	VarG(Ma)	0.046	0.006	0.035	0.058
WrT	VarE(I)	0.226	0.030	0.167	0.248
WrT	VarG(Ia)	0.257	0.013	0.230	0.284
WrT	VarG(Ia:a)	0.467	0.040	0.387	0.547
WrT	VarG(Ma)	0.049	0.006	0.037	0.060

Table 6 should be compared with Table 5 which are the MINQUE estimates with OLS estimates of fixed effects.

We see that the epistatic component (VarG(Ia:a)) has actually increased in Table 6 compared to Table 5, and the standard errors of estimates are smaller. The iterative estimation procedure only took 3 rounds to converge - the output is shown below

```
.....
GLS-b step:
Warning: Multivariate GLS is not same as multiple univariate GLS's
Round =  1  Stopcrit =  0.06876087
Round =  2  Stopcrit =  0.01187422
Round =  3  Stopcrit =  0.002260546
Iteration completed - count =  3
Convergence achieved
GLS-b step completed successfully:
....
```

This is a very well behaved iteration. It is a matter of experience that this iteration will misbehave if the model is not appropriate for the data. This is an indication that our estimate of epistatic variance (and the other 3 components) is free of interfering issues with the model or data.

B.3 Outlier effects

It is possible for analyses to be biased by presence of a small number of outliers. The package *dmm* has an option to use robust regression methods instead of ordinary least squares for variance component estimation. This is possible because *dmm* reduces variance component estimation to a regression problem.

We reran the analysis from Table 5 using robust regression. Robust regression is a univariate procedure. We had to do one trait at a time. W e only did WrN and WrB. That was sufficient to achieve our aim of looking at out lier bias. The results are shown in Table 7

Table 7: Robust regression estimates of proportion of phenotypic variance (VarP(I)) due to the four most significant components, with standard errors and confidence limits, for neck, and body wrinkle scores

Trait	Component	Estimate	StdErr	CI95lo	CI95hi
WrN	VarE(I)	0.311	0.110	0.094	0.527
WrN	VarG(Ia)	0.327	0.052	0.224	0.431
WrN	VarG(Ia:a)	0.340	0.153	0.039	0.640
WrN	VarG(Ma)	0.021	0.022	-0.023	0.065
WrB	VarE(I)	0.123	0.109	-0.091	0.338
WrB	VarG(Ia)	0.152	0.051	0.051	0.254
WrB	VarG(Ia:a)	0.668	0.152	0.368	0.967
WrB	VarG(Ma)	0.055	0.022	0.011	0.099

The resuts are similar, slight decreases in VarE((I) and VarG(Ia), and sligtht increases in VarG(Ia:a) and VarG(Ma). Standard errors are larger, because some observations have been discarded by the robust regression procedure.

So there is strong evidence that our analysis showing epistatic variance was not biased by outlier effects.

B.4 Correlation between estimates

The components we have chosen to include in our partitioning of phenotypic variance are correlated with one another. Table 8 shows correlations among the columns of the coefficient matrix W for the 9 compoonents included in Table 4.

Table 8: Correlations among columns of the W matrix used to estimate 9 components of variation in wrinkle scores

	VarE(I)	VarG(Ia)	VarG(Ia:a)	VarG(Ma)	VarE(M)	VarGs(Ia)	VarGs(Ma)	CovG(Ia,Ma)	CovG(Ma,Ia)
VarE(I)	1.00	0.54	0.89	0.50	0.60	0.53	0.42	0.35	0.35
VarG(Ia)	0.54	1.00	0.82	0.55	0.50	0.67	0.50	0.59	0.59
VarG(Ia:a)	0.89	0.82	1.00	0.60	0.63	0.68	0.52	0.53	0.53
VarG(Ma)	0.50	0.55	0.60	1.00	0.82	0.64	0.93	0.76	0.76
VarE(M)	0.60	0.50	0.63	0.82	1.00	0.53	0.70	0.57	0.57
VarGs(Ia)	0.53	0.67	0.68	0.64	0.53	1.00	0.65	0.61	0.61
VarGs(Ma)	0.42	0.50	0.52	0.93	0.70	0.65	1.00	0.71	0.71
CovG(Ia,Ma)	0.35	0.59	0.53	0.76	0.57	0.61	0.71	1.00	0.58
CovG(Ma,Ia)	0.35	0.59	0.53	0.76	0.57	0.61	0.71	0.58	1.00

The correlations of sufficient magnitude to be of concern are between VarE(I) and VarG(Ia:a) (0.89), and between VarG(Ia) and VarG(Ia:a) (0.82). Because these involve the major components of interest, we need to look further.

We reran the analysis from Table 4 using principal component regression instead of OLS. There were 9 variance components estimated, so we are talking about estimation in a 9-dimensional parameter space. Of these 9 dimensions, the principal component regression showed that only about 5 dimensions were significant. This conclusion is reached by examination of the proportins of variance explained by successively increasing numbers of principal components. This is shown in Table 9

Table 9: Cumulative proportions of variance accounted for by successively increasing numbers of principal components in a principal component regression analysis of wrinkle score data

Number of Principal Components	Percent variance explained
1	70.03
2	82.06
3	88.48
4	92.76
5	95.60
6	97.90
7	99.38
8	99.88
9	100.00

What happens in principal component regression is that the regression coefficients are estimated by regressing the data on the set of 9 (or fewer) principal components, rather than on the 9 variance component parameters of interest. This has the feature that the 9 components are independent, so the problem with correlations, noted above, disappears. We can then take the principal component regression coefficients, and convert them back to variance component estimates, ie to regressions on the original X variates, which in our case are columns of the W matrix. If we do this using all 9 principal components, we get exactly the same estimates of variance components as we get using OLS. The interest is in using fewer than 9 principal components, in the present case about 5 should be adequate.

The variance component parameter estimates we get using 5 principal components are shown in Table 10.

Table 10: Estimates of proportion of phenotypic variance (VarP(I)) due to nine variance components of Table 4, but estimated by principal component regression using only 5 principal components. With standard errors and confidence limits, for neck, body, and total wrinkle scores

Trait	Component	Estimate	StdErr	CI95lo	CI95hi
WrN	VarE(I)	0.185	0.005	0.174	0.196
WrN	VarG(Ia)	0.326	0.007	0.312	0.339
WrN	VarG(Ia:a)	0.231	0.002	0.225	0.236
WrN	VarG(Ma)	0.018	0.002	0.013	0.023
WrN	VarE(M)	0.164	0.008	0.147	0.180
WrN	VarGs(Ia)	0.002	0.004	0.016	0.033
WrN	VarGs(Ma)	0.000	NA	NA	NA
WrN	CovG(Ia,Ma)	0.024	0.014	-0.004	0.053
WrN	CovG(Ma,Ia)	0.024	0.014	-0.003	0.052
WrN	VarP(I)	1.000	0.000	1.000	1.000
WrB	VarE(I)	0.191	0.007	0.176	0.205
WrB	VarG(Ia)	0.304	0.008	0.286	0.321
WrB	VarG(Ia:a)	0.229	0.003	0.222	0.235
WrB	VarG(Ma)	0.011	0.003	0.222	0.235
WrB	VarE(M)	0.166	0.010	0.145	0.187
WrB	VarGs(Ia)	0.070	0.005	0.063	0.084
WrB	VarGs(Ma)	0.000	0.000	-0.000	0.000
WrB	CovG(Ia,Ma)	0.012	0.016	-0.019	0.045
WrB	CovG(Ma,Ia)	0.012	0.016	-0.018	0.043
WrB	VarP(I)	1.000	0.000	1.000	1.000
WrT	VarE(I)	0.172	0.005	0.160	0.1183
WrT	VarG(Ia)	0.337	0.006	0.323	0.350
WrT	VarG(Ia:a)	0.225	0.003	0.218	0.231
WrT	VarG(Ma)	0.014	0.002	0.009	0.019
WrT	VarE(M)	0.141	0.007	0.125	0.156
WrT	VarGs(Ia)	0.042	0.004	0.033	0.050
WrT	VarGs(Ma)	0.000	NA	NA	NA
WrT	CovG(Ia,Ma)	0.034	0.013	0.008	0.060
WrT	CovG(Ma,Ia)	0.034	0.013	0.007	0.061
WrT	VarP(I)	1.000	0.000	1.000	1.000

We see that there is only a small difference between Table 10 and Table 4. The difference mostly involves the VarG(Ma) component , which has become small and been replaced by VarE(M) accompanied by a shift in the sign of CovG(Ia,Ma) and CovG(Ma,Ia). For WrB the VarG(Ia:a) epistatic components has descreased, but is stll large and significant. For WrN the VarG(Ia:a) component is unchanged. For both WrB and WrN the VarG(Ia) component is slightly

increased and the VarE(I) component is slightly lower. The sex linked variance components remain low.

One can conclude that there is some doubt as to whether the maternal variance component is genetic or environmental, but there is no doubt that the epistatic genetic variance component is present.

Note that the standard errors of estimates from principal component regression are lower than those from the standard OLS regression. That is because constraints have been applied by omitting 4 of the 9 principal components. If one simply omits a variance component under OLS, that is equivalent to constraining the parameter estimates to lie on a plane in parameter space which is parallel to one of the axes. If , instead, one omits a principal component under PCR, that is equivalent to constraining the parameter estimates to lie on a plane which is at angles to the other axes. The equation of the constraint plane is given by the *loadings* for each principal component. So we will finish by looking at the *loadings*. These are given in Table 11

Table 11: Loadings of nine principal components on the nine variance components for wrinkle score data

Principal component	1	2	3	4	5	6	7	8	9
Variance component									
VarE(I)	-0.134		-0.345	-0.362		-0.319	0.528		0.583
VarG(Ia)	-0.288	0.323	-0.535	0.510		-0.133	-0.445		0.219
VarG(Ia:a)	-0.190	0.165	-0.404	-0.108		-0.252	0.295		-0.782
VarG(Ma)	-0.396	-0.395						0.823	
VarE(M)	-0.282	-0.267	-0.367	-0.524		0.481	-0.352	-0.292	
VarGs(Ia)	-0.549	0.637	0.465	-0.243		0.116			
VarGs(Ma)	-0.454	-0.454	0.285			-0.580	-0.175	-0.367	
CovG(Ia,Ma)	-0.244	-0.100		0.360	-0.707	0.339	0.372	-0.217	
CovG(Ma,Ia)	-0.244	-0.100		0.360	-0.707	0.339	0.372	-0.217	
VarP(I)									

The most obvious thing to note is the loadings for component 5. These say that the two cross-effect covariance components (CovG(Ia,Ma) and CovG(Ma,Ia)) are equal if component 5 is set to zero (ie omitted). We know these are equal for one trait, so the constraint plane of component 5 is not expected to lead to a serious reduction in variation.

However there are 4 other components which define constraint planes which are even less serious than component 5. We need to interpret these. In particular component 9 says that VarG(Ia:a) equals a weighted sum of VarE(I) and VarG(Ia). Component 9 only leads to a 0.2 percent reduction in variation if it is omitted (set to zero) so this effectively says that all observations lie on the plane defined by

$$.583VarE(I) + .219VarG(Ia) - .782VarG(Ia : a) = 0$$

That is the net effect of those correlations in Table 8. The pedigree structure of the data constrains it in this way. This is not to say that these three components cannot vary, they can, but can only vary in a way that maintains the above relationship.

Components 6, 7, and 8 are more complex. Component 8 says that VarG(Ma) is constrained to a weighted sum of the other components involving maternal effects. Components 6 and 7 we will leave.

Constraints on the parameter space which arise from the correlations of Table 8 are due to the data structure only. The actual data values do not contribute to Table 8. So the estimates of components we get will not be the same for all traits, despite the above constraints.

We will finish by having a look at estimates of variance components for a range of traits other than wrinkle scores. We do this to demonstrate that the result of a large VarG(Ia:a) estimate for wrinkle scores is not inevitable, given the data structure.

We divide our traits into 3 groups, according to the estimates obtained for VarG(Ia:a) and VarG(Ia).

only VarG(Ia) large weaning weight, adult body weight

only VarG(Ia:a) large follicle density, S/P ratio, crimp frequency

both VarG(Ia) and VarG(Ia:a) large clean wool weight, fibre diameter, crimp wavelength, follicle curvature, wrinkle scores

So results differ depending on the trait measurements. In particular the fact that some traits had zero VarG(Ia:a) indicates that the result of a significant VarG(Ia:a) for wrinkle scores weas not inevitable, it depends on the data.

We also note that crimp frequency had only VarG(Ia:a) but crimp wavelength had both. Wavelength is simply the reciprocal of frequency. So a transformation of th data can alter the result. We need to investigate that in relation to wrinkle scores.

We also need to look at some other data sets, hopefully with a diffferent set of correlations to that in Table 8.

We do both these follow up investigations in the following two sections.

B.5 Scale effects

We need to see whether changing the scale of wrinkle score alters the variance component estimates, in particular whether VarG(Ia:a) changes. We redo the analysis of Table 4 with transformed values of WrB. We use the reciprocal transform (actually $1/(WrB+0.1)$, to avoid dividing by zero when the wrinkle score is zero), and the square (WrB^2). Results are shown in Table 12

Table 12: Estimates of proportion of phenotypic variance (VarP(I)) due to all components found to be significant, with standard errors and confidence limits, for body wrinkle score, and its reciprocal, and square transformations

Trait	Component	Estimate	StdErr	CI95lo	CI95hi
WrB	VarE(I)	0.250	0.047	0.158	0.343
WrB	VarG(Ia)	0.236	0.023	0.191	0.282
WrB	VarG(Ia:a)	0.372	0.064	0.245	0.498
WrB	VarG(Ma)	0.237	0.033	0.171	0.303
WrB	VarE(M)	0.001	0.017	-0.033	0.035
WrB	VarGs(Ia)	0.050	0.008	0.033	0.067
WrB	VarGs(Ma)	0.006	0.018	-0.029	0.042
WrB	CovG(Ia,Ma)	-0.077	0.018	-0.115	-0.040
WrB	CovG(Ma,Ia)	-0.077	0.018	-0.115	-0.040
WrB	VarP(I)	1.000	0.000	1.000	1.000
1/WrB	VarE(I)	0.848	0.048	0.753	0.941
1/WrB	VarG(Ia)	0.184	0.024	0.136	0.230
1/WrB	VarG(Ia:a)	0.000	0.080	-0.157	0.159
1/WrB	VarG(Ma)	0.051	0.033	-0.014	0.118
1/WrB	VarE(M)	0.032	0.018	-0.004	0.070
1/WrB	VarGs(Ia)	0.059	0.009	0.040	0.077
1/WrB	VarGs(Ma)	0.000	0.020	-0.004	0.004
1/WrB	CovG(Ia,Ma)	-0.080	0.020	-0.127	-0.048
1/WrB	CovG(Ma,Ia)	-0.080	0.020	-0.127	-0.048
1/WrB	VarP(I)	1.000	0.000	1.000	1.000
WrB^2	VarE(I)	0.323	0.046	0.231	0.414
WrB^2	VarG(Ia)	0.181	0.022	0.136	0.226
WrB^2	VarG(Ia:a)	0.355	0.064	0.228	0.481
WrB^2	VarG(Ma)	0.225	0.033	0.158	0.291
WrB^2	VarE(M)	0.000	0.016	-0.031	0.032
WrB^2	VarGs(Ia)	0.044	0.008	0.027	0.061
WrB^2	VarGs(Ma)	0.000	0.003	-0.007	0.007
WrB^2	CovG(Ia,Ma)	-0.064	0.018	-0.101	-0.027
WrB^2	CovG(Ma,Ia)	-0.064	0.018	-0.101	-0.027
WrB^2	VarP(I)	1.000	0.000	1.000	1.000

The reciprocal transform reduces the VarG(Ia:a) epistatic component to near zero, the square transform leaves it unchanged at about 36 percent of the phenotypic variance. Both transforms increase the environmental variance, and both decrease VarG(Ia) . Reciprocal is a very severe transform.

It is well known that interaction effects can be altered by change of scale. This applies to variance components equally as well as to fixed effects. One can only make an interaction dissapear by change of scale if it does not involve change of rank. Epistasis for wrinkle is unlikely to involve change of rank. It is not unexpected, that the epistatic component is the one most affected by change of scale.

So you can get almost any result you want by choosing a scale. Does that invalidate the analysis? No. The epistatic effect (VarG(Ia:a)) is valid for wrinkle score on the scale at which it was observed.

What the scale effect does prove is that the structure of this dataset is not solely responsible for the estimation of an epistatic component of variance. It can be removed or augmented by changing the data, either by going to another trait, or by rescaling the wrinkle score.

B.6 Other datasets

References

[1] Chapman, R.E. (1965) The ovine arrector pili musculature and crimp formation in wool. In "Biology of the Skin and Hair Growth" Angus and Robertson, Sydney, Ed. A.G. Lyne and B.F. Short. pp 201-232

[2] Horio, M. and Kondo, T. (1953) Text. Res. J. 23:373

[3] Jackson, N.(2017) Genetic relationship between skin and wool traits in Merino sheep. Part I Responses to selection and estimates of additive genetic parameters. URL https://github.com/nevillejackson/Fleece-genetics/tree/master/skinandfleeceparameters/ab3220/skinwool1.pdf

[4] Jackson, N. and Watts, J.E. (2017) What is known about the genetics of wrinkle score in Merino sheep? URL https://github.com/nevillejackson/Fleece-genetics/tree/master/wrinkle/wrinkle.pdf

[5] Jackson, N., Nay T. and Turner, Helen Newton (1975) Response to selection in Australian Merino sheep. VII Phenotypic and genetic parameters for some wool follicle characteristics and their correlation with wool and body traits. Aust. J. Agric. Res. 26:937-57

[6] Jackson, N. and Watts, J.E. (2016) Staple crimp formation in the fleece of Merino sheep. Report available from the authors as a pdf document.

[7] Jackson, N. and Watts J.E. (2016) Can we predict intrinsic fibre curvature from follicle curvature score? Report available from the author as a pdf document.

[8] Jackson, N. (2015) An Overview of the R package dmm. From http://cran.r-project.org/package=dmm Or https://github.com/cran/dmm

[9] Jackson, N. Lax, J. and Wilson, R.L.(1986) Sex and selection for fleece weight in Merino sheep. Zeitschrift fur Tierzuchtung und Zuchtungsbiologie. Bd. 103:97-115

[10] Jackson, N. (2017) What are the defining characteristics of a primitive sheep relative to a modern Merino sheep? https://github.com/nevillejackson/atavistic-sheep/tree/master/mev-rewrite/supplementary/primitive/primitive.pdf

[11] Jackson, N. and Watts, J. E. (2018) Does follicle development affect the spatial layout of sheep skin? URL https://github.com/nevillejackson/Fleece-biology/tree/master/skinspace/skinspace.pdf

[12] Lynch, M. and Walsh, B. (1997) Genetics and Analysis of Quantitative Traits. Sinauer, Massachusetts, USA, 1997

[13] Moore, G.P.M, Jackson, N. and Lax, J. (1989) Evidence of a unique developmental mechanism specifting follicle density and fibre size in sheep selecterd for single skin and fleece characters. Genetical Reaearch. 53:57-62

[14] Nagorcka, B.N. (1981) Theoretical mechanism for crimp. Aust J. Biol. Sci. 34: 189-209

[15] Onions, W.J. (1962) Wool: an introduction to its properties, varieties, uses and production. Ernest Benn limited, London, 1962

[16] Rendel, J.M. and Nay, T. (1978) Selection for high and low ratio and high and low primary density in Merino sheep. Aust. J. Agric. Res. 29:1077-86

[17] R Core Team (2013). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. ISBN 3-900051-07-0, URL http://www.R-project.org/.

[18] Searle, S.R., Casella, G., and McCullock, C.E. (1992) Variance Components. John Wiley and Sons, New York.

[19] Swan, P.G. (1993) Objective measurement of fibre crimp curvature and the bulk compressional properties of Australian wools. PhD Thesis, University of NSW, March 1993

[20] Watson, N., Jackson, N. and Whiteley, K.J. (1977) Inheritance of the resistance to compression property of Austrailian Merino wool and its genetic correlation with follicle curvature and various wool and body characters. Aust. J. Agric. Res. 28:1083-94

[21] Wolak, M.E. (2014) nadiv: an R package to create relatedness matrices for estimating non-additive genetic variances in animal models. Methods in Ecology and Evolution 3:792-796.

[22] Turner, H.N., Dolling, C.H.S, and Kennedy, J.F. (1968) Response to selection in Australian Merino sheep. I Selection for high clean wool weight with aceiling on fibre diameter and degree of skin wrinkle. Aust.J.agric.Res. 19:79-112

[23] Turner, H.N., Hayman, R.H., Riches, J.H., Roberts, N.F., and Wilson, L.T. (1953) Physical definition of sheep and their fleece for breeding and husbandry studies, with particular reference to Merino sheep. CSIRO Aust. Div. Anim. Hlth. Prod. Divl. Rep. No 4 (Series S.W. -2)