Introduction; variance components and heritability

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Workshop on Evolutionary Quantitative Genetics

Introduction; variance components and heritability – p.1/30

Development of quantitative genetics theory









Empirical statistical models (their "Law of Ancestral Heredity") by Galton and Pearson from 1889 on were overwhelmed by R. A. Fisher's 1918 Mendelian tour-de-force ... which Jay Lush and his colleagues made the center of modern animal and plant breeding

$$P = \mu + \begin{pmatrix} AA & -2 \\ Aa & 0 \\ aa & 3 \end{pmatrix} + \begin{pmatrix} BB & 0.6 \\ Bb & 0.1 \\ bb & -0.2 \end{pmatrix} + \begin{pmatrix} CC & -1 \\ Cc & 6 \\ cc & 6 \end{pmatrix} + \begin{pmatrix} DD & 0.3 \\ Dd & 0.3 \\ dd & 0.7 \end{pmatrix} + \begin{pmatrix} EE & -0.4 \\ Ee & 0.3 \\ ee & -0.3 \end{pmatrix} + \frac{environmental}{effect}$$

arbitrary starting point (4)

AA Bb Cc dd Ee

$$\frac{E}{e} = \frac{A}{A} = \frac{c d}{C d} = \frac{B}{b}$$

$$P = \mu + \begin{pmatrix} AA & -2 \\ Aa & 0 \\ aa & 3 \end{pmatrix} + \begin{pmatrix} BB & 0.6 \\ Bb & 0.1 \\ bb & -0.2 \end{pmatrix} + \begin{pmatrix} CC & -1 \\ Cc & 6 \\ cc & 6 \end{pmatrix} + \begin{pmatrix} DD & 0.3 \\ Dd & 0.3 \\ dd & 0.7 \end{pmatrix} + \begin{pmatrix} EE & -0.4 \\ Ee & 0.3 \\ ee & -0.3 \end{pmatrix} + \frac{environmental}{effect}$$

arbitrary starting point (4)

AA Bb Cc dd Ee

$$4 + 0.3 - 2$$

$$E = A \qquad C d \qquad B \\ C d \qquad b$$

$$P = \mu + \begin{pmatrix} AA & -2 \\ Aa & 0 \\ aa & 3 \end{pmatrix} + \begin{pmatrix} BB & 0.6 \\ Bb & 0.1 \\ bb & -0.2 \end{pmatrix} + \begin{pmatrix} CC & -1 \\ Cc & 6 \\ cc & 6 \end{pmatrix} + \begin{pmatrix} DD & 0.3 \\ Dd & 0.3 \\ dd & 0.7 \end{pmatrix} + \begin{pmatrix} EE & -0.4 \\ Ee & 0.3 \\ ee & -0.3 \end{pmatrix} + \frac{environmental}{effect}$$

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arbitrary starting point (4)

AA Bb Cc dd Ee

$$A = B Cc DD EE$$

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$$A = C d B$$

$$B = D = D$$

$$P = \mu + \begin{pmatrix} AA & -2 \\ Aa & 0 \\ aa & 3 \end{pmatrix} + \begin{pmatrix} BB & 0.6 \\ Bb & 0.1 \\ bb & -0.2 \end{pmatrix} + \begin{pmatrix} CC & -1 \\ Cc & 6 \\ cc & 6 \end{pmatrix} + \begin{pmatrix} DD & 0.3 \\ Dd & 0.3 \\ dd & 0.7 \end{pmatrix} + \begin{pmatrix} EE & -0.4 \\ Ee & 0.3 \\ ee & -0.3 \end{pmatrix} + \frac{environmental}{effect}$$

arbitrary starting point (4)

AA Bb Cc dd Ee 10

Aa bb cc DD ee

$$A = B Cc DD EE$$

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$$A = C d E = 0.1 + 0.1 + 0.9$$

$$E = A = C d E = 0$$

Introduction; variance components and heritability – p.8/30

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arbitrary starting point (4)

AA Bb Cc dd Ee 10

Aa bb cc DD ee 8.8

aa bb Cc DD Ee

$$A = Bb Cc DD = Ee$$

$$A = C D = Ee$$

$$A = C B = EE$$

$$P = \mu + \begin{pmatrix} AA & -2 \\ Aa & 0 \\ aA & 3 \end{pmatrix} + \begin{pmatrix} BB & 0.6 \\ Bb & 0.1 \\ bb & -0.2 \end{pmatrix} + \begin{pmatrix} CC & -1 \\ Cc & 6 \\ cc & 6 \end{pmatrix} + \begin{pmatrix} DD & 0.3 \\ Dd & 0.3 \\ dd & 0.7 \end{pmatrix} + \begin{pmatrix} EE & -0.4 \\ Ee & 0.3 \\ ee & -0.3 \end{pmatrix} + \frac{environmental}{effect}$$

arbitrary starting point (4)

AA Bb Cc dd Ee 10

Aa bb cc DD ee 8.8

aa bb Cc DD Ee 6.5

aa bb Cc DD EE

Aa Bb Cc DD EE

Aa Bb Cc DD EE

$$A = Bb Cc DD EE$$

$$A = Bb Cc DC DE$$

$$A = B$$

Introduction; variance components and heritability – p.10/30

$$P = \mu + \begin{pmatrix} AA & -2 \\ Aa & 0 \\ aa & 3 \end{pmatrix} + \begin{pmatrix} BB & 0.6 \\ Bb & 0.1 \\ bb & -0.2 \end{pmatrix} + \begin{pmatrix} CC & -1 \\ Cc & 6 \\ cc & 6 \end{pmatrix} + \begin{pmatrix} DD & 0.3 \\ Dd & 0.3 \\ dd & 0.7 \end{pmatrix} + \begin{pmatrix} EE & -0.4 \\ Ee & 0.3 \\ ee & -0.3 \end{pmatrix} + \frac{environmental}{effect}$$

arbitrary starting point (4)

AA Bb Cc dd Ee 10

Aa bb cc DD ee 8.8

aa bb Cc DD Ee 6.5

aa bb Cc DD EE 12.2

Aa Bb Cc DD EE 12.2

Aa Bb Cc DD Ee

$$4 - 0.4 + 3 + 6 + 0.3 - 0.2 - 0.5$$

$$E = \frac{a}{a} \frac{c D}{C D} = \frac{b}{b}$$

$$P = \mu + \begin{pmatrix} AA & -2 \\ Aa & 0 \\ aa & 3 \end{pmatrix} + \begin{pmatrix} BB & 0.6 \\ Bb & 0.1 \\ bb & -0.2 \end{pmatrix} + \begin{pmatrix} CC & -1 \\ Cc & 6 \\ cc & 6 \end{pmatrix} + \begin{pmatrix} DD & 0.3 \\ Dd & 0.3 \\ dd & 0.7 \end{pmatrix} + \begin{pmatrix} EE & -0.4 \\ Ee & 0.3 \\ ee & -0.3 \end{pmatrix} + \frac{environmental}{effect}$$

arbitrary starting point (4)

AA Bb Cc dd Ee 10

Aa bb cc DD ee 8.8

aa bb Cc DD Ee 6.5

aa bb Cc DD EE 12.2

Aa Bb Cc DD Ee 8.9

4 + 0.3 + 0 + 6+0.3 + 0.1 - 1.8

$$E = A = C D = B$$

... to make a 0/1 character apply a threshold of 9

$$\mathbf{P} = \mathbf{\mu} + \begin{pmatrix} AA & -2 \\ Aa & 0 \\ aa & 3 \end{pmatrix} + \begin{pmatrix} BB & 0.6 \\ Bb & 0.1 \\ bb & -0.2 \end{pmatrix} + \begin{pmatrix} CC & -1 \\ Cc & 6 \\ cc & 6 \end{pmatrix} + \begin{pmatrix} DD & 0.3 \\ Dd & 0.3 \\ dd & 0.7 \end{pmatrix} + \begin{pmatrix} EE & -0.4 \\ Ee & 0.3 \\ ee & -0.3 \end{pmatrix} + \stackrel{\text{environmental}}{\text{effect}}$$

AA	Bb	Cc	dd	Ee	10	1
Aa	bb	cc	DD	ee	8.8	 0
aa	bb	CC	DD	Ee	6.5	 0
aa	bb	Cc	DD	EE	12.2	 1
Aa	Bb	Cc	DD	Ee	8.9	 0

(This is Sewall Wright's threshold model, of which more later).

Introduction; variance components and heritability - p.13/30

A single mendelian locus with environmental effects



In this arbitrary example, each genotype has background environmental variance distributed in a lognormal distribution. Those environmental variables get larger as we move from the top figure downwards.

Or many mendelian loci (and environmental effect)



(Each locus is dominant and all have the same effect and same gene frequency, but with the effect sizes scaled in each case so that the cases to have the same total genetic variance and the same environmental variance, with 30% of the phenotypic variance being genetic) provers and heritability – p.15/30

Additive effects and dominance deviations



R. A. Fisher (1918) defined additive effects α_i and dominance deviations δ_{ij} by fitting a straight line through the genotypic mean phenotypes, with points weighted by their Hardy-Weinberg population genotype frequency.

Fisher's model assumes

- Random mating, so Hardy-Weinberg proportions

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 - Random mating, so Hardy-Weinberg proportions
 - Linkage equilibrium between all loci
 - Environmental effects independent of the genotype
 - Environmental effects independent in different individuals
 - No interaction between loci (effects are additive between loci)

- The two α 's in a locus (by Hardy-Weinberg)

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- The α 's and the δ in a locus, as a result of having defined them by the weighted least squares regression (trust me)

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- The α 's and the δ in a locus, as a result of having defined them by the weighted least squares regression (trust me)
- All the effects (α 's and δ 's) at different loci (by linkage equilibrium)
- The environmental effect (by independence of the environment from the genotype)

So the phenotype is a sum of terms, all of which are uncorrelated (have zero covariance):

$$P = \mu + \alpha_{i}^{(1)} + \alpha_{j}^{(1)} + \delta_{ij}^{(1)} + \alpha_{k}^{(2)} + \alpha_{\ell}^{(2)} + \delta_{k\ell}^{(2)} + \alpha_{m}^{(3)} + \alpha_{m}^{(3)} + \delta_{mn}^{(3)} + \dots + \epsilon$$

Rearranging and adding up variances

$$P = \mu + (\alpha^{(1)} + \alpha^{(1)} + \alpha^{(2)} + \alpha^{(2)} + \alpha^{(3)} + \alpha^{(3)} + \dots) + (\delta^{(1)} + \delta^{(2)} + \delta^{(3)}) + \dots + \epsilon$$

(The μ + (all the α terms) is also called the "breeding value" of the individual).

Since random variables that are uncorrelated have variances that sum up, we have partitioned the phenotype into four parts (one a nonvarying starting point μ),

$$\mathsf{P} = \mu + \mathsf{A} + \mathsf{D} + \mathsf{E}$$

and that means their variances add up too (the variance of μ being 0:

$$\operatorname{Var}(\mathsf{P}) \;=\; \mathsf{V}_\mathsf{A} \;+\; \mathsf{V}_\mathsf{D} \;+\; \mathsf{V}_\mathsf{E}$$

Covariances and fraction of shared effects

If X, Y, and Z are independent random variables,

$$\operatorname{Cov}[X+Y, X+Z] = \operatorname{Var}(X)$$

So the covariance is the variance of the part shared between the two sums.

$$\begin{array}{rcl} \mathsf{P}_{\mathsf{x}} &=& \mu & + (\alpha + \alpha + \alpha + \alpha + \alpha + \dots) & + (\delta + \delta + \delta + \dots) & + & \varepsilon \\ & & \uparrow & & \uparrow & & \uparrow & \\ & & \mathsf{f}_1 \text{ of these shared} & & \mathsf{f}_2 \text{ of these shared} & & \downarrow & \\ & & \downarrow & & \downarrow & & \downarrow & \\ \mathsf{P}_{\mathsf{y}} &=& \mu & + (\alpha + \alpha + \alpha + \alpha + \dots) & + (\delta + \delta + \delta + \dots) & + & \varepsilon \end{array}$$

If a fraction f_1 of the α are shared, that fraction of the variance from them is shared, and similarly for the δ s, and environment is not shared,

$${\rm Cov}\,({\sf P}_x,{\sf P}_y)\;=\;f_1\,V_A\;+\;f_2\,V_D$$

Variance components and ANOVA

Does all this look a lot like analysis of variance (ANOVA)?

It ought to: that was also developed by R. A. Fisher in the same era, and published in the early 1920s, very soon after his 1918 paper.

- Each additive effect is a single-factor ("row" or "column") effects
- The dominance deviations are two-way interaction effects
- All interaction effects between loci, and between the environment and anything else, have been forced to be zero by the assumed model
- The least squares regression is the same one used to assign fixed effects in ANOVA

Variance components and covariances of relatives

This can be done be computing, from the kind of relationship:

- the probability that a single copy of a gene is also found in the relative, owing to identity by descent (f1)
- the probability that both copies at a locus are found in the relative (f₂)

These give the fraction of V_A and of V_D that contribute to the covariance of pairs of relatives.

$$Cov(this kind of relative) = f_1V_A + f_2V_D$$

It establishes algebraic relationships between covariances of different kinds of relatives (and the associated correlation coefficients).

The important case for us is parents and offspring ($f_1 = 1/2, f_2 = 0$):

$$\operatorname{Cov}(\mathsf{P},\mathsf{O}) = \frac{1}{2} \mathsf{V}_{\mathsf{A}}$$

Coefficients f_1 and f_2 in relatives

Relationship	f_1	f_2
Onesself	1	1
Identical twin	1	1
Parent	1/2	0
Offspring	1/2	0
Full sib	1/2	1/4
Half sib	1/4	0
Aunt/Uncle	1/4	0
Niece/Nephew	1/4	0
First cousin	1/8	0

Heritability

Heritability is the fraction of the total phenotypic variance that is from the additive genetic variance V_A . Note that

$$h^2 = \frac{V_A}{V_A + V_D + V_E}$$

- It is *not* the fraction of all variance that is genetic, as it does not include the dominance variance V_D
- It depends on the gene frequencies (the weights in the regression) so that it can be different from population to population
- For that matter, it can be different from generation to generation as gene frequencies change by genetic drift and selection
- Which is comforting, since when the population has fixed or lost all alleles, we'd think there would be no genetic variance at all

Heritability is denoted by h^2 for historical reasons (Sewall Wright in 1921) and no one ever uses unsquared h.

Slope of parent-offspring regression



Expected slope is $Cov(O, P)/Var(P) = \frac{1}{2}h^2$

Mean of offspring of a selected parent



Expected slope is $Cov(O, P)/Var(P) = \frac{1}{2}h^2$ When lots of genes of small effect add up, get bivariate normality which implies this linear dependence.

Response to truncation selection on one parent



The bivariate normality of the joint distribution implied this linear dependence. The linearity of expectations of linear dependence guarantees this.

Response to truncation selection on both parents

This response, with response doubled for selection on both parents, is simply "The Breeder's Equation":

Response = heritability \times selection differential

(if selection is on both sexes of parent)

References on variance components and heritability

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- Falconer, D. S. and T. F. C. MacKay. 1996. *An Introduction to Quantitative Genetics*. 4th Edition. Benjamin-Cummings, San Francisco. [Falconer's classic 1960 textbook, updated in recent editions by Trudy MacKay]
- Lynch, M. and B. Walsh. 1998. *Genetics and Analysis of Quantitative Traits*. Sinauer Associates, Sunderland, Massachusetts. [A recent and more intensive and comprehensive text]

References on variance components and heritability

Felsenstein, J. 2016. *Theoretical Evolutionary Genetics*. Available as a free download from the Department of Genome Sciences, University of Washington, Seattle at

http://evolution.gs.washington.edu/pgbook/pgbook.html [My population genetics theory class text; chapter IX covers quantitative genetics theory, and chapter XI covers quantitative characters under optimizing selection.]