

Outline of lectures 9-11

Genetics of quantitative characters

1. When we have a measurable (quantitative) character, we may not be able to discern which phenotypes correspond to which genotypes. If each genotype gives a distribution of possible phenotypes, and these overlap, the distribution of phenotypes will have peaks that correspond to the genotypic classes but these peaks can overlap, leaving us uncertain which genotype a given phenotype corresponds to.
2. As the overlap gets more extreme we can lose all the peaks and just have one distribution with a single peak.
3. If there are multiple loci contributing to the phenotype, the peaks also become confused with each other. Either way, we cannot do traditional Mendelian genetics, even though the underlying basis of the trait is Mendelian.
4. The traits we are talking about include not only sizes and weights but behavioral traits (such as a measure of geotaxis), susceptibility to disease, lymphocyte count, and (most significant economically) racehorse speed.
5. Such traits have been worked on for centuries by animal and plant breeders. They apply artificial selection (usually by breeding from the best extreme of the distribution of phenotypes).
6. Typically one sees response to the artificial selection. After a time one can appear to reach a "selection limit" where further response appears to have stopped. This can be tested by reverse selection and by relaxed selection. It is usually helpful to also have an unselected control line, to check for environmental changes, and to have replicates of the selection lines.
7. If genetic variation has been lost, we expect that reverse selection of the selected line will not get a response.
8. An alternative possibility is that genetic variation is still present, but that natural selection is opposing artificial selection (that the individuals you judge best have lower survival or fertility under your breeding conditions, enough to stop progress). This can be tested by relaxing selection; if there is natural selection opposing progress, it will then start pushing the population mean back towards the starting point.
9. Selection can be carried out long-term. An important experiment is the Illinois Corn Selection Experiment, at the University of Illinois, where four open-pollinated (random mating) lines of corn were selected since 1896. There were up and down lines for protein

content of kernel, and up and down lines for oil content of kernel. Continued progress has been made and the means are now far outside the original range of the population. It is probable that the genetic variation that is being utilized was not all present at the outset but some of it has been generated by mutation since the start of the selection. This experiment involves 1 generation per year.

10. R. A. Fisher introduced a statistical theory of quantitative inheritance in 1918. It assumes that the trait is controlled by adding up effects of individual loci, and then adding on an environmental effect. The individual loci can have any number of alleles and any dominance pattern, and some can have much larger effects than others. But interaction between the loci is not allowed. In real life loci interact in complex ways, and environments interact with genetic effects. Fisher's theory is a rough approximation, but is surprisingly effective in practice.
11. The width of a distribution of a character is measured by its *standard deviation*. The square of this quantity is easier to use statistically. It is called the *variance*. (Fisher's 1918 paper is the first place that the word "variance" is used for this!)
12. Under his model's assumptions, Fisher showed that the variance can be broken down into three components, V_A , V_D , and V_E , the additive, dominance, and environmental variances. The environmental variance is the contribution made by the environmental variation to the variance. The additive and dominance terms are both genetic effects. The additive variance is (in effect) the effect of single copies of genes, and the dominance effect is the effect of the interaction of pairs of copies at a locus.
13. This distinction between additive and dominance variance seems very artificial. It is related to the breakdown of variance and its attribution to causes in the statistical theory of the *analysis of variance*. This is not surprising because that theory was developed by Fisher in 1922, shortly after his quantitative genetic work. In analysis of variance we have variance components due to (say) rows and due to columns, and an interaction component between them. The dominance variance is an interaction component of this sort.
14. Fisher showed how covariances (and correlations) between relatives can be written in terms of these three variance components. This in turn means that we can measure the three variance components by measuring correlations between a number of different kinds of relatives, and then solving for the values of V_A , V_D , and V_E that fit these correlations.
15. Fisher and Sewall Wright showed how to predict the response to artificial selection from these variance components. Jay Lush of Iowa State University widely publicized the resulting theory of quantitative genetics in books starting in 1937.
16. The fraction of the variance contributed by the V_A term is called the *heritability*, and denoted by h^2 , where

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

17. Note that the heritability is *not* the degree of genetic variation because the V_D term is left out of the numerator. Note also that the variance components can vary from population to population, as gene frequencies and environmental regimes vary, and can change during a selection experiment. For example, if we select a line until all alleles get fixed or lost, heritability within that line will drop to zero.
18. The response to artificial selection is the heritability times the *selection differential*. The selection differential is the difference between the individuals that you select, and the original population mean. Thus if we have a population with a mean of 100 pounds, and breed from the biggest individuals such that the ones we breed from have a mean of 108 pounds, the selection differential is 8 pounds.
19. If R is the selection differential and ΔZ is the gain in one generation,

$$\Delta Z = h^2 R$$

20. So if the heritability is 0.4 in the above case, and R is 8 pounds, the expected gain is 3.2 pounds.
21. the reason why the additive genetic variance is the important genetic component is that individual genes get passed on, but the particular genotypes that result in dominance effects get ripped apart by Mendelian segregation and not passed on intact.
22. The Fisher-Wright-Lush theory has been essential to animal and plant breeding for 75 years, but is being superseded by the use of molecular markers. They can be used to map *QTLs*, “quantitative trait loci” to specific places in the genome, and we can then hope to understand them biochemically, and perhaps manipulate them genetically. Anyone want a hamburger from an artificial cow?
23. However for a long time it will be hard to detect loci of small effect this way, and some traits have many of them and have much of their variance contributed by them.
24. Natural selection is often acting not by carrying out this kind of “truncation selection” but by selecting for an intermediate phenotype, “optimizing selection”. This can be seen in studies of survival of individuals of different phenotypes in natural populations.
25. Even though the pattern of optimizing selection is different from truncation selection, the theory still applies, with the response being a fraction h^2 of the selection differential.