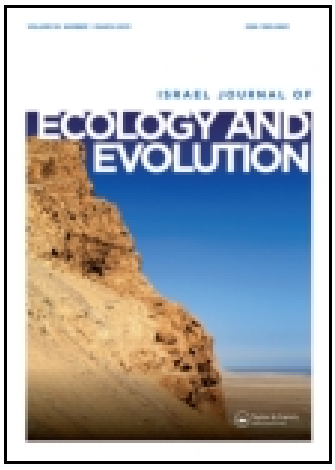

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Gene-culture co-evolution: teaching, learning, and correlations between relatives

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Gene-culture co-evolution: teaching, learning, and correlations between relatives

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Heritability, the fraction of phenotypic variance attributable to the action of genes, is usually derived from a linear statistical partition of variance. In this paper we study a dichotomous phenotype whose transmission from parents to offspring depends on the parents' phenotypes and the offspring's genotype. Each individual is then represented as a phenogenotype. We derive expressions for each component of phenotypic variance and for covariances between relatives of various degrees. The resulting heritability estimates vary with the rates of phenotypic transmission as well as with the genetic contribution to the phenotype. Assortative mating by phenotype in parents is also shown to contribute to the correlations between relatives. In addition, we show that the frequency of alleles at genes affecting the phenotypes strongly affects standard heritability measures. This is important because for most complex traits these allele frequencies cannot be ascertained.

Keywords: gene-culture coevolution; correlations between relatives; heritability; assortative mating

Notes on contributors

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Introduction

Inheritance patterns are multifaceted and yet many evolutionary models as well as statistical inferences of heritability fail to account for the complex interplay between genetics and environment that shapes phenotypes and their transmission. In this paper, we develop a model that tracks the dynamics of a phenotype that is culturally influenced as well as being under partial genetic control. We assume a single underlying diploid locus that, along with the phenotypes of parents, alters the probability that a focal individual develops or does not develop a dichotomous trait. We also consider the influence of non-random mating patterns among the parents. Our analysis focuses first on the evolutionary dynamics of the trait itself and secondly on how standard statistical estimates of genetic heritability depend on the interplay of genetic and cultural inheritance and on the mating patterns.

Background

Recent empirical and theoretical studies of cultural transmission have addressed the efficacy of active teaching (either vertically by parents or obliquely from non-parental elders, or horizontally from peers) and learning in driving the evolution of discrete-valued phenotypes (Hewlett et al. 2011; Creanza et al. 2012; Fogarty & Feldman 2012). One class of analyses has considered the dynamic and equilibrium properties of these phenotypes using deterministic models (effectively assuming an infinite population size). A second class has modeled various probabilistic rules of transmission when offspring sample from a parental population and choose whose trait to emulate (Henrich 2004; Borenstein et al. 2008; Aoki et al. 2011; Aoki & Feldman 2014). This second class of models allows for cultural drift (by analogy with genetic drift; Cavalli-Sforza & Feldman 1981), where population size plays a key role for the evolution of culture in the population and where calculations often focus on the probability that a culturally transmitted character spreads within the population. Both classes of models address the roles of cultural transmission and assortative mating in phenotypic evolution. However, they do not explore how statistical relationships between relatives are affected by the rules of transmission and mating. In this paper, we examine the evolutionary dynamics of a trait under both genetic and

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cultural transmission, and the covariances between relatives expected to result from joint cultural and genetic determination of phenotypes.

Parents affect their offspring through a variety of mechanisms, and our model encompasses genetic inheritance, direct teaching, as well as epigenetic inheritance, and niche construction. Epigenetic variation, representing differences in degrees of methylation or acetylation, for example, contributes to variation in timing and/or expression of genes and hence has important phenotypic effects. While many of these epigenetic signals are reset during gametogenesis in animals (Morgan et al. 2005), it is becoming increasingly clear that some epigenetic signals are inherited (Chong & Whitelaw 2004; Blewitt et al. 2006) and that many are strongly influenced by parents, either through parental imprinting (Sasaki and Matsui 2008) or in utero effects (Rhee et al. 2012). Because these epigenetic phenomena do not obey the usual rules of genetic transmission, they can have a variety of effects on familial correlations among quantitative phenotypes and on the likelihood of a discretely defined disease, such as rheumatoid arthritis (Slatkin 2009; Tal et al. 2009; Feinberg & Irizarry 2010; Furrow et al. 2011; Liu et al. 2013).

In many cases, whether or not an epigenetic mark is established depends on the environment, providing a direct mechanism by which the environment created by parents can alter the expression of coding genes in the offspring (Furrow & Feldman 2013). This more complicated view of phenotype-environment interdependence can be viewed as an example of cultural niche construction (Ihara & Feldman 2004; Creanza et al. 2012), whereby one class of culturally transmitted traits (e.g. some aspects of an individual's environment) affects the transmission of another trait. In this case, both the rules of environmental transmission and those of epigenetic modification of the genetic contribution to the phenotype will affect correlations among relatives, often summarized in terms of heritability.

A standard method for inferring the genetic heritability underlying a trait involves the statistical analysis of correlations between relatives, following from the seminal work by Fisher (1918). These inferences assume a quantitative genetic underpinning to a trait. By contrast, our model assumes a dichotomous character under both genetic and/or cultural influences. Nevertheless, we can investigate the relationship between standard heritability estimates and the parameters of our underlying evolutionary model, describing genetic effects, cultural transmission, and patterns of non-random mating.

Statistical methods have also been developed that treat dichotomous traits as "threshold characters", again assuming an underlying quantitative trait ("liability"). Falconer (1960) introduced a method for inferring heritability for threshold characters and in 1965 applied the method to data on the incidence of diseases such as club foot and cleft palate. His aim was "to get further towards an answer to the question of the relative importance of heredity and environment" (Falconer, 1965, p. 51). To this end he adopted the concept due to Carter (1961, 1964) of a continuously varying (Gaussian) liability function such that any individual whose liability score exceeded a threshold

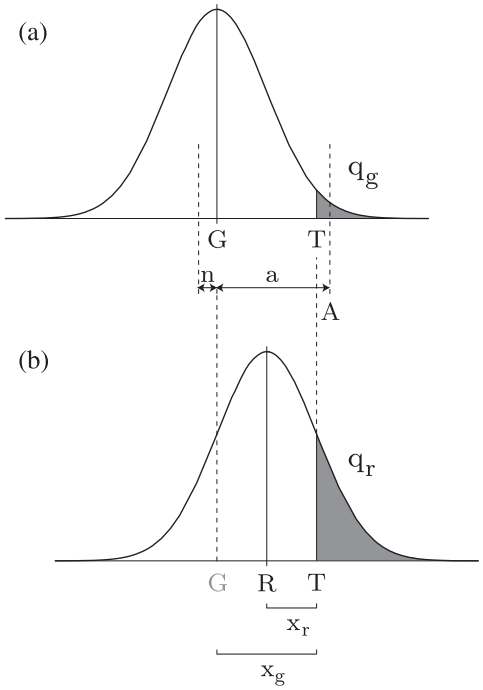

Figure 1. The upper curve (a) represents the distribution of liabilities in the general population with a scale measured in standard deviations from G, the mean liability in the general population. T is threshold. A is the mean liability of individuals with the disease (of type 1) in the general population. In the lower curve, (b) R is the mean liability of relatives of type 1 individuals with the disease. The shaded areas represent the incidences q_g and q_r, i.e. the proportions of individuals in the upper and lower distributions whose liabilities exceed T. x_g and x_r are the deviations of T from the means (on the standard deviation scale). a is the mean deviation of type 1 individuals with the disease from $G(a = z/q_g)$, and n is the mean deviation of the liabilities of healthy (type 2) individuals in the population from G $(n = z/(1 - q_g))$. z is the height of the normal curve at T. The subscripts g and r refer to the general population and the relatives of individuals with the disease, respectively.

T had the disease while those who scored less than T did not (Figure 1). From the observed incidences of the disease in the general population and among relatives of a specific degree, e.g. sibs, of an individual with the disease, the heritability of the liability could be calculated.

Falconer's method assumed that the variances of the liability distribution in different focal groups are the same, but more general methods for treating threshold characters were developed by Edwards (1969). Here the distribution of liabilities among propositi on the one hand and their relatives on the other is taken to be bivariate normal. Edwards (1969) proposed an approximate simple relationship between the expected correlation, ρ, of this bivariate distribution and the incidences in the population and in the relatives of propositi. The heritability can then be found from $h^2 = \rho/r$, where r is the coefficient of relationship, provided there is no assortative mating. This method of tetrachoric correlations was based on the work of Pearson (1900) and Everitt (1910) and can be combined with maximum likelihood techniques to infer heritability of dichotomized traits (e.g. see Eaves et al. 1989 for an analysis of personality traits). A review of the principles underlying these treatments of liability for dichotomous

traits can be found in Chapter 9 of Cavalli-Sforza and Bodmer (1971).

We first describe the model, using a general vertical transmission scheme for a dichotomous trait, and explore the dynamic and equilibrium properties of the coevolving system of genotypes and phenotypes. We then examine in more detail a slightly less general form of the transmission scheme. Next some of the statistics commonly used to summarize heritability are reviewed and computed based on simulations of our model. The purpose here is to explore to what extent standard statistics, such as heritability, actually reflect a known genetic-cultural transmission regime. Finally, similar calculations are carried out using methods typically applied to the study of threshold characters.

The model

Our model follows that of Feldman and Cavalli-Sforza (1976). We consider two phenotypes labeled 1 and 2 that occur in equal frequencies within the two sexes. The frequencies of the two phenotypes within groups of individuals and the frequencies of various phenotypic combinations within families are treated as observable quantities. The genetic interpretation of such data uses tools from quantitative genetics. In the following we develop a population model that describes the genetic and cultural transmission of the phenotypes. This framework will subsequently permit evaluation of the expected values of the population variances and familial covariances, which are tools used in quantitative genetics to interpret data on the variation and transmission of the phenotypes.

The phenotype of an individual is influenced by its genotype at an autosomal gene with two alleles A and a. Individuals thus come in six phenogenotypes, namely AA_1, AA_2, Aa_1, Aa_2, aa_1, aa_2. The phenotype of an individual is partly determined by the phenotypes of its parents; that is, there is vertical cultural transmission. The probability that an individual acquires a given phenotype depends on the genotype of the individual and on the phenotypes of the parents. The rules of transmission are shown in Table 1. Thus, $\alpha_i, \beta_i, \gamma_i$ and δ_i describe the frequency of phenotype 1 among offspring of genotype i from the four different parental phenotypic combinations; the three genotypes AA, Aa and aa are numbered 1, 2 and 3, respectively.

The frequencies of the six phenogenotypes AA_1, AA_2, Aa_1, Aa_2, aa_1, aa_2 are u_1, v_1, u_2, v_2, u_3, v_3, respectively. The frequency of phenotype 1 in the population is $k = u_1 + u_2 + u_3$ and that of phenotype 2 is $1 - k = v_1 + v_2 + v_3$. The frequencies of the genotypes AA, Aa and aa are $u_1 + v_1$, $u_2 + v_2$ and $u_3 + v_3$, respectively. The frequencies of alleles A and a among individuals with phenotype 1 are

$$p_1 = (u_1 + u_2/2)/k, \quad q_1 = (u_3 + u_2/2)/k, \tag{1a}$$

while the frequencies of these alleles among individuals with phenotype 2 are

$$p_2 = (v_1 + v_2/2)/(1-k), \quad q_2 = (v_3 + v_2/2)/(1-k). \tag{1b}$$

The frequencies of A and a in the whole population are $p = u_1 + v_1 + u_2/2 + v_2/2 = kp_1 + (1-k)p_2$ and $q = 1 - p$, respectively.

Parents are assumed to mate assortatively according to their phenotypes with probability m and to mate randomly with probability $1 - m$. The four types of families in terms of parental phenotypes are 1×1, 1×2, 2×1 and 2×2 and these occur with frequencies

$$\begin{aligned} &\mu_1 = (1-m)k^2 + mk, \ \ \mu_2 = \mu_3 = (1-m)k(1-k), \\ &\mu_4 = (1-m)(1-k)^2 + m(1-k), \end{aligned} \tag{2}$$

respectively. For given parental phenotypes, the mating among genotypes is random. The resulting mating frequencies are shown in Table 2. This table also shows the phenogenotypic distributions among offspring from the various matings calculated from Mendelian segregation frequencies and the phenotypic transmission rules of Table 1. The genetic influence is in the ability of the offspring to acquire a trait; no genetic variation in parents' ability to culturally transmit the character is included. This amounts to genetic variation in learning. Writing $u_1', u_2', u_3', v_1', v_2', v_3'$ for the frequencies of the phenogenotypes in the next (i.e. the offspring) generation, and assuming equal fitnesses, the evolution of the system is described by the recursions

$$u_1' = \alpha_1 p_1^2 \mu_1 + p_1 p_2 (\beta_1 + \gamma_1)\mu_2 + \delta_1 p_2^2 \mu_4, \tag{3a}$$

$$u_2' = 2\alpha_2 p_1 q_1 \mu_1 + (p_1 q_2 + p_2 q_1)(\beta_2 + \gamma_2)\mu_2 + 2\delta_2 p_2 q_2 \mu_4, \tag{3b}$$

$$u_3' = \alpha_3 q_1^2 \mu_1 + q_1 q_2 (\beta_3 + \gamma_3)\mu_2 + \delta_3 q_2^2 \mu_4, \tag{3c}$$

with the recursions for v_1, v_2, v_3 obtained by replacing $\alpha_i, \beta_i, \gamma_i, \delta_i$ by $1 - \alpha_i$, $1 - \beta_i$, $1 - \gamma_i$, $1 - \delta_i$.

From the recurrence equations (3) we obtain the genotypic frequencies in the population of offspring:

$$u_1' + v_1' = p^2 + mk(1-k)(p_1 - p_2)^2, \tag{4a}$$

$$u_2' + v_2' = 2pq - 2mk(1-k)(p_1 - p_2)^2, \tag{4b}$$

$$u_3' + v_3' = q^2 + mk(1-k)(p_1 - p_2)^2. \tag{4c}$$

These equations are independent of the phenotypic transmission parameters because the phenotypic differences

Table 1. Rules of phenotypic transmission.

parental phenotypes M × F	offspring probabilities (given offspring's genotype)					
	AA_1	AA_2	Aa_1	Aa_2	aa_1	aa_2
1×1	α_1	$1 - \alpha_1$	α_2	$1 - \alpha_2$	α_3	$1 - \alpha_3$
1×2	β_1	$1 - \beta_1$	β_2	$1 - \beta_2$	β_3	$1 - \beta_3$
2×1	γ_1	$1 - \gamma_1$	γ_2	$1 - \gamma_2$	γ_3	$1 - \gamma_3$
2×2	δ_1	$1 - \delta_1$	δ_2	$1 - \delta_2$	δ_3	$1 - \delta_3$

Table 2. Mating and transmission.

Mating		Offspring Probabilities					
M × F	Frequency	AA_1	AA_2	Aa_1	Aa_2	aa_1	aa_2
$AA_1 \times AA_1$	$u_1^2(1-m)+mu_1^2/k$	α_1	$1-\alpha_1$				
$AA_1 \times AA_2$	$u_1v_1(1-m)$	β_1	$1-\beta_1$				
$AA_2 \times AA_1$	$u_1v_1(1-m)$	γ_1	$1-\gamma_1$				
$AA_2 \times AA_2$	$v_1^2(1-m)+mv_1^2/(1-k)$	δ_1	$1-\delta_1$				
$AA_1 \times Aa_1$	$u_1u_2(1-m)+mu_1u_2/k$	$\frac{1}{2}\alpha_1$	$\frac{1}{2}(1-\alpha_1)$	$\frac{1}{2}\alpha_2$	$\frac{1}{2}(1-\alpha_2)$		
$AA_1 \times Aa_2$	$u_1v_2(1-m)$	$\frac{1}{2}\beta_1$	$\frac{1}{2}(1-\beta_1)$	$\frac{1}{2}\beta_2$	$\frac{1}{2}(1-\beta_2)$		
$AA_2 \times Aa_1$	$u_2v_1(1-m)$	$\frac{1}{2}\gamma_1$	$\frac{1}{2}(1-\gamma_1)$	$\frac{1}{2}\gamma_2$	$\frac{1}{2}(1-\gamma_2)$		
$AA_2 \times Aa_2$	$v_1v_2(1-m)+mv_1v_2/(1-k)$	$\frac{1}{2}\delta_1$	$\frac{1}{2}(1-\delta_1)$	$\frac{1}{2}\delta_2$	$\frac{1}{2}(1-\delta_2)$		
$AA_1 \times aa_1$	$u_1u_3(1-m)+mu_1u_3/k$			α_2	$1-\alpha_2$		
$AA_1 \times aa_2$	$u_1v_3(1-m)$			β_2	$1-\beta_2$		
$AA_2 \times aa_1$	$u_3v_1(1-m)$			γ_2	$1-\gamma_2$		
$AA_2 \times aa_2$	$v_1v_3(1-m)+v_1v_3m/(1-k)$			δ_2	$1-\delta_2$		
$Aa_1 \times AA_1$	$u_1u_2(1-m)+mu_1u_2/k$	$\frac{1}{2}\alpha_1$	$\frac{1}{2}(1-\alpha_1)$	$\frac{1}{2}\alpha_2$	$\frac{1}{2}(1-\alpha_2)$		
$Aa_1 \times AA_2$	$u_2v_1(1-m)$	$\frac{1}{2}\beta_1$	$\frac{1}{2}(1-\beta_1)$	$\frac{1}{2}\beta_2$	$\frac{1}{2}(1-\beta_2)$		
$Aa_2 \times AA_1$	$u_1v_2(1-m)$	$\frac{1}{2}\gamma_1$	$\frac{1}{2}(1-\gamma_1)$	$\frac{1}{2}\gamma_2$	$\frac{1}{2}(1-\gamma_2)$		
$Aa_2 \times AA_2$	$v_1v_2(1-m)+mv_1v_2/(1-k)$	$\frac{1}{2}\delta_1$	$\frac{1}{2}(1-\delta_1)$	$\frac{1}{2}\delta_2$	$\frac{1}{2}(1-\delta_2)$		
$Aa_1 \times Aa_1$	$u_2^2(1-m)+mu_2^2/k$	$\alpha_1/4$	$(1-\alpha_1)/4$	$\frac{1}{2}\alpha_2$	$\frac{1}{2}(1-\alpha_2)$	$\alpha_3/4$	$(1-\alpha_3)/4$
$Aa_1 \times Aa_2$	$u_2v_2(1-m)$	$\beta_1/4$	$(1-\beta_4)/4$	$\frac{1}{2}\beta_2$	$\frac{1}{2}(1-\beta_2)$	$\beta_3/4$	$(1-\beta_3)/4$
$Aa_2 \times Aa_1$	$u_2v_2(1-m)$	$\gamma_1/4$	$(1-\gamma_1)/4$	$\frac{1}{2}\gamma_2$	$\frac{1}{2}(1-\gamma_2)$	$\gamma_3/4$	$(1-\gamma_3)/4$
$Aa_2 \times Aa_2$	$v_2^2(1-m)+mv_2^2/(1-k)$	$\delta_1/4$	$(1-\delta_1)/4$	$\frac{1}{2}\delta_2$	$\frac{1}{2}(1-\delta_2)$	$\delta_3/4$	$(1-\delta_3)/4$
$Aa_1 \times aa_1$	$u_2u_3(1-m)+mu_2u_3/k$			$\frac{1}{2}\alpha_2$	$\frac{1}{2}(1-\alpha_2)$	$\frac{1}{2}\alpha_3$	$\frac{1}{2}(1-\alpha_3)$
$Aa_1 \times aa_2$	$u_2v_3(1-m)$			$\frac{1}{2}\beta_2$	$\frac{1}{2}(1-\beta_2)$	$\frac{1}{2}\beta_3$	$\frac{1}{2}(1-\beta_3)$
$Aa_2 \times aa_1$	$u_3v_2(1-m)$			$\frac{1}{2}\gamma_2$	$\frac{1}{2}(1-\gamma_2)$	$\frac{1}{2}\gamma_3$	$\frac{1}{2}(1-\gamma_3)$
$Aa_2 \times aa_2$	$v_2v_3(1-m)+mv_2v_3/(1-k)$			$\frac{1}{2}\delta_2$	$\frac{1}{2}(1-\delta_2)$	$\frac{1}{2}\delta_3$	$\frac{1}{2}(1-\delta_3)$
$aa_1 \times AA_1$	$u_1u_3(1-m)+mu_1u_3/k$			α_2	$(1-\alpha_2)$		
$aa_1 \times AA_2$	$u_3v_1(1-m)$			β_2	$(1-\beta_2)$		
$aa_2 \times AA_1$	$u_1v_3(1-m)$			γ_2	$(1-\gamma_2)$		
$aa_2 \times AA_2$	$v_1v_3(1-m)+mv_1v_3/(1-k)$			δ_2	$(1-\delta_2)$		
$aa_1 \times Aa_1$	$u_2u_3(1-m)+mu_2u_3/k$			$\frac{1}{2}\alpha_2$	$\frac{1}{2}(1-\alpha_2)$	$\frac{1}{2}\alpha_3$	$\frac{1}{2}(1-\alpha_3)$
$aa_1 \times Aa_2$	$u_3v_2(1-m)$			$\frac{1}{2}\beta_2$	$\frac{1}{2}(1-\beta_2)$	$\frac{1}{2}\beta_3$	$\frac{1}{2}(1-\beta_3)$
$aa_2 \times Aa_1$	$u_2v_3(1-m)$			$\frac{1}{2}\gamma_2$	$\frac{1}{2}(1-\gamma_2)$	$\frac{1}{2}\gamma_3$	$\frac{1}{2}(1-\gamma_3)$
$aa_2 \times Aa_2$	$v_2v_3(1-m)+mv_2v_3/(1-k)$			$\frac{1}{2}\delta_2$	$\frac{1}{2}(1-\delta_2)$	$\frac{1}{2}\delta_3$	$\frac{1}{2}(1-\delta_3)$
$aa_1 \times aa_1$	$u_3^2(1-m)+mu_3^2/k$					α_3	$1-\alpha_3$
$aa_1 \times aa_2$	$u_3v_3(1-m)$					β_3	$1-\beta_3$
$aa_2 \times aa_1$	$u_3v_3(1-m)$					γ_3	$1-\gamma_3$
$aa_2 \times aa_2$	$v_3^2(1-m)+mv_3^2(1-k)$					δ_3	$1-\delta_3$

have no impact on the transmission of genetic variants between generations in the absence of selection. Equations (4) are therefore ordinary recurrence equations in the genotypic frequencies. Because selection is absent, the allele frequency remains constant, $p' = u_1' + v_1' + u_2'/2 + v_2'/2 = p$, and we can rewrite the recurrence equations (4) in terms of Wright's inbreeding coefficient in the next generation, F':

$$u_1' + v_1' = p^2 + F'pq, \tag{5a}$$

$$u_2' + v_2' = 2pq(1-F'), \tag{5b}$$

$$u_3' + v_3' = q^2 + F'pq, \tag{5c}$$

where

$$F' = \frac{mk(1-k)(p_1-p_2)^2}{pq} \tag{6}$$

measures the deviation of the genotypic frequencies from Hardy–Weinberg proportions. As long as the allele frequencies differ between phenotypic classes, i.e. $p_1 \neq p_2$, the heterozygote frequency is reduced by the combined effects of genotype–phenotype interactions and assortment by phenotype, and the homozygotes are correspondingly more frequent. The allele frequencies in the offspring generation can also be calculated. Thus, from

Equations (3) we have

$$k'p_1' = \mu_1(\alpha_1 p_1^2 + \alpha_2 p_1 q_1) + \mu_2\left[(\beta_1+\gamma_1)p_1p_2 + \frac{\beta_2+\gamma_2}{2}(p_1q_2+p_2q_1)\right] + \mu_4\left[\delta_1 p_2^2 + \delta_2 p_2 q_2\right], \quad (7a)$$

$$(1-k')p_2' = \mu_1\left[(1-\alpha_1)p_1^2 + (1-\alpha_2)p_1q_1\right] + \mu_2\left[(2-\beta_1-\gamma_1)p_1p_2 + \left(1-\frac{\beta_2+\gamma_2}{2}\right)(p_1q_2+p_2q_1)\right] + \mu_4\left[(1-\delta_1)p_2^2 + (1-\delta_2)p_2q_2\right], \quad (7b)$$

where the overall frequency of phenotype 1 among the offspring is

$$k' = \mu_1\left(\alpha_1 p_1^2 + 2\alpha_2 p_1 q_1 + \alpha_3 q_1^2\right) + \mu_2[(\beta_1+\gamma_1)p_1p_2 + (\beta_2+\gamma_2)(p_1q_2+p_2q_1) + (\beta_3+\gamma_3)q_1q_2] + \mu_4\left(\delta_1 p_2^2 + 2\delta_2 p_2 q_2 + \delta_3 q_2^2\right). \quad (8)$$

The allele frequencies in the whole population are invariant, but the frequencies within the phenotypes can change as a consequence of the genotype-dependent vertical cultural transmission.

Since p is invariant, the dynamical system can be expressed in terms of two variates, namely the frequency k of phenotype 1 and the frequency p_1 of allele A within phenotype 1; these parameters determine the allele frequency within phenotype 2 as $p_2 = (p - kp_1)/(1-k)$. Thus, Equations (7) and (8) describe a two-dimensional dynamical system. The parameters of the model are the initial allele frequency, p, the propensity towards assortative mating, m, and the twelve phenotypic transmission parameters in Table 1. To help in the analysis of various phenomena, we also consider a simpler transmission scheme, which we call bilinear and which is specified by just five parameters.

A bilinear transmission scheme

We introduce probabilities of acquisition of the phenotype that, in terms of the offspring genotypes, are reminiscent of Fisher's original model of genotypic effects. In addition, these transmission probabilities include a component that represents the phenotypes of both parents. Table 3 presents these special values of the general model of Table 1.

We can interpret the transmission rules of Table 3 as a kind of parental niche construction acting on the phenotype of the offspring. The phenotypic configurations of the parents constitute an environmental niche that, along with the offspring's genotype, determines the distribution of offspring phenotypes in the population. When the offspring become parents, they will, in turn, provide the niche in which their offsprings' phenotypes develop.

An alternative interpretation in terms of epigenetics is also possible. The probability that an offspring of genotype AA, say, expresses phenotype 1, for example, depends on η (and τ as well), which might be interpreted as the level of methylation of AA due to the effects of a parent having phenotype 1. In other words, η can be viewed as an epigenetic regulator of the phenotype expressed by the three genotypes AA, Aa, and aa. A more general model might include a second site B/b, which is the direct target of the epigenetic mark, whose state depends on the parental phenotypes and alters the chance the A/a genotypes express phenotype 1.

The parameter β is a baseline probability of acquiring the trait 1 in the absence of parental transmission. The parameters α and σ describe the effect of the offspring's genotype on its phenotype. The effect of allele A is given by α, in that the homozygote AA has an added probability of 2α of acquiring the trait compared to the aa homozygote. The effect of heterozygote Aa is described in relative terms by σ so the added probability that a heterozygote acquires the trait is $\sigma\alpha$. As a matter of choice we assume $\alpha > 0$, i.e. genotype AA has an increased chance of becoming phenotype 1. In Fisherian terms, σ reflects the degree of genetic dominance of allele A with respect to allele a; $\sigma = 2$ means that A is completely dominant, $\sigma = 1$ means that A is additive, and $\sigma = 0$ means that A is completely recessive to a with respect to acquisition of phenotype 1. The parameters η and τ describe the effects of the parental phenotypes on the offspring phenotype. Positive η means that offspring of parents possessing phenotype 1 have an increased probability of acquiring phenotype 1, whereas for a negative η, parental phenotype 1 discourages the development of a similar phenotype among the offspring. The model is sex symmetric, and η describes the influence of a parental phenotype 1 in the sense that the mating 1×1 adds the effect 2η to the probability of phenotype 1 among offspring compared to 2×2 matings. The effect of the mating 1×2 (or 2×1) on the phenotype of an offspring is described by $\tau\eta$, where τ represents a kind of environmental dominance in parental status. If, e.g., $\tau = 2$, the probability that an offspring is

Table 3. Bilinear transmission scheme.[a]

Mating M × F	Probability that offspring is phenotype 1		
	AA	Aa	aa
1 × 1	$\alpha_1 = 2\eta + 2\alpha + \beta$	$\alpha_2 = 2\eta + \sigma\alpha + \beta$	$\alpha_3 = 2\eta + \beta$
1 × 2	$\beta_1 = \gamma_1 = \tau\eta + 2\alpha + \beta$	$\beta_2 = \gamma_2 = \tau\eta + \sigma\alpha + \beta$	$\beta_3 = \gamma_3 = \tau\eta + \beta$
2 × 1	$\beta_1 = \gamma_1 = \tau\eta + 2\alpha + \beta$	$\beta_2 = \gamma_2 = \tau\eta + \sigma\alpha + \beta$	$\beta_3 = \gamma_3 = \tau\eta + \beta$
2 × 2	$\delta_1 = 2\alpha + \beta$	$\delta_2 = \sigma\alpha + \beta$	$\delta_3 = \beta$

[a] See Table 1 for the definition of $\alpha_i, \beta_i, \gamma_i, \delta_i$. $0 \le \sigma, \tau \le 2$ and all transmission probabilities are nonnegative, e.g. $0 \le 2\eta + 2\alpha + \beta \le 1$.

phenotype 1 is the same in the case that both parents have phenotype 1 as in the case that only one has phenotype 1. If the parents' phenotypes have no effect, then $\eta = 0$, while an absence of genetic effects is expressed by $\alpha = 0$.

Substitution of the transmission parameters from Table 3 into Equation (8) produces the simpler recursion

$$k' = \beta + 2\alpha[p + (\sigma - 1)pq(1 - F')] + 2\eta[k - (1 - \tau)(1 - m)k(1 - k)] \quad (9)$$

for the phenotypic frequency. If cultural transmission is absent ($\eta = 0$) the phenotypic frequency is $k' = \beta + 2\alpha p$, which remains constant because p is constant. In the analytical treatment of cultural and genetic transmission we assume no genetic dominance and set $\sigma = 1$, since this results in significant simplification of this equation. The effect of this assumption will be explored in the numerical treatment. Likewise Equation (9) simplifies considerably if we assume no environmental dominance in parental status, i.e. $\tau = 1$ and it becomes

$$k' = \beta + 2\alpha p + 2\eta k. \quad (10)$$

In the following analysis of the dynamics of the model we shall assume $\tau = 1$, and the analysis for the general case $0 \le \tau \le 2$ is given in Appendix 1.

Recursion (10) has a unique equilibrium given by

$$\hat{k} = \frac{\beta + 2\alpha p}{1 - 2\eta} \quad (11)$$

and convergence to this equilibrium always occurs, because (10) may be written

$$k' - \hat{k} = 2\eta(k - \hat{k}) \quad (12)$$

and $0 \le 2\eta \le 1$.

Recursion (7a) describing the change in allele frequency within phenotype 1 simplifies in the bilinear model with $\sigma = \tau = 1$ to become

$$k'(p_1' - p) = \alpha pq + \eta(1 + m)k(p_1 - p) + \frac{\alpha m k}{1 - k}(p_1 - p)^2. \quad (13)$$

Equilibria of (13) are the two roots of $g(\hat{p}_1 - p) = 0$ where

$$g(\pi) = \alpha pq + \hat{k}[(1 + m)\eta - 1]\pi + \frac{\alpha m \hat{k}}{1 - \hat{k}}\pi^2. \quad (14)$$

We have $g(0) \ge 0$, and in Appendix 1 we show that $g(1 - p) \le 0$. Thus there exists a unique valid equilibrium $\hat{p}_1$ in the interval $p \le \hat{p}_1 \le 1$.

In evaluating the convergence of p_1 to the equilibrium, $\hat{p}_1$, it may be assumed that k is as close to its equilibrium value as we wish, because from (12) the convergence of k is independent of p_1. Thus, from Equation (13) with $k = \hat{k}$ and the equilibrium equation $g(\hat{p}_1 - p) = 0$ we obtain

$$p_1' - \hat{p}_1 = (p_1 - \hat{p}_1)\left[\eta(1 + m) + \frac{(p_1 + \hat{p}_1 - 2p)m\alpha}{1 - \hat{k}}\right]. \quad (15)$$

The bracketed term in (15) may be rewritten as $\eta(1 + m) + \alpha m[(p_1 - p_2) + (\hat{p}_1 - \hat{p}_2)]$ and, since $2\alpha + 2\eta < 1$, this sum is less than unity in absolute value. This assures convergence of p_1 to $\hat{p}_1$.

These results can be extended to include phenotypic dominance, i.e. $0 \le \tau \le 2$ (see Appendix 1). The phenotype frequency k converges to the unique valid root, $\hat{k}$, of the quadratic equation

$$\beta + 2\alpha p + k[2\tau\eta + 2\eta m(1 - \tau) - 1] + 2k^2(1 - m)\eta(1 - \tau) = 0 \quad (16)$$

and the allele frequency p_1 converges to the unique valid root of the quadratic equation $f(p_1 - p) = 0$ where

$$f(p_1 - p) = \frac{\alpha m(p_1 - p)^2}{1 - \hat{k}} + \left\{2\eta[(1 - m)\hat{k} + m] + \tau\eta(1 - m)(1 - 2\hat{k}) - 1\right\}(p_1 - p) + \frac{\alpha pq}{\hat{k}}. \quad (17)$$

Variance analysis

In the calculations of the quantitative genetic variances and covariances, it is convenient to assign the value 1 to phenotype 1 and the value 0 to phenotype 2. The observable quantity is then a Bernoulli random variable; the population mean is k and the population variance is $V_p = k(1 - k)$. We will assume that the population is at equilibrium, and although it is difficult to prove convergence to equilibrium in the general case, numerical iterations suggest that convergence always occurs. For simplicity we delete the carets from equilibrium frequencies, i.e. k, p_i, F, u_i and v_i should be understood as $\hat{k}$, $\hat{p}_i$, $\hat{F}$, $\hat{u}_i$ and $\hat{v}_i$ unless otherwise indicated.

The average phenotype of individuals with a given genotype is called the *genotypic value* of that genotype (Table 4). Since the frequency of AA is $u_1 + v_1$ and within AA the chance that an individual is phenotype 1 is $u_1/(u_1 + v_1)$, the average phenotypic value of AA is $u_1/(u_1 + v_1)$. It is convenient to express the genotypic values as deviations from the population mean, the so-called *genotypic effects* g_{AA}, g_{Aa} and g_{aa} (Table 4). The mean genotypic effect in the population is then zero (see Falconer, 1996, ch. 7).

The *genotypic variance* V_G is defined as the variance among the genotypic values, or equivalently the variance

Table 4. Genotypic values.[a]

	genotype		
	AA	*Aa*	*aa*
frequency	$u_1 + v_1$	$u_2 + v_2$	$u_3 + v_3$
genotypic value	$\frac{u_1}{u_1 + v_1}$	$\frac{u_2}{u_2 + v_2}$	$\frac{u_3}{u_3 + v_3}$
genotypic effect	$g_{AA} = \frac{u_1}{u_1 + v_1} - k$	$g_{Aa} = \frac{u_2}{u_2 + v_2} - k$	$g_{aa} = \frac{u_3}{u_3 + v_3} - k$
additive specification	$2e_1$	$e_1 + e_2$	$2e_2$

[a] e_1 and e_2 are the average effects of alleles A and a, respectively, and these are estimated by $\hat{e}_1$ and $\hat{e}_2$ given in Equations (25) and (26).

among the genotypic effects. Thus

$$\begin{aligned} V_G &= [u_1/(u_1+v_1) - k]^2(u_1+v_1) + [u_2/(u_2+v_2) - k]^2 \\ &\quad \times (u_2+v_2) + [u_3/(u_3+v_3) - k]^2(u_3+v_3) \\ &= \frac{u_1^2}{u_1+v_1} + \frac{u_2^2}{u_2+v_2} + \frac{u_3^2}{u_3+v_3} - k^2. \end{aligned} \tag{18}$$

The variance among individuals within genotype i is again the Bernoulli variance, with probability corresponding to the genotypic value $u_i/(u_i + v_i)$, that is,

$$V_{WG_i} = \frac{u_i}{u_i+v_i}\left(1 - \frac{u_i}{u_i+v_i}\right) = \frac{u_i v_i}{(u_i+v_i)^2}.$$

The population average of these within-genotype variances is referred to as the *environmental variance*

$$\begin{aligned} V_E &= \frac{u_1 v_1}{(u_1+v_1)^2}(u_1+v_1) + \frac{u_2 v_2}{(u_2+v_2)^2}(u_2+v_2) \\ &\quad + \frac{u_3 v_3}{(u_3+v_3)^2}(u_3+v_3) \\ &= \frac{u_1 v_1}{u_1+v_1} + \frac{u_2 v_2}{u_2+v_2} + \frac{u_3 v_3}{u_3+v_3}. \end{aligned} \tag{19}$$

The environmental variance describes the variation residual to that given by the genotypic variance. The population variance is therefore given by

$$k(1-k) = V_G + V_E. \tag{20}$$

The environmental variance describes the unavoidable variance due to the probabilistic nature of the transmission in our model and to the phenotypic differences between an individual's parents.

It is customary to partition the genotypic variance into a component due to the variation in allelic effects, usually called the genic or *additive variance*, V_A, and a residual variance, which in a one-locus model is ascribed to genotypic variation due to effects of dominance between alleles. The additive variance is defined in terms of the additive effects of the genotypes, and these are defined as the sum of the average effects of the alleles in the genotype, which for A and a are denoted by e_1 and e_2, respectively (Table 4). The additive specification of the genotypic effects implies that the mean additive effect of the alleles in the population is zero,

$$e_1 p + e_2 q = 0. \tag{21}$$

The concept of the average (additive) effects of alleles is discussed at length by Falconer (1989, p. 115 et sequ). They are functions of the genotypic deviations and in our context we may derive these average effects by following the method of Moran (1962) (see also Ewens, 2004, pp. 6–11). This approach minimizes the residual variance obtained by fitting a linear model of the allelic contributions to the genotypic values. Thus,

$$\begin{aligned} V_R &= (g_{AA} - 2e_1)^2(u_1+v_1) + (g_{Aa} - e_1 - e_2)^2(u_2+v_2) \\ &\quad + (g_{aa} - 2e_2)^2(u_3+v_3) \end{aligned}$$

is minimized with respect to e_1 and e_2. The result is the so-called dominance variance

$$\begin{aligned} V_D &= (g_{AA} 2\hat{e}_1)^2(u_1+v_1) + (g_{Aa} - \hat{e}_1 - \hat{e}_2)^2(u_2+v_2) \\ &\quad + (g_{aa} - 2\hat{e}_2)^2(u_3+v_3), \end{aligned} \tag{22}$$

where $\hat{e}_1$ and $\hat{e}_2$ are the average effects at the minimum of V_R.

Differentiating V_R with respect to e_1 and e_2 and setting the derivatives to zero produces the equations

$$2(g_{AA} - 2e_1)(u_1+v_1) + (g_{Aa} - e_1 - e_2)(u_2+v_2) = 0 \tag{23a}$$

and

$$2(g_{aa} - 2e_2)(u_3+v_3) + (g_{Aa} - e_1 - e_2)(u_2+v_2) = 0, \tag{23b}$$

which allow us to determine e_1 and e_2. Adding these equations produces (21). Substituting the values for g_{AA}, g_{Aa}, g_{aa} from Table 4, rewriting (23a) as

$$k(p - p_1) + 2e_1(u_1+v_1) + \frac{1}{2}(e_1+e_2)(u_2+v_2) = 0,$$

and substituting $e_2 = -e_1 p/q$ from (21), we obtain

$$k(p_1 - p) = \left[2(u_1 + v_1) + \frac{(q-p)}{2q}(u_2 + v_2)\right] e_1. \quad (24)$$

Writing $(u_1 + v_1)$ and $(u_2 + v_2)$ as in Equations (5) and collecting terms yields the solution

$$\hat{e}_1 = \frac{k(p_1 - p)}{p(1+F)} = k(1-k)\frac{(p_1 - p_2)}{p(1+F)}. \quad (25)$$

Similarly,

$$\hat{e}_2 = \frac{k(q_1 - q)}{q(1+F)} = \frac{-k(p_1 - p)}{q(1+F)} = -k(1-k)\frac{(p_1 - p_2)}{q(1+F)}. \quad (26)$$

Note that the average of the allelic effects derived in this way is indeed zero (see Equation (21)) as was the average of the genotypic values. The average effect of substituting allele A for a is

$$\hat{e}_1 - \hat{e}_2 = k(1-k)\frac{(p_1 - p_2)}{pq(1+F)} = \hat{e}, \quad (27)$$

say. In terms of the average effect of substitution we may therefore write

$$\hat{e}_1 = q\hat{e}, \quad \hat{e}_2 = -p\hat{e}. \quad (28)$$

The average effect of substitution, $\hat{e}$, is a function of the phenotype frequencies, of the allele frequencies within phenotypes, and of the deviation from Hardy–Weinberg proportions in the population. These effects are defined for a given frequency configuration within a population and they are not valid for populations with other phenotype frequencies, allele frequencies within phenotypes, or genotypic frequencies, even when the genotypic effects are the same.

The additive genetic variance is the variance in the additive genotypic effects. From Table 4 it is given by

$$V_A = 4\hat{e}_1^2(u_1 + v_1) + (\hat{e}_1 + \hat{e}_2)^2(u_2 + v_2) + 4\hat{e}_2^2(u_3 + v_3). \quad (29)$$

This expression simplifies by inserting the average allele effects in the form (26) and the genotypic frequencies from Equations (5) to give

$$\begin{aligned} V_A &= \{4(p^2 + Fpq)q^2 + 2pq(1-F)(p-q)^2 \\ &\quad + 4(q^2 + Fpq)p^2)\}\hat{e}^2 \\ &= 2pq(1+F)\hat{e}^2. \end{aligned} \quad (30)$$

Equation (30) assumes the form derived by Fisher (1918) for the additive genetic variance when $F = 0$ as in the case of random mating ($m = 0$). Equation (30) is also reminiscent of the form for the genetic variance with inbreeding exhibited by Falconer (1996) in his Table 15.1 when $m = 0$.

The residual variance is the dominance variance, V_D (22), and after considerable algebra, it reduces to

$$V_D = \frac{\{u_2(1+F) + 2(1-F)k[p_1(2p-1) - p(p+Fq)]\}^2}{4(1-F^2)pq(p+qF)(q+pF)}, \quad (31)$$

and with random mating ($F = 0$),

$$V_D = \frac{1}{p^2q^2}\left[k(p_1q^2 + q_1p^2) - \frac{1}{2}u_2\right]^2. \quad (32)$$

The additive and dominance variances partition the genotypic variance into two components, namely

$$V_G = V_A + V_D, \quad (33)$$

thus extending the classical variance partition in (20). This partition has proven useful in describing population variation because it is closely related to familial correlations in classical genetic models, where the only source of familial aggregation of phenotypes is genetic. Thus, the covariance between a parent and its offspring is $\frac{1}{2}V_A$, so V_A is an expression of the part of the phenotypic variation that is transmissible via the passage of genetic material from parents to offspring. This has motivated the consideration of the *heritability*

$$h^2 = \frac{V_A}{V_P} \quad (34)$$

as the fraction of the phenotypic variance that is genetically transmissible. This is sometimes called the *narrow sense* heritability, because it only considers the additive part of the genetic variation while the *broad sense* heritability also includes non-additive genetic variation, i.e. V_G/V_P, with $V_P = k(1-k)$.

Heritability was originally designed to measure the genetic transmission from parents to offspring. The additive variance is the variance of the allele effects e_1 (25) and e_2 (26), and these depend on the details of the genetic and phenotypic frequencies in the population. Therefore, a value of heritability estimated in one population cannot be expected to describe the genetic transmission of the character in another population. It follows that an observed value of the heritability of a trait does not contribute to an assessment of the genetic basis of population differences in mean phenotype.

Cultural transmission breaks the simple relationship between the familial correlations and the genetic components of the variance derived in this section. For instance, the parent–offspring correlation will be inflated due to the direct vertical transmission of parental phenotypes to their offspring. To separate this phenotypic transmission from effects of genetic transmission, we need to study familial aggregation of the trait in cases where either the biological or the cultural link has been broken. For parent–offspring relations this can be achieved (to some extent) by studying relations between foster parents and adopted offspring and

between biological parents and their offspring adopted away.

Adoptions

The cultural link between biological parents and offspring is broken in early adoption, and with no subsequent contact between the child and the biological parents cultural transmission is unlikely. The genetic transmission of a studied trait can thus be independently evaluated. Breaking the cultural link is a special case of the general need to control the effects of common environment in the study of inheritance of quantitative traits. Adoption does not break the effects of the environment experienced by the fetus in utero, however.

In the proper statistical estimation of the relative contributions of genotype and environment to a phenotype, adoptions have played an important role. Our goal is to estimate the non-genetic transmission of a trait and to this end we compute means and variances of adopted individuals and see how these differ from those of offspring reared by their biological families.

Computation of variances among adopted individuals is straightforward using the resemblance between individuals and foster parents from Table 1. An individual of genotype AA, brought up in the first type of family in Table 1, acquires phenotype 1 with probability α_1. If an individual is Aa and is brought up in a family of the second type, it acquires phenotype 1 with probability β_2, etc. Thus, the mean phenotype among adopted offspring is

$$\mu_A = (u_1 + v_1)M_1 + (u_2 + v_2)M_2 + (u_3 + v_3)M_3 \quad (35)$$

where

$$\begin{aligned} M_1 &= \mu_1\alpha_1 + \mu_2(\beta_1 + \gamma_1) + \mu_4\delta_1, \\ M_2 &= \mu_1\alpha_2 + \mu_2(\beta_2 + \gamma_2) + \mu_4\delta_2, \\ M_3 &= \mu_1\alpha_3 + \mu_2(\beta_3 + \gamma_3) + \mu_4\delta_3. \end{aligned}$$

The variance among randomly adopted offspring is then

$$V_{A0} = \mu_A(1 - \mu_A). \quad (36)$$

The average variance within adoptive families is

$$\begin{aligned} V_{WAF} = {} & \mu_1 z_1(1 - z_1) + \mu_2[z_2(1 - z_2) + z_3(1 - z_3)] \\ & + \mu_4[z_4(1 - z_4)], \end{aligned} \quad (37)$$

where

$$\begin{aligned} z_1 &= \alpha_1(u_1 + v_1) + \alpha_2(u_2 + v_2) + \alpha_3(u_3 + v_3), \\ z_2 &= \beta_1(u_1 + v_1) + \beta_2(u_2 + v_2) + \beta_3(u_3 + v_3), \\ z_3 &= \gamma_1(u_1 + v_1) + \gamma_2(u_2 + v_2) + \gamma_3(u_3 + v_3), \\ z_4 &= \delta_1(u_1 + v_1) + \delta_2(u_2 + v_2) + \delta_3(u_3 + v_3) \end{aligned}$$

are the probabilities that a child adopted into each of the four types of families acquires phenotype 1. Clearly, we may rewrite our Equation (35) for the mean as

$$\mu_A = \mu_1 z_1 + \mu_2 z_2 + \mu_2 z_3 + \mu_4 z_4. \quad (38)$$

Then the variance between adoptive families is the difference

$$\begin{aligned} V_{BAF} &= V_{A0} - V_{WAF} \\ &= \mu_1 z_1^2 + \mu_2(z_2^2 + z_3^2) + \mu_4 z_4^2 - \mu_A^2. \end{aligned} \quad (39)$$

Covariances between relatives

Throughout the following, we assume that the population is at equilibrium, i.e. $k' = k$. Computation of the covariance between the phenotypic values of monozygous (MZ) twins, for example, is carried out by assuming that their genotypes are identical. In the general model of Table 1, for example, a pair of Aa_1 twins occurs in an $AA_1 \times Aa_2$ family with probability $\frac{1}{2}\beta_2^2$. The resulting covariance between MZ twins reared in the same family is given by

$$\begin{aligned} \mathrm{cov(MZT)} + (k)^2 = {} & \mu_1(\alpha_1^2 p_1^2 + 2\alpha_2^2 p_1 q_1 + \alpha_3^2 q_1^2) \\ & + \mu_2\Big[(\beta_1^2 + \gamma_1^2)p_1 p_2 + (\beta_2^2 + \gamma_2^2) \\ & \times (p_1 q_2 + p_2 q_1) + (\beta_3^2 + \gamma_3^2) q_1 q_2\Big] \\ & + \mu_4(\delta_1^2 p_2^2 + 2\delta_2^2 p_2 q_2 + \delta_3^2 q_2^2). \end{aligned} \quad (40)$$

The covariance between sibs reared together, cov(SST), is the same as that of dizygous (DZ) twins reared together, cov(DZT), in our model. This and the covariance between a parent and its biological offspring living together, cov (OPT), are given in Appendix 2. Note that for this dichotomous trait the parent–offspring covariance is the same whether we use the mid-parent or a randomly chosen parent. If $\beta_i \neq \gamma_i$, however, the mother–offspring and father–offspring covariances differ in a simple way.

Covariances that involve adopted offspring may be computed in a manner analogous to that used to derive the variances (36), (37) and (39). For example, the covariance between MZ twins each raised in a randomly chosen adoptive family is

$$\begin{aligned} & \mathrm{cov(MZA)} \\ & = (u_1 + v_1)M_1^2 + (u_2 + v_2)M_2^2 + (u_3 + v_3)M_3^2 - \mu_A^2. \end{aligned} \quad (41)$$

In the same way the covariance between a foster parent and its adopted child is

$$\mathrm{cov(FOP)} = \mu_1 z_1 + \mu_2 \frac{(z_2 + z_3)}{2} - k\mu_A, \quad (42)$$

since z_i represent the probabilities that a random offspring placed in a family of type i acquires phenotype 1 while k and μ_A are the parental and adopted offspring means, respectively. In Appendix 2 we record the covariances between biological sibs that are each randomly adopted, and between an adopted sib and the biological child of its adopting parents.

In the bilinear model of Table 3 the covariances simplify somewhat if we assume no genetic dominance,

$\sigma = 1$, and we have

$$\begin{aligned}\operatorname{cov}(\mathrm{MZT}) &= 2\alpha^2 pq + 2m\alpha^2 k(1-k)(p_1-p_2)^2 \\ &\quad + 4\alpha\eta(1+m)k(1-k)(p_1-p_2) \\ &\quad + 4\alpha(\tau-1)\eta\mu_2(1-2k)(p_1-p_2) \\ &\quad + 2\eta^2(1+m)k(1-k) \\ &\quad + 2(\tau-1)^2\eta^2\mu_2(1-2\mu_2) \\ &\quad + 4(\tau-1)\eta^2\mu_2(1-2k).\end{aligned} \tag{43}$$

With $\eta = 0$ this reduces to

$$\operatorname{cov}(\mathrm{MZT}) = 2\alpha^2 pq + 2m\alpha^2 k(1-k)(p_1-p_2)^2. \tag{44}$$

In addition, the covariance between full biological sibs (including DZ twins) is

$$\begin{aligned}\operatorname{cov}(\mathrm{SST}) &= \alpha^2[pq + 3mk(1-k)(p_1-p_2)^2] \\ &\quad + 2(1+m)k(1-k)\eta^2 \\ &\quad + 4(\tau-1)\eta^2\mu_2(1-2k) \\ &\quad + 2(\tau-1)^2\eta^2\mu_2[1-2k(1-k)(1-m)] \\ &\quad + 4\alpha\eta(1+m)k(1-k)(p_1-p_2) \\ &\quad + 4\alpha(\tau-1)\eta\mu_2(1-2k)(p_1-p_2).\end{aligned} \tag{45}$$

Finally,

$$\begin{aligned}\operatorname{cov}(\mathrm{OPT}) &= (1+m)k(1-k)[\alpha(p_1-p_2)+\eta] \\ &\quad + (\tau-1)\eta(1-m)k(1-k)(1-2k).\end{aligned} \tag{46}$$

Correlations between a pair of relatives may be obtained from the covariance between them by dividing by the product of the phenotypic standard deviations for each of the two types of individuals. Assuming that the population is at equilibrium, the appropriate denominator becomes the phenotypic variance in the general population, $V_P = k(1-k)$, for any relationship in which both individuals were raised by their biological parents (e.g. for $r_{\mathrm{MZT}}, r_{\mathrm{DZT}}, r_{\mathrm{SST}}, r_{\mathrm{OPT}}$). If both individuals were raised in an adoptive family, the denominator becomes $\mu_A(1-\mu_A)$ (e.g. for $r_{\mathrm{MZA}}, r_{\mathrm{DZA}}, r_{\mathrm{SSA}}, r_{\mathrm{SAA}}$). Finally, if one relative is raised by its biological parents and the other by adoptive parents, the denominator becomes $\sqrt{(k(1-k)\mu_A(1-\mu_A)}$ (e.g. for $r_{\mathrm{SAB}}, r_{\mathrm{FOP}}$).

Discrete traits with continuous liabilities

The liability models of Carter (1961, 1964) and Falconer (1965) describe correlations among relatives for a dichotomous character as a consequence of an underlying continuously varying character, which is heritable. This character was envisioned to determine the liability of the individual to a disease, such that individuals whose liability exceeds a value, called the *threshold*, would have the disease (Figure 1). Individuals with a liability below the threshold are healthy. This formulation was originally made with reference to the dichotomy between diseased and healthy for such cases as pyloric stenosis or cleft palate, which are examples of diseases with a complex etiology, where familial aggregation exists but with unknown laws of transmission. For such diseases an analysis based on an assumption of a distribution of liabilities seems reasonable, although the model is applicable to any dichotomous character. The phenotype 1 for the observable discrete trait develops in individuals with a liability above the threshold T, and individuals whose liability falls below the threshold would have the phenotype 2.

The ideas of liability and threshold are shown in Figures 1(a) and (b) where a Gaussian distribution of liability is assumed and an individual whose liability exceeds the threshold T takes the discrete trait value 1. Falconer's idea was that the affected individuals, whose mean is A, should be regarded as selected from the general population (Figure 1(a)) in the same way as desirable animals whose character value exceeds T are selected by a breeder. The difference $A - G$ is then called the *selection differential*. Among the relatives (e.g. offspring or sibs) of these type 1 individuals, the mean liability is R (Figure 1(b)) and the variances of the two curves are assumed to be equal. The difference $R - G$ is called the *selection response* in animal breeding. The ratio

$$b = \frac{R-G}{A-G} \tag{47}$$

is the regression of the liability of the relatives on that of the selected individuals (who, when phenotype 1 is a disease, are called propositi). From Figures 1 we have

$$b = \frac{1}{a}(x_g - x_r). \tag{48}$$

Now if P represents the liability of any individual in the population and R that of a relative, b may be written as

$$b = \frac{\operatorname{cov}(P,R)}{V}, \tag{49}$$

where V is the variance of liability in the population. As Falconer points out, Fisher's expressions for the covariances in terms of coefficients of relationship allows the heritability of liability to be estimated. For example, if there is no genotype-environment covariance and the propositi and their relatives are parents and children

$$b = \frac{1}{2}h^2, \tag{50}$$

where h^2 is the heritability of liability. If the selected individuals and their relatives are sibs, we must assume that there is no dominance variance to obtain $b = \frac{1}{2}h^2$. Of course assortative mating for liability is ignored in these calculations as is cultural inheritance. In general, under these assumptions

$$b = rh^2, \tag{51}$$

where r is the coefficient of relationship between the selected individuals and their relatives.

In order to tie together the relations (48) and (51), Falconer used the relationship between the incidences q_g and q_r of type 1 individuals in the population and their relatives, and the distances x_g and x_r. Thus, given q_g, x_g is obtained from tables of the normal distribution; for example, if $q_g = 0.025$, x_g is about 1.96. Further, it is well known that

$$a = \frac{z}{q_g}, \tag{52}$$

where z is the height of the normal distribution at T, namely

$$z = \frac{1}{\sqrt{2\pi}} \exp\left(-\frac{1}{2}x_g^2\right), \tag{53}$$

which can be found in standard tables. Thus

$$h_F^2 = \frac{b}{r} = \frac{x_g - x_r}{ra} = \frac{q_g(x_g - x_r)}{rz}. \tag{54}$$

Falconer (1965) provides a table of values x and a for given incidences q.

The analysis just described has been widely used to estimate the heritability of liability to diseases whose transmission is complex. One example cited by Cavalli-Sforza and Bodmer (1971, p. 557) concerns harelip, whose incidence in the general population is 0.1% and in first degree relatives is 3.5%. Using Falconer's tables these proportions give $x_g = 3.09$, $x_r = 1.81$ and $a = 3.37$ (note the misprint in Cavalli-Sforza and Bodmer's book where 3.7 is used). From (54) this gives an estimate of $h^2 = 0.77$ for the heritability of the liability to the disease. Note that this is *not* the heritability of harelip itself which is 0.07 if estimated from $2r_{\mathrm{OPT}}$.

The application of this liability analysis in our system of discrete phenotypes takes phenotype 1 as the disease and phenotype 2 as the normal phenotype. The incidence of phenotype 1 in the general population is k and for most purposes it would be reasonable to assume that equilibrium has been attained. To obtain the incidence, q_r, in relatives of individuals of phenotype 1 observe that

$$\begin{aligned} q_r &= \text{prob [relative is 1|propositus is 1]} \\ &= \frac{\text{prob [propositus and relative both 1]}}{\text{prob [propositus is 1]}} \qquad (55) \\ &= \frac{\text{cov [propositus, relative]} + k^2}{k}. \qquad (56) \end{aligned}$$

For example, if the relatives are sibs, then the incidence in relatives is $q_r = [\text{cov (SST)}/k] + k$, while if the propositus is a parent and the relative its offspring, then (56) is $q_r = [\text{cov (OPT)}/k] + k$. These are computed using (45) and (46) when the transmission is of the bilinear form.

Another way to view the application of Falconer's method is to observe that (56) may be rewritten as

$$q_r = (1 - k)\rho + k, \tag{57}$$

Table 5.

	Propositus		
Relatives	phenotype 1	phenotype 2	Total
phenotype 1	$k[k + (1-k)\rho]$	$k(1-k)(1-\rho)$	k
phenotype 2	$k(1-k)(1-\rho)$	$(1-k)[(1-k) + k\rho]$	$1-k$
Total	k	$1-k$	1

where ρ is the correlation between the liabilities of an individual and its relative, since the variance in both groups is $k(1-k)$. In a similar way, the fraction q_n of phenotype 1 among the relatives of phenotype 2 individuals is

$$q_n = k(1 - \rho), \tag{58}$$

which reflects that relatives of an unaffected individual are less likely to be affected than a random individual in the population by a factor $(1 - \rho)$. This allows us to construct a 2×2 table of frequencies, as shown in Table 5. From this table the usual χ^2 turns out to be exactly ρ^2. Another way of saying this is that ρ is the Pearson correlation coefficient.

Falconer's method has been criticized because of the key assumption that the variance of the distribution of liability among the relatives of propositi is the same as in the general population. Edwards (1969) suggested that a procedure, often termed "tetrachoric" analysis and due originally to Pearson (1900, 1904) and Everitt (1910), could overcome this difficulty. In this analysis, liability in propositi and their relatives is assumed to have a bivariate Gaussian distribution as shown in Figure 2. The plane of liabilities in the propositi and relatives is divided into four quadrants by threshold T in propositi measured in units of standard deviation from the respective means and

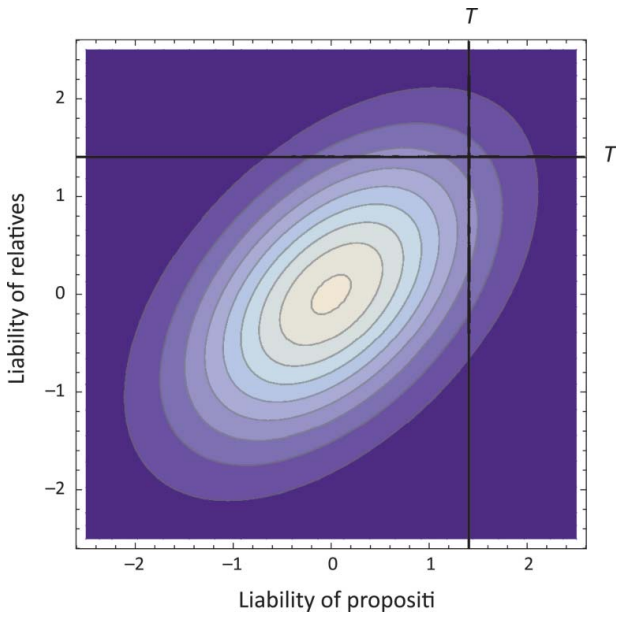

Figure 2. Two-dimensional graph showing the incidence of a trait in individuals and in their relatives. Based on a threshold model of disease susceptibility. Here $\rho = 0.5$.

relatives. The other important parameter is the correlation, ρ, between the two liabilities, which is 0.5 in Figure 2. It should be noted that for some values of the phenotype population frequency, and frequencies of the phenotype in relatives, Falconer's method may give heritabilities greater than unity.

Within this framework, Edwards (1969) suggests the approximate estimate for the correlation ρ:

$$\hat{\rho} = \frac{0.57 \log \kappa}{-\log q_g - 0.44 \log \kappa - 0.26}, \tag{59}$$

where $\kappa = q_r/q_g$. Then the heritability h^2 is estimated by

$$h_E^2 = \frac{\hat{\rho}}{r}, \tag{60}$$

where r is the coefficient of relationship. Cavalli-Sforza and Bodmer (1971, p. 563) use the harelip data to apply (59). In this case $q_g = 0.001$ and $q_r/q_g = 35$. Hence from (59) $\hat{\rho} = 0.427$ and since these are first degree relatives, from (60) $h_E^2 = 0.854$ which is higher than the estimate of 0.77 obtained using Falconer's method. Again this estimate of the heritability of liability assumes no assortative mating for liability, no cultural transmission, and, if the relatives are sibs, no dominance variance.

Even though there may be an empirical estimate for the extent of assortative mating for a dichotomous trait, no such estimate can be obtained for the correlation between the liabilities of mates. This must give us pause as we attempt to interpret estimates of heritability of liability that are obtained under the assumption of no assortative mating. In fact, assortment for liability may have a significant effect on the estimate of heritability. Let us assume that the correlation between the liability of mates is m_L. Fisher's theory predicts that when the relatives are parents and offspring, (50) should be replaced by

$$b = \frac{1}{2} h^2 (1 + m_L). \tag{61}$$

The estimate in (54) based on *parent–offspring* data therefore would become

$$h^2 = \frac{2(x_g - x_r)}{a(1 + m_L)}. \tag{62}$$

Compared to the value in (54), this is reduced by the factor $(1 + m_L)$. For sibs or dizygous twins, Fisher's value for b is more complex:

$$b = \frac{1}{2} h^2 (1 + m_L h^2), \tag{63}$$

and, to obtain the heritability of liability from data on *sibs*, we solve the quadratic equation

$$\frac{1}{2} m_L (h^2)^2 + \frac{1}{2} h^2 - \frac{1}{a}(x_g - x_r) = 0 \tag{64}$$

using the root closest to the interval $(0, 1)$. For example, in the case of harelip, (54) gave an estimate of $h^2 = 0.77$ with first degree relatives, but the assumption of a marital correlation for liability of $m_L = 0.5$ would produce new estimates of $h^2 = 0.51$ from parents and offspring (using (62)) and $h^2 = 0.59$ from sibs (using (64)).

Assortative mating may be taken into account in Edward's analysis in a similar way. For parent–offspring data $r = \frac{1}{2}(1 + m_L)$ and for sib data $r = \frac{1}{2}(1 + m_L h^2)$ may be used in Equation (60).

Whether assortative mating occurs at the level of liability or at the observable level of the trait may be difficult to distinguish in practice. However, when the trait is an ability or a skill, assortment may occur on the basis of the trait (Creanza et al. 2012).

Numerical analysis

In order to explore the relationship between the model of transmission and the statistics of familial aggregation, a numerical analysis of the bilinear model of Table 3 was carried out. A parametric grid of α, β and η was set up with $0 \le 2\alpha + 2\eta + \beta \le 1$. For each choice of the triplet (α, β, η) the genetic dominance, σ, and parental dominance τ were each set in turn to 1.0, 1.5 and 2.0. Recessivity, with values less than 1, is considered by interchanging A and a. Two values of the assortative mating parameter were used, $m = 0.0$ and $m = 0.5$. Then for each specification of $(\alpha, \beta, \eta, \sigma, \tau)$, the allele frequency, p, was chosen uniformly from 0.01 to 0.99 in 0.01 intervals; for each of these 99 p values, the equilibrium of Equations (7) and (8) was determined numerically (see supplemental Mathematica file). To assess the speed with which this equilibrium was attained, we also iterated the recursions starting with a population composed entirely of individuals bearing phenotype 2 ($k = 0$), hence simulating a new trait that appears within a population, which varies genetically in its predilection to adopt the trait. In general, equilibrium was rapidly approached. Across all of the combinations of parameters considered in Tables 7–9 (see later in this section), the distances that both k and p_1 were away from their equilibrium values fell to below 1% of their initial distances by ten generations, with equilibration taking longer when cultural transmission exhibited dominance ($\tau = 2$). Sample plots of the dynamics of k and p_1 are provided in the supplemental Mathematica file.

At equilibrium we recorded the phenotypic mean k (the frequency of phenotype 1), the population variance $k(1-k)$, the gene frequency p of A, the variance among adopted individuals, namely $V_{A0} = \mu_A(1 - \mu_A)$ from (36), the additive genetic variance V_A (from (29)), and the dominance variance V_D (from (30)). Covariances and correlations between the most commonly treated relatives listed in Table 6 were also computed at equilibrium.

From these frequencies and covariances four quantities that have been used to estimate heritability of a trait were computed. The first of these is based on the standard calculation of additive genetic variance for additive traits (Falconer 1996). Ignoring cultural transmission and assortment, half the difference in mean phenotype between AA and aa homozygotes provides an estimate of

Table 6. List of correlations between relatives.

symbol	relationship
r_{MZT}	monozygous twins raised together
r_{MZA}	monozygous twins raised separately
r_{DZT}	dizygous twins raised together
r_{DZA}	dizygous twins raised separately
r_{SST}	full sibs raised together
r_{SSA}	full sibs raised separately
r_{SAB}	two unrelated individuals raised by the biological parents of one
r_{SAA}	two unrelated adopted individuals raised in the same home
r_{OPT}	a parent and his or her natural child raised by that parent
r_{FOP}	a parent and his or her foster child

the average effect of the allele, which we denote by ξ: $\xi = [u_1/(u_1 + v_1) - u_3/(u_3 + v_3)]/2$, so that the estimated heritability is

$$h_1^2 = 2pq\xi^2/k(1-k).$$

This will generally not give a good estimate of the true heritability $h^2 = V_A/V_P$ using Equations (26) and (29) evaluated at the equilibrium of Equations (7) and (8) unless assortment is absent ($m = 0$), the genes are additive ($\sigma = 1$), and cultural transmission is either absent ($\eta = 0$) or additive ($\tau = 1$). The second tabulated heritability is

$$h_2^2 = 2r_{OPT}/(1+m)$$

(Cavalli-Sforza & Bodmer 1971, p. 547), and when $\beta = \eta = 0$ and $\sigma = 1$ this is exactly equal to h^2 as we show in Appendix 3. In other words, when the family environment (interpreted in terms of the parents' phenotypes) plays no role, the parent–offspring statistic gives an accurate estimate of the heritability as long as it accounts for assortative mating.

We also record the two widely used estimates of heritability based on twin correlations. These have been widely used in human behavioral genetics to estimate heritability from observations on sets of MZ and DZ twins (see Hay 1985, p. 221). The first, usually called Holzinger's H, is computed as

$$h_3^2 = (r_{MZT} - r_{DZT})/(1 - r_{DZT}).$$

The second, Nichols' HR, has the form

$$h_4^2 = 2(r_{MZT} - r_{DZT})/r_{MZT}.$$

It should be noted that an alternative form of h_4^2, namely $2(r_{MZT} - r_{DZT})$, has also been used in the literature.

The remaining estimates of heritability do not refer to the trait itself, but to the liability of the trait, namely Falconer's and Edwards' heritabilities h_F^2 and h_E^2, given by Equations (54) and (60). We record these estimates based on sibs and parent–offspring pairs and list values that do and do not take assortative mating into account according to Equations (62) and (64). In making the adjustments we have used a correlation $m_L = 0.5$ between the liabilities of mates. The simulations, however, were based on a phenotypic model of assortment with $m = 0$ or $m = 0.5$.

In our investigations, the role of the baseline parameter β was found to be relatively uninteresting, except insofar as it affected k and therefore the total variance $k(1-k)$. Thus if $\eta = 0$, for example, the change in r_{MZT} caused by changing β is due entirely to the change in the value of the variance $k(1-k)$. Therefore, in order to concentrate on the roles of genetic and cultural effects (α and η, respectively), $\beta = 0.1$ will be assumed in the following discussion, except where noted.

An example of the complete output for one parameter sets is shown in Table 7. Each derived statistic is averaged over the 99 different starting conditions, and the standard deviation computed in the usual way. All values are computed at the equilibrium of the dynamical system (7) and (8). Even from the single parameter set examined in Table 7 it is obvious that the estimates of heritability h_1^2, h_2^2, h_3^2 and h_4^2 are widely discrepant. Table 7 also records the standard and adjusted values of Falconer's and Edwards' heritabilities of liabilities of the trait. For the majority of p values used, both the standard and adjusted Edwards' estimates violated the validity criterion

Table 7. Example of results for the bilinear model with $\alpha = 0.2$, $\eta = 0.2$, $\beta = 0.1$, $\alpha = \sigma = 1$, $m = 0.5$. Equilibrium values for each statistic were calculated using allele frequencies from $p = 0.01$ to 0.99 in intervals of 0.01, and we report the means and standard deviations of these statistics across these 99 values of p. The number of cases where heritability estimates fell outside of (0,1) is reported in square brackets (not reported if all heritability values were valid).

statistic	mean	s.d.
k	0.500	0.191
$k(1-k)$	0.214	0.033
$\mu_A(1-\mu_A)$	0.214	0.033
p	0.500	0.287
V_A	0.029	0.013
V_D	0.000	0.000
h_1^2	0.129	0.044
h_2^2	0.489	0.032
h_3^2	0.037	0.013
h_4^2	0.236	0.056
h^2	0.127	0.045

	Covariance		Correlation	
Relationship	mean	s.d.	mean	s.d.
MZT	0.052	0.015	0.235	0.041
MZA	0.014	0.006	0.062	0.022
DZT = SST	0.045	0.013	0.206	0.031
DZA = SSA	0.007	0.003	0.033	0.012
OPT	0.079	0.016	0.367	0.024
FOP	0.064f	0.010	0.300	0.000
SAB	0.032	0.007	0.147	0.009
SAA	0.026	0.004	0.120	0.000

heritabilities of liability		SST	OPT	SST(adj)	OPT(adj)
	h_F^2	0.705	1.283 [99]	0.552	0.855 [3]
	h_E^2	2.996 [81]	2.890 [99]	0.954 [44[a]]	1.927 [94]

[a] For 24 of the remaining 99 values of p, h_E^2 was complex and not included.

Table 8. Bilinear model: $\sigma = 1$, $\tau = 1$.[a]

	$m = 0$			$m = 0.5$		
	$\alpha = 0.4$ $\eta = 0$	$\alpha = 0.2$ $\eta = 0.2$	$\alpha = 0$ $\eta = 0.4$	$\alpha = 0.4$ $\eta = 0$	$\alpha = 0.2$ $\eta = 0.2$	$\alpha = 0$ $\eta = 0.4$
k	0.500	0.500	0.500	0.500	0.500	0.500
$k(1-k)$	0.198	0.214	0.250	0.198	0.214	0.250
p	0.500	0.500	0.500	0.500	0.500	0.500
V_A	0.054	0.021	0.000	0.058	0.029	0.000
V_D	0.000	0.000	0.000	0.000	0.000	0.000
r_{MZT}	0.255	0.170	0.320	0.276	0.235	0.480
r_{DZT}	0.128	0.140	0.320	0.159	0.206	0.480
r_{OPT}	0.128	0.237	0.400	0.207	0.367	0.600
h_1^2	0.255	0.094	0.000	0.276	0.129	0.000
h_2^2	0.255	0.475	0.800	0.276	0.489	0.800
h_3^2	0.148	0.035	0.000 [99]	0.142	0.037	0.000
h_4^2	1.000 [22]	0.338	0.000 [99]	0.862	0.236	0.000
h^2	0.255	0.094	0.000	0.276	0.127	0.000
Liability heritabilities: Falconer (h_F^2)						
	$m = 0$			$m = 0.5$		
	$\alpha = 0.4$ $\eta = 0$	$\alpha = 0.2$ $\eta = 0.2$	$\alpha = 0$ $\eta = 0.4$	$\alpha = 0.4$ $\eta = 0$	$\alpha = 0.2$ $\eta = 0.2$	$\alpha = 0$ $\eta = 0.4$
SST	0.447	0.476	1.034 [99]	0.554	0.705	1.613 [99]
OPT	0.447	0.817	1.314 [99]	0.725	1.283 [99]	2.110 [99]
SST (adj)[b]	0.374	0.397	0.752	0.448	0.552	1.056 [99]
OPT (adj)	0.298	0.545	0.876	0.483	0.855 [3]	1.406 [99]
Liability heritabilities: Edwards (h_E^2)						
	$m = 0$			$m = 0.5$		
	$\alpha = 0.4$ $\eta = 0$	$\alpha = 0.2$ $\eta = 0.2$	$\alpha = 0$ $\eta = 0.4$	$\alpha = 0.4$ $\eta = 0$	$\alpha = 0.2$ $\eta = 0.2$	$\alpha = 0$ $\eta = 0.4$
SST	1.282 [63]	0.220 [66]	−11.433 [99]	−1.082 [71]	2.996 [81]	−5.728 [99]
OPT	1.282 [63]	−0.011 [92]	−7.160 [99]	0.626 [80]	2.890 [99]	−4.770 [99]
SST (adj)[b]	0.538 [42]	0.493 [40]	[always complex]	0.494 [43]	0.954 [44]	[always complex]
OPT (adj)	0.855 [57]	−0.007 [72]	−4.773 [99]	0.417 [68]	1.927 [94]	−3.180 [99]

[a] See legend for Table 7.
[b] Across this row of parameter values, h_E^2 was complex in (15, 18, 99, 19, 24, 99) of the 99 values for p explored.

$0 \le h^2 \le 1$, as did the standard Falconer estimate based on OPT.

In order to demonstrate some of the more interesting outcomes of the numerical analysis, we have chosen two cases, a completely additive case $\sigma = 1$, $\tau = 1$ and a case with genetic and environmental dominance $\sigma = 2$, $\tau = 2$. The case $\sigma = 1$, $\tau = 1$ is shown in Table 8 and $\sigma = 2$, $\tau = 2$ in Table 9. In both tables we have chosen three transmission arrangements: $(\alpha, \eta) = (0.4, 0.0)$, $(0.2, 0.2)$ and $(0.0, 0.4)$, with two levels of assortative mating: $m = 0$ and $m = 0.5$.

The main result seen from Tables 8 and 9 is that all estimates of heritability are sensitive to the mode of transmission. As transmission switches from being primarily genetic ($\alpha = 0.4$, $\eta = 0$) to primarily cultural ($\alpha = 0$, $\eta = 0.4$), the true heritability (h^2, measured exactly from V_A/V_P) declines. Heritability estimated from offspring–parent correlations (h_2^2), however, exhibits the opposite pattern, confounding cultural transmission with genetic transmission. Estimates of heritability based on liability similarly tend to rise when cultural transmission replaces genetic transmission. Heritability estimated from twins (h_3^2) exhibits better behavior in the sense of declining when genetic transmission weakens, but the point estimates for h_3^2 often lie far from the true heritability.

Assortative mating increases all correlations between relatives in a way that is enhanced by increased cultural transmission. Heritabilities are also generally increased by the assortment, although with $\eta = 0$, h_3^2 may actually decrease as m goes from 0 to 0.5. For all of the heritabilities of liability there is also an increase with m.

Larger dominance values (σ and τ) produce higher equilibrium values of k. As expected, however, there is no detectable effect on the additive genetic variance. The dominance component V_D obviously is affected by the value of σ. MZ twin correlations are all higher in Table 9 than in Table 8. Comparing the two tables, we see that with $\sigma = \tau = 1$, r_{MZT} is not monotone decreasing as the genetic contribution to transmission decreases, but r_{DZT} and r_{OPT} are increasing as α decreases. With $\sigma = \tau = 2$, r_{MZT} is decreasing as α decreases with $m = 0$, but is not monotone when $m = 0.5$.

Table 9. Bilinear model: $\sigma = 2$, $\tau = 2$.[a]

	$m = 0$			$m = 0.5$		
	$\alpha = 0.4$ $\eta = 0$	$\alpha = 0.2$ $\eta = 0.2$	$\alpha = 0$ $\eta = 0.4$	$\alpha = 0.4$ $\eta = 0$	$\alpha = 0.2$ $\eta = 0.2$	$\alpha = 0$ $\eta = 0.4$
k	0.635	0.727	0.890	0.621	0.670	0.809
$k(1-k)$	0.176	0.172	0.098	0.178	0.187	0.155
p	0.500	0.500	0.500	0.500	0.500	0.500
V_A	0.065	0.022	0.000	0.066	0.032	0.000
V_D	0.022	0.006	0.000	0.023	0.007	0.000
r_{MZT}	0.425	0.201	0.078	0.432	0.297	0.418
r_{DZT}	0.183	0.136	0.078	0.246	0.243	0.418
r_{OPT}	0.154	0.156	0.088	0.255	0.350	0.476
h_1^2	0.308	0.102	0.000	0.327	0.132	0.000
h_2^2	0.308	0.311	0.175	0.341	0.467	0.635
h_3^2	0.316	0.078	0.000 [99]	0.270	0.074	0.000
h_4^2	1.193 [99]	0.665	0.000 [99]	0.961 [32]	0.339	0.000
h^2	0.308	0.107	0.000	0.312	0.145	0.000
Liability heritabilities: Falconer (h_F^2)						
	$m = 0$			$m = 0.5$		
	$\alpha = 0.4$ $\eta = 0$	$\alpha = 0.2$ $\eta = 0.2$	$\alpha = 0$ $\eta = 0.4$	$\alpha = 0.4$ $\eta = 0$	$\alpha = 0.2$ $\eta = 0.2$	$\alpha = 0$ $\eta = 0.4$
SST	0.665	0.509	0.445	0.896 [55]	0.917 [49]	2.054 [99]
OPT	0.542	0.589	0.503	0.916 [57]	1.397 [99]	2.421 [99]
SST (adj)[b]	0.511	0.411	0.374	0.646	0.677	1.260 [99]
OPT (adj)	0.361	0.393	0.335	0.611	0.931 [25]	1.614 [99]
Liability heritabilities: Edwards (h_E^2)						
	$m = 0$			$m = 0.5$		
	$\alpha = 0.4$ $\eta = 0$	$\alpha = 0.2$ $\eta = 0.2$	$\alpha = 0$ $\eta = 0.4$	$\alpha = 0.4$ $\eta = 0$	$\alpha = 0.2$ $\eta = 0.2$	$\alpha = 0$ $\eta = 0.4$
SST	0.625 [92]	0.021 [99]	−0.022 [99]	0.153 [94]	0.306 [99]	−0.250 [99]
OPT	−0.408 [92]	−0.774 [99]	−0.025 [99]	93.200 [96]	0.073 [99]	−0.280 [99]
SST (adj)[b]	0.471 [67]	0.197 [78]	−0.023 [99]	0.564 [65]	0.426 [70]	−0.293 [99]
OPT (adj)	−0.272 [85]	−0.516 [99]	−0.017 [99]	62.133 [92]	0.049 [99]	−0.187 [99]

[a] See legend for Table 7.
[b] Across this row of parameter values, h_E^2 was complex in (19, 17, 0, 24, 25, 0) of the 99 values for p explored.

The values of the heritabilities of liability serve to emphasize the care that must be taken in using this concept when the trait under study is not a rare disease. A key illustration of this is the fact that for almost every parameter set in Tables 8 and 9, the heritability of liability computed using Edwards' measure (59) turned out to be greater than unity, negative, or, when adjusted for assortative mating using $m_L = 1/2$, complex. Falconer's estimate of the heritability based on liability (h_F^2) more often lies between 0 and 1, except when levels of assortment and cultural transmission are high. Even in cases where the average value of h_F^2 is valid, however, many of the point estimates from a particular simulation with a given allele frequency, p, lie outside of 0 and 1. For example, the majority of point estimates for h_F^2(SST) and h_F^2(OPT) were above 1 in Table 9 when $m = 0.5$.

The first point to observe about Falconer's measure is that as the level of cultural transmission, η, increases, the estimated heritability of liability computed from sibs or parents and offspring increases. When these values are adjusted for assortment on liability, this may not be the case, especially with sibs. These heritabilities also increase when there is assortment for the trait itself ($m > 0$). The fractional adjustment for $m_L = 1/2$ is greater in the parent–offspring case than with sibs; it would be of interest to determine whether this is a general phenomenon. Finally, the estimated heritabilities vary with p in ways that differ from the true heritability, h^2, causing biases that are highly sensitive to the underlying genetic details.

An aspect of quantitative inheritance that has received less attention than it deserves is the role of gene frequency in estimates of heritability. Since we kept track of both equilibrium gene frequency and additive genetic varaince, we are in a position to explore this relationship for different vertical transmission schemes. Figure 3 shows how the true heritability V_A/V_P varies with p for $(\alpha, \eta) = (0.4, 0)$ and $(0.2, 0.2)$ for each of $m = 0$, $m = 0.5$ using the baseline transmission rate $\beta = 0.1$ (panels (a) and (b)) or assuming a lower tendency of all individuals to adopt the trait ($\beta = 0.0$ in panels (c) and (d)). First, observe that m does not affect the qualitative role of p; the curves with $m = 0$ and $m = 0.5$ are quite close. However, as p increases, h^2 varies dramatically in all panels, particularly when genetic and familial dominance are high.

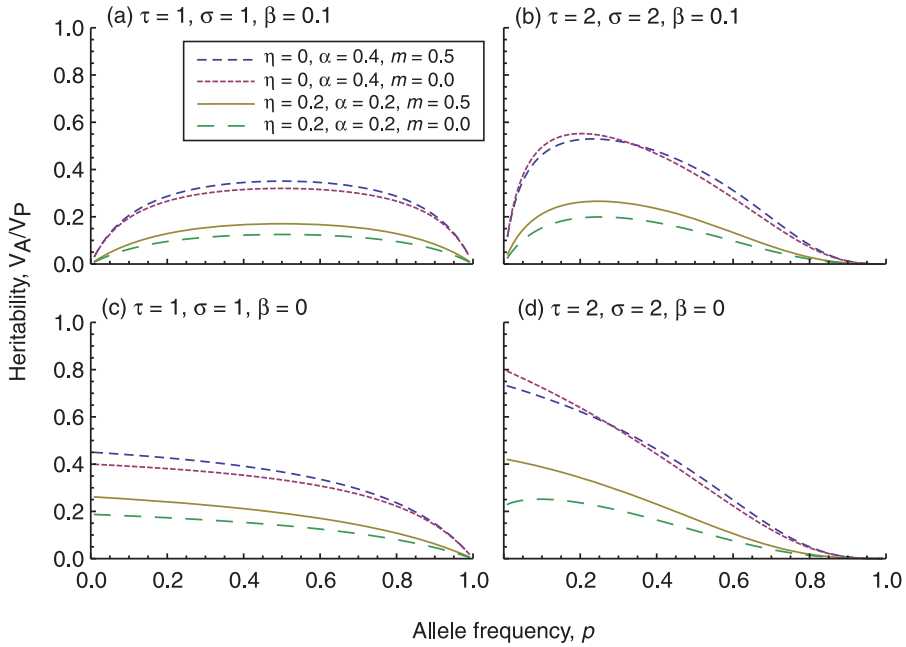

Figure 3. Heritability V_A/V_P as a function of the equilibrium gene frequency when $\sigma = \tau = 1$ (panels (a) and (c)) or $\sigma = \tau = 2$ (panels (b) and (d)), using the default value of $\beta = 0.1$ (panels (a) and (b)) or $\beta = 0$ (panels (c) and (d)). With $\beta = 0.1$, the probability of adopting phenotype 1 (see Table 3) ranges from 0.1 (β) to 0.9 ($2\eta + 2\sigma + \beta$), and heritability is highest when the allele frequency is intermediate (panels (a) and (b)). With $\beta = 0$, the probability of adopting phenotype 1 ranges from 0 (β) to 0.8 ($2\eta + 2\sigma + \beta$), creating an asymmetry where the heritability is higher when allele frequencies are low because nearly all aa individuals then develop phenotype 2 (i.e. stochastic variation, which depresses heritability, is virtually absent).

Furthermore, the nature of the relationship between p and h^2 depends on the inherent tendency to adopt the trait, β. With $\beta = 0.1$, the probability that an individual adopts a trait based on Table 2 ranges from 0.1 to 0.9, leading to a symmetric humped relationship between p and h^2 (panel (a)). With $\beta = 0$, however, the probability of adopting a trait ranges from only 0.0 to 0.8, causing heritability to be very high (little stochasticity) when p is near 0.0 and the trait is rarely expressed in families that transmit the trait (panel (c)). Of course, in practice the frequencies of genes

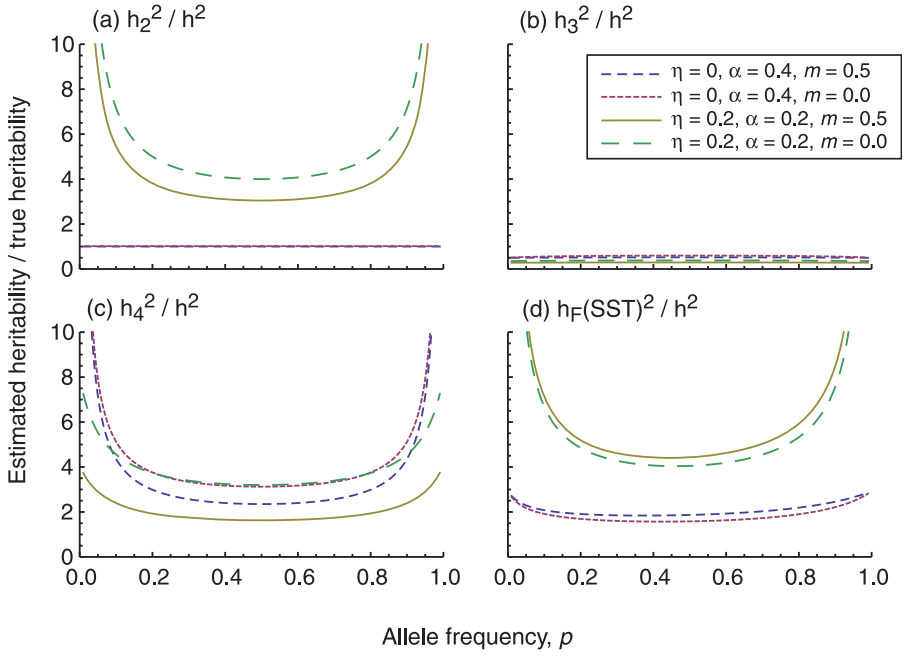

Figure 4. Heritability estimated from familial correlations relative to the true underlying heritability, h^2, varies as a function of the underlying allele frequency, p. Panels: (a) h_2^2, (b) h_3^2, (c) h_4^2, (d) h_F^2 (SST). In all figures: $\beta = 0.1$, $\tau = 1$, and $\sigma = 1$. Two combinations of η and α are used, namely $\eta = \alpha = 0.2$ (green curves) and $\eta = 0$ and $\alpha = 0.4$ (purple curves). The full lines are results for assortative mating ($m = 0.5$), and broken lines show results for random mating ($m = 0$). Because of the sensitivity of the various heritability estimates of p, it is impossible to determine the extent of bias in a given estimate without knowing the underlying genetic details, including allele frequencies.

that contribute to quantitative traits are not estimable. This makes it virtually impossible to infer the extent of genetic transmission from heritability. For instance, a heritability of 25% is compatible in our model, with $\alpha = 0.2$, $\eta = 0.2$, $m = 0.5$ and $p = 0.1$, as well as $\alpha = 0.4$, $\eta = 0$ and $p = 0.8$ with either $m = 0$ or $m = 0.5$ $(\sigma = \tau = 1, \beta = 0)$. These rules of transmission are very different in terms of the relative role of cultural transmission, and the gene frequencies are not extreme. However, the heritability is the same for the two transmission regimes.

Importantly, the estimated heritabilities vary with p in ways that differ from the true heritability, h^2, causing biases to be highly sensitive to the underlying genetic details. This sensitivity is illustrated in Figure 4, which plots various estimates of heritability divided by h^2. Severe biases are often seen when the trait is very rare (p near 0) or very common (p near 1). Even when dealing with intermediate allele frequencies, none of the heritability measures explored in this figure perform well, particularly in the presence of cultural transmission.

Discussion and conclusions

The most common procedures used to infer the relative importance of genetic and non-genetic contributions to a trait in humans have their origins in biometrical analysis developed early in the twentieth century. Fisher's fundamental study in 1918 showed that correlations between relatives could be expressed in terms of genetic contributions, assortative mating, and allele frequencies. Although the effect of environmental variation was lurking in the background, it was never made specific. Thus, in applications of Fisher's analysis, first to animal breeding but later to human behaviors, the genetic assumptions inherent in Fisher's work were rarely questioned, and no particular model for environmental transmission was considered. Indeed, almost no quantification of potential cultural contributions that might aggregate in families was introduced until the 1970s (Cavalli-Sforza and Feldman 1973). It is still generally the case that genetic and non-genetic contributions to human quantitative variation are expressed using linear regression models.

The introduction of more detailed descriptions of the process of cultural transmission has both advantages and disadvantages. We have seen in this paper that simple models of vertical cultural transmission superimposed on simple one-locus genetic transmission produce closed form expressions for correlations between relatives. Different ways of estimating heritability can then yield substantially different results, and the extent of these differences depends on the relative importance of cultural and genetic transmission. For the correlations themselves, MZ twin and parent–offspring correlations are clearly more strongly affected by the transmission rule than is the sib–sib correlation (Tables 8 and 9). There is, however, an interesting effect of assortative mating. In Table 9, for example, r_{MZT} decreases with increasing cultural transmission when $m = 0$, but not when $m = 1/2$, while r_{OPT} increases with increasing cultural transmission for both $m = 0$ and $m = 1/2$ in Table 8. This increase of r_{OPT} with increasing η might have been predicted because, after all, the cultural transmission in our model is from parent to child. But the non-monotonicity observed for r_{MZT} is difficult to justify from first principles.

Our analysis has highlighted some unpleasant features of estimates of the heritability of liability. These properties, notably estimates greater than unity, are not important for traits that are rare in the population and relatively rare in the relatives of propositi. But it does appear that liability analysis may well be inappropriate for traits whose frequencies are well above those of rare congenital diseases such as pyloric stensis, cleft palate or club foot.

Our final point concerns the role of gene frequency. For most quantitative traits, the value of p is completely unknown. Yet even in Fisher's original analysis, the various components of genotypic variance depended on allele frequencies. This dependence is highlighted in Figures 3 and 4, where the heritability decreases with p at a rate which increases with the strength of genetic transmission. This relationship between h^2 and p must be kept in mind when heritability is used to infer the model of transmission. The same heritability may be produced by quite different proportions of cultural and genetic transmission with different gene frequencies. Since the latter are never known, it is very risky to infer the relative importance of α and η from h^2.

Thus, secreted beneath commonly used summary statistics for any trait with complex transmission is a universe of possible transmission rules. By starting with these rules and proceeding in reverse to produce the summary statistics, the sensitivity of these statistics to the assumptions commonly made in quantitative genetics becomes clear.

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Appendix 1. Convergence of the bilinear model for $\sigma = 1, \tau \neq 1$

In the analytical treatment of the bilinear transmission scheme of Table 3 we assume $\sigma = 1$, $\eta > 0$ and $0 \leq \tau \leq 2$.

The right side of (9) is a monotone increasing function of k. There is a unique valid equilibrium $\hat{k}$ of (9) that solves

$$\begin{aligned}&\beta + 2\alpha p + k[2\tau\eta + 2\eta m(1-\tau) - 1]\\&\quad + k^2(1-m)2\eta(1-\tau) = 0.\end{aligned} \tag{65}$$

Recursion (4a) simplifies to become

$$\begin{aligned}k'(p_1' - p) = \alpha pq + \alpha m\frac{k}{1-k}(p_1 - p)^2 + \eta(p_1 - p)\\ \times\{(1+m)k + (\tau - 1)(1-m)k(1-2k)\},\end{aligned} \tag{66}$$

where we have used $(1-k)p_2 = p - kp_1$ and $p_1 - p_2 = (p_1 - p)/(1-k)$.

Consider first the case $\eta = 0$ so that, from (9), k is constant over time and equal to $\beta + 2\alpha p$. Then using (10) with $\eta = 0$ we may rewrite (66) as

$$p_1' - p = \frac{\alpha pq}{\beta + 2\alpha p} + \frac{\alpha m(p_1 - p)^2}{1 - \beta - 2\alpha p}. \tag{67}$$

Clearly since $\alpha > 0$ we have $p_1' > p$ in every generation and $d(p_1' - p)/d(p_1 - p) = 2\alpha m(p_1 - p)/(1 - \beta - 2\alpha p) > 0$ so that p_1' is monotone increasing in p_1.

The fixed points of the recursion (67) are the roots of the quadratic equation $g(p_1 - p) = 0$ where

$$g(\pi) = \pi^2\frac{\alpha m}{1-k} - \pi + \frac{\alpha pq}{k}. \tag{68}$$

Now obviously $g(0) > 0$ and for $p_1 = 1$ we get

$$g(q) = q\left[\frac{\alpha p}{k} + \frac{\alpha mq}{1-k} - 1\right]. \tag{69}$$

Substituting $k = \beta + 2\alpha p$ we see that $g(q) < 0$ if

$$\begin{aligned}&\alpha p(1 - \beta - 2\alpha p) + \alpha mq(\beta + 2\alpha p)\\&\quad - (\beta + 2\alpha p)(1 - \beta - 2\alpha p) < 0.\end{aligned}$$

The left side of this inequality is less than

$$\begin{aligned}&-(\beta + \alpha p)(1 - \beta - 2\alpha p) + \alpha q(\beta + 2\alpha p)\\&= -(\beta + \alpha p)(1 - \beta - 2\alpha) - \alpha\beta q < 0.\end{aligned}$$

There is therefore a single valid equilibrium, $\hat{p}_1$, of (67) to which there is global convergence.

The case $\eta \neq 0$ is more difficult to analyze. Since (9) is independent of p_1 and p_2 we may take k to be as close as we please to its equilibrium value. Then using this value of k we may rewrite

(66) as $p_1' - p = h(p_1 - p)$ where

$$h(\pi) = \frac{\alpha pq}{k} + \frac{\alpha m\pi^2}{1-k} + 2\eta[(1-m)k + m]\pi + \tau\eta(1-m)(1-2k)\pi. \tag{70}$$

Since

$$\frac{\partial h}{\partial \pi} = \frac{2\alpha m\pi}{1-k} + \eta\{2[(1-m)k+m] + \tau(1-m)(1-2k)\}, \tag{71}$$

provided that $\pi > 0$, $h(\pi)$ is a monotone increasing function of π. On substitution of $\pi/(1-k) = p_1 - p_2$ into the right-hand side of (71), and using the fact that $2\alpha + 2\eta < 1$, we have $|\partial h/\partial \pi| < 1$.

The equilibria of (70), namely the roots of $p_1 - p = h(p_1 - p)$, solve the quadratic equation $f(\pi) = 0$ where

$$f(\pi) = \frac{\alpha m\pi^2}{1-k} + \{2\eta[(1-m)k+m] + \tau\eta(1-m)(1-2k) - 1\}\pi + \frac{\alpha pq}{k}. \tag{72}$$

Now

$$f(0) = \frac{\alpha pq}{k} > 0.$$

Further

$$f(q) = \frac{\alpha mq^2}{1-k} + q\{2\eta[(1-m)k+m] + \tau\eta(1-m)(1-2k) - 1\} + \frac{\alpha pq}{k}. \tag{73}$$

We claim that $f(q) < 0$. In order to prove this note first that $f(q)/q < 0$ if

$$\frac{\alpha mq}{1-k} + 2\eta\{(1-m)k + m + \tau(1-m)(1-k)\} - 1 + \frac{\alpha p}{k} < 0. \tag{74}$$

On substitution from (9) into (74) the latter becomes

$$\frac{\alpha mq}{1-k} - \frac{\beta + 2\alpha p}{k} + \frac{\alpha p}{k} < 0. \tag{75}$$

Clearly for the truth of (75) it is sufficient that

$$(\beta + \alpha p)(1-k) > \alpha qk,$$

or

$$\beta + \alpha p > (\beta + \alpha)k. \tag{76}$$

In order to prove (76) we return to (65), and show that the valid root $\hat{k}$ of (65) satisfies

$$\hat{k} < \frac{\beta + 2\alpha p}{1 - 2\eta}. \tag{77}$$

If (77) is true, then it is sufficient for (76) that $(\beta + \alpha p)(1-2\eta) > (\beta + \alpha)(\beta + 2\alpha p)$. But $(1-2\eta) > \beta + 2\alpha$, and

$$(\beta + \alpha p)(\beta + 2\alpha) - (\beta + \alpha)(\beta + 2\alpha p) = \alpha\beta q > 0.$$

It remains to prove (77). The quadratic (65) is positive at $k = 0$ and negative at $k = 1$. We show that it is also negative at $k = (\beta + 2\alpha p)/(1 - 2\eta)$. Substitute $k = (\beta + 2\alpha p)/(1-2\eta)$ into the left side of (65) to obtain

$$\beta + 2\alpha p + \frac{\beta + 2\alpha p}{1-2\eta}[2\tau\eta + 2\eta m(1-\tau) - 1] + \frac{(\beta + 2\alpha p)^2}{(1-2\eta)^2} 2\eta(1-m)(1-\tau) = 2\eta\frac{\beta + 2\alpha p}{1-2\eta}\left\{\left[\frac{\beta + 2\alpha p}{1-2\eta} - 1\right](1-m)(1-\tau)\right\}. \tag{78}$$

But $1 - 2\eta > \beta + 2\alpha > \beta + 2\alpha p$ so that (78) is negative. Together with the fact that the quadratic (65) is negative at $k = 1$ this shows that the valid root of (65) is less than $(\beta + 2\alpha p)/(1-2\eta)$. This concludes the proof that $f(q) < 0$.

Since $f(0) > 0$ and $f(q) < 0$ there is a unique valid equilibrium, $\hat{p}_1$, of (70). Since $|\partial p_1'/\partial p_1| < 1$ this root must be globally stable. This completes the proof of convergence to valid roots of (16) and (17).

Appendix 2. Covariances

$$\begin{aligned}
&\mathrm{Cov}(\mathrm{DZT}) + (k)^2 \\
&= \mu_1\left\{\alpha_1^2\left(p_1 - \frac{u_2}{4k}\right)^2 + 2\alpha_2^2\left[\left(p_1 - \frac{u_2}{4k}\right)\left(q_1 - \frac{u_2}{4k}\right) + \frac{u_2^2}{16k^2}\right]\right. \\
&\quad + \alpha_3^2\left(q_1 - \frac{u_2}{4k}\right)^2 + \alpha_2\frac{u_2}{k}\left[\alpha_1\left(p_1 - \frac{u_2}{4k}\right) + \alpha_3\left(q_1 - \frac{u_2}{4k}\right)\right] + \alpha_1\alpha_3\frac{u_2^2}{8k^2}\Big\} \\
&\quad + \mu_2\left\{(\beta_1^2 + \gamma_1^2)\left(p_1 - \frac{u_2}{4k}\right)\left(p_2 - \frac{v_2}{4(1-k)}\right)\right. \\
&\quad + (\beta_3^2 + \gamma_3^2)\left(q_1 - \frac{u_2}{4k}\right)\left(q_2 - \frac{v_2}{4(1-k)}\right) + (\beta_2^2 + \gamma_2^2) \\
&\quad \times\left[\left(p_1 - \frac{u_2}{4k}\right)\left(q_2 - \frac{v_2}{4(1-k)}\right) + \left(p_2 - \frac{v_2}{4(1-k)}\right)\left(q_1 - \frac{u_2}{4k}\right) + \frac{u_2v_2}{8k(1-k)}\right] \\
&\quad + \left(\frac{\beta_1\beta_2 + \gamma_1\gamma_2}{2}\right)\left[\frac{u_2}{k}\left(p_2 - \frac{v_2}{4(1-k)}\right) + \frac{v_2}{1-k}\left(p_1 - \frac{u_2}{4k}\right)\right] \\
&\quad + (\beta_1\beta_3 + \gamma_1\gamma_3)\frac{u_2v_2}{8k(1-k)} + \left(\frac{\beta_3\beta_2 + \gamma_3\gamma_2}{2}\right) \\
&\quad \times\left.\left[\frac{u_2}{k}\left(q_2 - \frac{v_2}{4(1-k)}\right) + \frac{v_2}{1-k}\left(q_1 - \frac{u_2}{4k}\right)\right]\right\} + \mu_4\left\{\delta_1^2\left(p_2 - \frac{v_2}{4(1-k)}\right)^2\right. \\
&\quad + 2\delta_2^2\left[\left(p_2 - \frac{v_2}{4(1-k)}\right)\left(q_2 - \frac{v_2}{4(1-k)}\right) + \frac{v_2^2}{16(1-k)^2}\right] \\
&\quad + \delta_3^2\left(q_2 - \frac{v_2}{4(1-k)}\right)^2 + \frac{\delta_2v_2}{1-k}\left[\delta_1\left(p_2 - \frac{v_2}{4(1-k)}\right) + \delta_3\left(q_2 - \frac{v_2}{4(1-k)}\right)\right] \\
&\quad + \delta_1\delta_3\frac{v_2^2}{8(1-k)^2}\Big\}.
\end{aligned} \tag{79}$$

$$\begin{aligned}
&\mathrm{Cov}(\mathrm{OPT}) + (\text{mean Parent})\ (\text{mean Offspring}) \\
&\quad = \mathrm{Cov}(\mathrm{OPT}) + k^2 \\
&\quad = \mu_1(\alpha_1p_1^2 + \alpha_3q_1^2 + 2\alpha_2p_1q_1) + \mu_2\left[p_1p_2\left(\frac{\beta_1 + \gamma_1}{2}\right)\right. \\
&\quad + \left.q_1q_2\left(\frac{\beta_3 + \gamma_3}{2}\right) + (p_1q_2 + p_2q_1)\left(\frac{\beta_2 + \gamma_2}{2}\right)\right].
\end{aligned} \tag{80}$$

Formula (80) gives the standard midparent–offspring covariance.

Covariance between biological sibs raised in randomly chosen adoptive families

Cov(SSA)

$$
\begin{aligned}
&= \left\{\left[(u_1+v_1)+\frac{1}{4}(u_2+v_2)\right]^2(1-m)+\left(u_1+\frac{1}{4}u_2\right)^2\frac{m}{k}\right.\\
&\quad\left.+\left(v_1+\frac{1}{4}v_2\right)^2\frac{m}{1-k}\right\}M_1^2\\
&+\left\{(u_2+v_2)\left[(u_1+v_1)+\frac{1}{4}(u_2+v_2)\right](1-m)\right.\\
&\quad\left.+u_2\left(u_1+\frac{1}{4}u_2\right)\frac{m}{k}+v_2\left(v_1+\frac{1}{4}v_2\right)\frac{m}{1-k}\right\}M_1M_2\\
&+\left\{\frac{1}{8}(u_2+v_2)^2(1-m)+\frac{1}{8}\left[u_2^2\frac{m}{k}+v_2^2\frac{m}{1-k}\right]\right\}M_1M_3\\
&+\left\{\left[(u_1+v_1)+\frac{1}{2}(u_2+v_2)\right]\left[(u_3+v_3)+\frac{1}{2}(u_2+v_2)\right](1-m)\right.\\
&\quad+(u_1+v_1)(u_3+v_3)(1-m)+u_1u_3\frac{m}{k}+\left(u_1+\frac{1}{2}u_2\right)\left(u_3+\frac{1}{2}u_2\right)\frac{m}{k}\\
&\quad\left.+v_1v_3\frac{m}{1-k}+\left(v_1+\frac{1}{2}v_2\right)\left(v_3+\frac{1}{2}v_2\right)\frac{m}{1-k}\right\}M_2^2\\
&+\left\{(u_2+v_2)\left[(u_3+v_3)+\frac{1}{4}(u_2+v_2)\right](1-m)+u_2\left(u_3+\frac{1}{4}u_2\right)\frac{m}{k}\right.\\
&\quad\left.+v_2\left(v_3+\frac{1}{4}v_2\right)\frac{m}{1-k}\right\}M_2M_3\\
&+\left\{\left[(u_3+v_3)+\frac{1}{4}(u_2+v_2)\right]^2(1-m)+\left(u_3+\frac{1}{4}u_2\right)^2\frac{m}{k}\right.\\
&\quad\left.+\left(v_3+\frac{1}{4}v_2\right)^2\frac{m}{1-k}\right\}M_3^2-\mu_A^2. \qquad (81)
\end{aligned}
$$

$$\mathrm{Cov(SAA)} = \mu_1 z_1^2+\mu_2 z_2^2+\mu_3 z_3^2+\mu_4 z_4^2-\mu_A^2, \qquad (82)$$

where M_i and z_i are given following Equations (35) and (37), respectively

Covariance between natural sib and foster sib raised by the biological parents of one is

$$
\begin{aligned}
\mathrm{Cov(SAB)} &= z_1\mu_1[p_1^2\alpha_1+2p_1q_1\alpha_2+q_1^2\alpha_3]\\
&\quad+z_2\mu_2[p_1p_2\beta_1+(p_1q_2+q_1p_2)\beta_2+q_1q_2\beta_3]\\
&\quad+z_3\mu_3[p_1p_2\gamma_1+(p_1q_2+q_1p_2)\gamma_2+q_1q_2\gamma_3]\\
&\quad+z_4\mu_4[p_2^2\delta_1+2p_2q_2\delta_2+q_2^2\delta_3]-\mu_A k. \qquad (83)
\end{aligned}
$$

Appendix 3. When $\beta=\eta=0, \sigma=1, 2r_{OPT}/(1+m) = V_A/k(1-k)$

The total phenotypic variance is $k(1-k)$ so that $V_A/k(1-k)$ is the usual "narrow sense" heritability. When $\eta=0$ we have from (46)

$$\mathrm{Cov}(OPT) = \alpha k(1-k)(1+m)(p_1-p_2), \qquad (84)$$

so that

$$2r_{OPT}/(1+m) = 2\alpha(p_1-p_2). \qquad (85)$$

From (13) and (67) at equilibrium with $\eta=0$

$$(1-k)(p_1-p_2) = \frac{\alpha pq}{k}+\alpha m(1-k)(p_1-p_2)^2,$$

so that

$$
\begin{aligned}
k(1-k)(p_1-p_2) &= \alpha pq\left[1+\frac{mk(1-k)(p_1-p_2)^2}{pq}\right] \qquad (86)\\
&= \alpha pq(1+F).
\end{aligned}
$$

Now we can rewrite (30) as

$$\frac{V_A}{k(1-k)} = \frac{2k(1-k)(p_1-p_2)^2}{pq(1+F)}.$$

Therefore to prove our result we must show

$$2\alpha(p_1-p_2) = \frac{2k(1-k)(p_1-p_2)^2}{pq(1+F)}$$

or

$$\alpha pq = \frac{k(1-k)(p_1-p_2)}{(1+F)}, \qquad (87)$$

which is true by (86).