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Evolutionary effects of contagious and familial transmission

(genetics/epidemics/population dynamics/polymorphism/cultural transmission)

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ABSTRACT **Two models involving non-Mendelian transmission of a discrete valued trait through within- and across-generation contagion are proposed in an investigation of the joint evolution of phenotype and genotype. A single locus with two alleles determines susceptibility to contagion. The incorporation of within-generation contagious transmission extends the parameter ranges allowing phenotypic polymorphism and introduces a new phenotypic equilibrium configuration. The latter is characterized by a threshold in the initial value of the trait which determines whether the trait can increase. Phenotypic evolution is accelerated by within-generation contagion, but the rate of genetic evolution is retarded relative to that under uniparental transmission across generations. The second model studied allows the trait to be acquired, at genotype-dependent rates, even if the transmitting parent does not have the trait. Both the pattern of phenotypic transmission and the selection on the trait influence the course of evolution. Some important aspects of the structure of the one locus–two allele model are shown to be preserved with more alleles. At equilibrium, the leading eigenvalue of the transmission-selection matrix assumes the role of genotypic fitness.**

Natural selection acts on phenotypes and indirectly affects genes contributing to them. The effects of such genes on a phenotype are direct or due to interaction with environmental influences. In either case a complete description of the evolutionary process requires knowledge of the joint population distribution of phenotypes and genotypes. Investigations dealing with continuously varying phenotypes include refs. 1–6. The evolutionary theory of discretely valued phenotypes under genetic influence is less well developed. Watson (7) and Uyenoyama and Feldman (8) have analyzed models of the cytoplasmic sex-ratio system in *Drosophila*, while Feldman and Cavalli-Sforza (9) introduced a general uniparental transmission scheme for two phenotypes at one diallelic locus.

In ref. 9 we considered a dichotomous trait that was transmitted exclusively from parent to child by contagion (for an infectious disease) or by teaching/learning (for a skill, custom, etc.). The rate of acquisition was a function of the child's genotype at a single diallelic locus. In the present paper we add another type of contagious transmission between members of the same generation at rates dependent on the same locus. In analogy with epidemiological terminology, such transmission is termed *horizontal* to contrast it with the contagious phenotypic transmission from parent to child, which is called *vertical*. As in ref. 9, vertical transmission is uniparental. A new generalization of our analysis of vertical transmission is presented in the second part of the paper. We use contagious to be synonymous with horizontal and familial to be synonymous with vertical transmission in the rest of the paper.

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Contagious vertical and horizontal transmission

The phenotype of an individual is described by 1 if the individual possesses the trait and 0 if it is absent. For brevity, "the phenotype" will mean the presence of the trait value 1. Individuals may acquire the phenotype through familial transmission from the transmitting parent who has the phenotype or through contact with randomly encountered members of the same offspring generation who have the phenotype. Two alleles A and a with frequencies p and $q = 1 - p$, respectively, segregate at an autosomal locus. If the transmitting parent possesses the trait, offspring of genotype AA acquire it with probability ν_1 (note that ν_1 here is equivalent to $1 - N_1$ in ref. 9). The proportion of AA individuals who have the trait is k_1, a variable whose value will change from generation to generation. The corresponding quantities for Aa and aa are ν_2 and k_2 and ν_3 and k_3, respectively. After this uniparental transmission, the offspring randomly encounter one another. An encounter between *any* individual with the phenotype and one of genotype AA who does not have it results in contagious transmission to the latter with probability h_1. For offspring of genotypes Aa and aa, the corresponding probabilities are h_2 and h_3, respectively. Selection occurs after all transmission is complete. Individuals with the phenotype have fitness $1 + s$ $(-1 \leq s)$ relative to those without it, irrespective of genotypes.

Following the assumptions of ref. 9, p, k_1, k_2, and k_3 characterize the parental generation censused after both stages of transmission and before selection occurs. After random mating and vertical transmission, but before contagious transmission, the variables assume the following values:

$$p' = \frac{p(1 + sK_1)}{1 + sK} \qquad [1a]$$

$$k_1^* = \frac{K_1\nu_1(1 + s)}{1 + sK_1} \qquad [1b]$$

$$k_2^* = (1/2)\nu_2(1 + s)\left[\frac{K_1}{1 + sK_1} + \frac{K_2}{1 + sK_2}\right] \qquad [1c]$$

$$k_3^* = \frac{K_2\nu_3(1 + s)}{1 + sK_2} \qquad [1d]$$

in which $K_1 = pk_1 + qk_2$, $K_2 = pk_2 + qk_3$, and $K = pK_1 + qK_2$. Asterisks indicate that the variables are observed before contagious transmission. At this stage, random (mass action) encounters occur, resulting in contagious transmission of the trait such that

$$k_i' = k_i^* + (1 - k_i^*)h_iK^*, \qquad [2]$$

in which

$$K^* = (p')^2k_1^* + 2p'q'k_2^* + (q')^2k_3^* \qquad [3]$$

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and the gene frequency, p', is unaltered by the horizontal transmission.

From Eq. **1a** the equilibria fall into one of the following categories according to the gene frequency: (*i*) $p = 0$, (*ii*) $p = 1$, or (*iii*) $p = \hat{p} = (\hat{k}_2 - \hat{k}_3)/(2\hat{k}_2 - \hat{k}_1 - \hat{k}_3)$. The existence and stability conditions for the $p = 0$ fixation equilibrium will be examined in detail. Analogous results for $p = 1$ may be obtained by substituting ν_1 for ν_3 and h_1 for h_3. The polymorphic equilibrium $p = \hat{p}$ will be examined in detail in the cases for which all N_i are equal or all h_i are equal.

Fixation Equilibrium $p = 0$. At the $p = 0$ boundary, $\hat{K} = \hat{K}_2 = \hat{k}_3$ so that, from Eq. **1d**, either $\hat{K} = 0$ or $\hat{K}$ corresponds to the valid roots ($0 \leq \hat{K} \leq 1$) of the quadratic equation

$$E_0(K) = s^2K^2 + K\{2s - \nu_3(1 + s)[s(1 + h_3) - h_3\nu_3(1 + s)]\} + 1 - \nu_3(1 + h_3)(1 + s) = 0. \quad [4]$$

The $\hat{K} = 0$ equilibrium is denoted the *Type 0* equilibrium. A *Type I* equilibrium corresponds to the root of Eq. **4** when exactly one root is valid. If two roots of Eq. **4** are valid, they are called *Type II* equilibria.

Type 0 Equilibrium Class. The equilibrium value of K_1 (namely, $\hat{K}_1 = \hat{k}_2$) assumes one of the following values:

$$(i)\ \hat{K}_1 = 0 \text{ or } (ii)\ \hat{K}_1 = [\nu_2(1 + s)(1/2) - 1]/s. \quad [5]$$

The second of these is valid if

$$\nu_2(1 + s) > 2, \quad [6]$$

but is unstable whenever it exists. From Eq. **1a**, the Type 0 equilibrium with $\hat{K} = \hat{K}_1 = 0$ corresponds to a neutral curve of equilibria (which we denoted $S^{(n)}$ in ref. 9) parametrized by the values of p. The point $p = \hat{K} = \hat{K}_1 = 0$ is neutrally stable at best and is unstable if either [**6**] holds or if the following inequality is true:

$$\nu_3(1 + s)(1 + h_3) > 1. \quad [7]$$

Type I Equilibrium Class. A single valid root of Eqs. **5** exists and is stable within the $p = 0$ plane if [**7**] is satisfied; i.e., if the $\hat{K} = 0$ point is unstable within the $p = 0$ plane. From Eq. **2**, at equilibrium the value for $\hat{K}_1 = \hat{k}_2$ is determined uniquely as the valid root of the quadratic equation

$$K_1 = \frac{\nu_2(1 + s)}{2}[K_1/(1 + sK_1) + \hat{K}/(1 + s\hat{K})]\left(1 - \frac{h_2\nu_3(1 + s)\hat{K}}{1 + s\hat{K}}\right) + h_2\nu_3(1 + s)\hat{K}/(1 + s\hat{K}), \quad [8]$$

in which $\hat{K}$ is the valid root of Eq. **4**. Feldman and Cavalli-Sforza (9) found that a phenotype under strictly vertical transmission is maintained only if the trait is sufficiently advantageous to its carriers (i.e., s large enough). The incorporation of contagion within generations, represented by h_i here, allows the stable maintenance of even a deleterious phenotype ($s < 0$) provided [**7**] holds. Near the Type I equilibrium, the A allele fails to increase when rare if

$$s\left[\nu_3 - \nu_2 + \nu_3(h_3 - h_2) + \frac{\nu_3(1 + s)\hat{K}(\nu_2h_2 - \nu_3h_3)}{1 + s\hat{K}}\right] > 0, \quad [9]$$

in which $\hat{K}$ is the valid root of Eq. **4**. This reduces to

$$(i)\ s(\nu_3 - \nu_2) > 0 \text{ or } (ii)\ s(h_3 - h_2) > 0 \quad [10]$$

in the special cases for which all h_i are equal or all ν_i are equal, respectively.

Type II Equilibrium Class. These two roots of Eq. **4** come into existence when [**7**], the existence condition for the Type I equilibrium, is violated and the following conditions are met:

$$\nu_3 > (1 + h_3)/(1 + h_3 + h_3^2) \quad [11a]$$

and

$$(1 + s) > (1 + s^*), \quad [11b]$$

in which $(1 + s^*)$ is the larger root of the quadratic equation

$$g_0(1 + s) = (1 + s)^2(1 + h_3 - h_3\nu_3) + 2(1 + s)[2h_3 - (1 + h_3)(1 + h_3 - h_3\nu_3)] + (1 - h_3)^2 = 0. \quad [12]$$

From [**7**] and [**11a**], Type II equilibria arise only if the phenotype is deleterious ($s < 0$) and is transmitted vertically at a sufficiently high rate. The equilibrium value of $\hat{K}_1 = \hat{K}_2$ corresponding to each Type II root is equal to the valid root of Eq. **8** in which, in Eq. **8**, $\hat{K}$ is the appropriate Type II root. As with a Type I root, at Type II equilibria the $p = 0$ plane is stable to the introduction of the A allele if [**9**] is satisfied. Within the $p = 0$ plane, the equilibrium associated with the larger root of Eq. **4** is stable and that associated with the smaller root is unstable. The smaller Type II root represents a threshold in the sense that traits that are introduced in frequencies below threshold rapidly decline. Because [**11**] requires that the contagious transmission rate h_3 be sufficiently large (for fixed ν_3), the Type II equilibria were termed "epidemiological" by Uyenoyama and Feldman (8) in their consideration of the infectious cytoplasmic sex-ratio condition.

Polymorphic Equilibrium ($p = \hat{p}$). From the fact that $\hat{p} = (\hat{k}_2 - \hat{k}_3)/(2\hat{k}_2 - \hat{k}_1 - \hat{k}_3)$, so that the equilibrium value $\hat{K} = (\hat{k}_2^2 - \hat{k}_1\hat{k}_3)/(2\hat{k}_2 - \hat{k}_1 - \hat{k}_3)$, it is possible to derive an equilibrium ninth-order polynomial for p. The high degree is due to variation in both ν_i and h_i simultaneously. The properties of this equilibrium polynomial will be reported elsewhere. Here we consider the two cases (I) $\nu_i = \nu$, h_i varying, and (II) ν_i varying, $h_i = h$. In these cases, apart from the Type 0 equilibrium $\hat{K} = \hat{K}_1 = \hat{K}_2 = 0$, within the $p = \hat{p}$ plane the equilibrium values are the roots of the quadratic

$$sK^2 + K\{2s - \nu(1 + s)[s(1 + \bar{h}) - \bar{h}\nu(1 + s)]\} + 1 - \nu(1 + \bar{h})(1 + s) = 0 \quad [13]$$

in Case I and of

$$s^2K^2 + K\{2s - \bar{\nu}(1 + s)[s(1 + h) - h\bar{\nu}(1 + s)]\} + 1 - \bar{\nu}(1 + h)(1 + s) = 0 \quad [14]$$

in Case II, in which $\bar{h} = p^2h_1 + 2pqh_2 + q^2h_3$ and $\bar{\nu} = p^2\nu_1 + 2pq\nu_2 + q^2\nu_3$. In Case I, $\hat{p} = (h_2 - h_3)/(2h_2 - h_1 - h_3)$ and in Case II $\hat{p} = (\nu_2 - \nu_3)/(2\nu_2 - \nu_1 - \nu_3)$. In both cases, the Type 0 equilibrium is neutrally stable at best and is unstable if

$$(i)\ \nu(1 + s)(1 + \bar{h}) > 1 \text{ or } (ii)\ \bar{\nu}(1 + s)(1 + h) > 1 \quad [15]$$

in Case I or Case II, respectively. The single Type I equilibrium comes into existence and is stable if the appropriate inequality in [**15**] is satisfied. When this inequality fails, then Type II equilibria exist provided that conditions identical to [**11**] hold with ν substituted for ν_3 and $\bar{h}$ for h_3 in Case I and $\bar{\nu}$ substituted for ν_3 with h for h_3 in Case II. As was true at the gene frequency fixation, the larger Type II root is stable and the smaller root is unstable. The conditions that the gene frequency polymorphism plane $p = \hat{p}$ be stable are that at equilibrium

$$\text{Case I: } s(h_2 - \bar{h}) > 0; \text{ Case II: } s(\nu_2 - \bar{\nu}) > 0. \quad [16]$$

Vertical and extrafamilial transmission

In this section the genotypes AA, Aa, and aa determine the probability that an individual will acquire the phenotype both from its transmitting parent who has the phenotype and from other sources when the transmitting parent does not have the

phenotype. In the latter case, the transmission is like that from a constant background source and in this sense is extrafamilial. (It might also be considered as genotype-dependent mutation or migration from an external source.) An individual is denoted 1 if the phenotype is present and by 0 if it is absent. As before, individuals of phenotype 1 have fitness $1 + s$ relative to individuals of phenotype 0. Individuals of genotype AA can be characterized by a transmission matrix A:

$$\mathrm{A} = \begin{pmatrix} a_{11} & a_{10} \\ a_{01} & a_{00} \end{pmatrix}, \qquad [17]$$

in which a_{ij} is the probability that an offspring of genotype AA has phenotype i, given that the transmitting parent has phenotype j, with $\Sigma_i a_{ij} = 1$ for $j = 1, 0$. Analogous transmission matrices B and C are associated with genotypes Aa and aa, respectively. There is no contagious transfer among members of the same generation. The variables p, K_1, and K_2, as defined earlier, are measured in the parental generation before selection occurs. After selection, random mating, and transmission according to A, B, and C, the variables assume the following values:

$$p' = \frac{p(1 + sK_1)}{1 + sK} \qquad [18]$$

$$K_1' = \frac{p[a_{10}(1 - K_1) + a_{11}(1 + s)K_1]}{1 + sK} + (q/2)\left\{\frac{[b_{10}(1 - K_1) + b_{11}(1 + s)K_1]}{1 + sK}\frac{(1 + sK_2)}{(1 + sK_1)} + \frac{b_{10}(1 - K_2) + b_{11}(1 + s)K_2}{1 + sK}\right\} \qquad [19]$$

$$K_2' = (p/2)\left\{\frac{b_{10}(1 - K_1) + b_{11}(1 + s)K_1}{1 + sK} + \frac{[b_{10}(1 - K_2) + b_{11}(1 + s)K_2]}{1 + sK}\frac{(1 + sK_1)}{(1 + sK_2)}\right\} + \frac{q[c_{10}(1 - K_2) + c_{11}(1 + s)K_2]}{1 + sK}. \qquad [20]$$

Eqs. **18–20** are identical to those given by Feldman and Cavalli-Sforza (9) for the general uniparental transmission and selection scheme under the following identifications:

$$N_1 = a_{01} \qquad n_1 = a_{00}$$
$$N_2 = b_{01} \qquad n_2 = b_{00}$$
$$N_3 = c_{01} \qquad n_3 = c_{00}$$
$$s_1 = s_2 = s_3 = s \qquad t_1 = t_2 = t_3 = 0.$$

Fixation Equilibrium ($p = 0$). Eq. **20** at equilibrium may be written in the following form for $p = 0$:

$$w_C \begin{pmatrix} \hat{K}_2 \\ 1 - \hat{K}_2 \end{pmatrix} = \begin{pmatrix} c_{11}(1 + s) & c_{10} \\ c_{01}(1 + s) & c_{00} \end{pmatrix} \begin{pmatrix} \hat{K}_2 \\ 1 - \hat{K}_2 \end{pmatrix}, \qquad [21]$$

in which $w_C = 1 + s\hat{K}$ and $\hat{K} = \hat{K}_2$. From Eq. **21** it is clear that the equilibrium vector $(\hat{K}_2, 1 - \hat{K}_2)$ is an eigenvector of the matrix shown. When all $c_{ij} > 0$, the Frobenius theorem for irreducible matrices (ref. 10, p. 53) indicates that the largest eigenvalue of the matrix is positive and it is associated with a non-negative eigenvector. Further, the eigenvector associated with the maximal eigenvalue is the only non-negative eigenvector of the matrix (ref. 10, p. 63). In terms of Eq. **21**, the mean fitness w_C is equal to the maximal eigenvalue of the matrix in Eq. **21** and the equilibrium value for $\hat{K}_2$, which is obtained from the eigenvector associated with the maximal eigenvalue, is valid and unique. Thus w_C is equal to the larger root of the following quadratic:

$$f_C(w) = w^2 - w[c_{11}(1 + s) + c_{00}] + (1 + s)(c_{11}c_{00} - c_{10}c_{01}) = 0. \qquad [22]$$

The definition of $(\hat{K}_2, 1 - \hat{K}_2)$ as the eigenvector associated with the maximal eigenvalue specifies the equilibrium value of $\hat{K}_2$ up to a multiplicative constant. This constant is determined by the constraint $\hat{K}_2 + (1 - \hat{K}_2) = 1$. In addition, the equilibrium vector must also be consistent with the definition of $w_C = 1 + s\hat{K}_2$. One can show that the two constraints are satisfied by the same vector by multiplying Eq. **21** on the left by (1, 1). The equilibrium value for $\hat{K}_2$ obtained from Eq. **21** is given by

$$K_2 = \frac{c_{10}}{w_C - c_{11}(1 + s) + c_{10}}. \qquad [23]$$

Feldman and Cavalli-Sforza (9) considered the case $a_{00} = b_{00} = c_{00} = 1$, which corresponds to substitution of the following reducible matrix in Eq. **21**:

$$\begin{pmatrix} c_{11}(1 + s) & 0 \\ c_{01}(1 + s) & 1 \end{pmatrix}.$$

In this case, two linearly independent non-negative eigenvectors exist for which $K_2 = 0$ and $\hat{K}_2 = [c_{11}(1 + s) - 1]/s$. Complete existence and stability conditions for this case were given by Feldman and Cavalli-Sforza (9). The remainder of the analysis will be presented under the assumption that A, B, and C are irreducible matrices.

At equilibrium Eq. **19** may be written as follows:

$$(2w_1\mathrm{I} - \mathrm{B})\begin{pmatrix} \hat{K}_1 \\ 1 - \hat{K}_1 \end{pmatrix} = \frac{w_1}{w_C}\mathrm{B}\begin{pmatrix} \hat{K}_2 \\ 1 - \hat{K}_2 \end{pmatrix}, \qquad [24]$$

in which $w_1 = 1 + s\hat{K}_1$ and I is the identity matrix. The vector $(\hat{K}_2, 1 - \hat{K}_2)$ is known from Eq. **23**, and $(\hat{K}_1, 1 - \hat{K}_1)$ may be found from Eq. **24** in terms of w_1 from Cramer's rule. The value of w_1, determined under the constraint that $\hat{K}_1 + (1 - \hat{K}_1) = 1$, is given by the larger root of the following quadratic:

$$2w_C f_B(w) + (1 + s)(b_{11} + b_{00} - 1)(w - w_C) = 0,$$

in which $f_B(w)$ is a quadratic similar to Eq. **22** involving the elements of B. As before, multiplication of Eq. **24** on the left by (1, 1) indicates that the two constraints $\hat{K}_1 + (1 - \hat{K}_1) = 1$ and $w_1 = 1 + s\hat{K}_1$ are satisfied by the same vector. The equilibrium value for $\hat{K}_1$ is unique and is given by

$$\hat{K}_1 = w_1\{[b_{11}(1 + s)\hat{K}_2 + b_{10}(1 - \hat{K}_2)](2w_1 - b_{00}) + b_{10}[b_{01}(1 + s)\hat{K}_2 + b_{00}(1 - \hat{K}_2)]\}\Delta^{-1}, \qquad [25]$$

in which

$$\Delta = \{w_C[2w_1 - b_{11}(1 + s)](2w_1 - b_{00}) - w_C(1 + s)b_{10}b_{01}\}.$$

The equilibrium defined by $p = 0$ and Eqs. **23** and **25** is always valid and is stable only if

$$w_C > w_B, \qquad [26]$$

in which w_B is the larger root of $f_B(w)$. By symmetry, a unique equilibrium exists at the $p = 1$ boundary and this equilibrium is stable only if

$$w_A > w_B. \qquad [27]$$

Internal Equilibrium. From Eq. **17**, $\hat{K}_1 = \hat{K}_2 = \hat{K}$ for all interior equilibria. Eqs. **19** and **20** may therefore be represented as follows:

$$\bar{w}\begin{pmatrix} \hat{K} \\ 1 - \hat{K} \end{pmatrix} = (p\mathrm{A} + q\mathrm{B})\begin{pmatrix} (1 + s) & 0 \\ 0 & 1 \end{pmatrix}\begin{pmatrix} \hat{K} \\ 1 - \hat{K} \end{pmatrix} \qquad [28]$$

$$\bar{w}\begin{pmatrix} \hat{K} \\ 1 - \hat{K} \end{pmatrix} = (p\mathrm{B} + q\mathrm{C})\begin{pmatrix} (1 + s) & 0 \\ 0 & 1 \end{pmatrix}\begin{pmatrix} \hat{K} \\ 1 - \hat{K} \end{pmatrix}, \qquad [29]$$

in which $\bar{w} = 1 + s\hat{K}$. The equilibrium value(s) of p is determined such that the mean fitness $\bar{w}$ corresponds to the largest eigenvalue of both matrices above. This condition leads to the following expression for $\hat{p}$:

$$\hat{p} = \frac{f_C(\bar{w}) - f_B(\bar{w})}{f_A(\bar{w}) + f_C(\bar{w}) - 2f_B(\bar{w})}, \quad [30]$$

in which $f_A(w)$, $f_B(w)$, and $f_C(w)$ are quadratics similar to Eq. **22.** The equilibrium mean fitness $\bar{w}$ is a root of the following cubic:

$$[f_B(w)]^2 - f_A(w)f_C(w) = 0. \quad [31]$$

For validity of $\hat{p}$ given by Eq. **30,** $\bar{w}$ must lie in one of the following ranges:

$$w_B > \bar{w} > w_A, w_C \quad [32a]$$

$$w_A, w_C > \bar{w} > w_B. \quad [32b]$$

Under the conditions in [**32**], a single valid root for Eq. **31** exists. As before, the equilibrium vector $(\hat{K}, 1 - \hat{K})$ is determined as an eigenvector of Eq. **28** or **29**. Therefore, a unique equilibrium with gene frequency $\hat{p}$ given by Eq. **30** comes into existence only if both stability conditions [**26**] and [**27**] for the boundary equilibria are satisfied or both conditions are violated. If [**32b**] holds, then the interior equilibrium is unstable and both boundary equilibria are stable. Condition [**32a**] ensures that both boundary equilibria are unstable and represents a necessary condition for stability of the interior equilibrium [**30**]. Although the local stability of the interior equilibrium under condition [**32a**] has eluded analysis, the considerations above suggest that the interior equilibrium is locally stable when [**32b**] holds.

Multiple Alleles. For multiple alleles at the susceptibility locus, the leading eigenvalue of the transmission-selection matrix retains its role as the two-dimensional analogue of genotypic fitness. The recursion equations for the n-allele case are given by:

$$p_i' = \frac{(1 + sK_i)p_i}{(1 + sK)} \qquad i = 1, 2, \ldots, n$$

$$K_i' = \frac{p_i[t_{11}^{(ii)}(1 + s)K_i + t_{10}^{(ii)}(1 - K_i)]}{1 + sK} + \sum_{j \neq i} p_j \left\{ \frac{t_{11}^{(ij)}(1 + s)K_j + t_{10}^{(ij)}(1 - K_j)}{1 + sK} + \frac{[t_{11}^{(ij)}(1 + s)K_i + t_{10}^{(ij)}(1 - K_i)](1 + sK_j)}{(1 + sK)(1 + sK_i)} \right\} / 2,$$

in which p_i is the frequency of the ith allele A_i and $T^{(ij)}$ is the transmission matrix for A_iA_j given by:

$$T^{(ij)} = \begin{pmatrix} t_{11}^{(ij)} & t_{10}^{(ij)} \\ t_{01}^{(ij)} & t_{00}^{(ij)} \end{pmatrix}.$$

For the two-allele case presented earlier, $T^{(11)} = A$, $T^{(12)} = B$, and $T^{(22)} = C$. K_i is the phenotypic marginal for the ith allele defined by

$$K_i = \sum_j p_j k^{(ij)},$$

in which $k^{(ij)}$ is the proportion of individuals of genotype A_iA_j that bear the trait.

In traditional one-locus, multiple-allele models with constant fitness parameters, the conditions for external stability to the introduction of $n - l$ new alleles of an internally stable equilibrium involving l alleles are

$$\bar{w} > \sum_{i-1}^{l} \sigma_{im} p_i \qquad m = l + 1, l + 2, \ldots, n,$$

in which $\sigma_{im} = \sigma_{mi}$ is the fitness of A_iA_m and $\bar{w}$ is the mean fitness associated with the stable equilibrium involving the original alleles $p_1, p_2, \ldots, p_l$ (11). It can be shown that the analogous condition for the multiple allele version of the nonfamilial learning model is given by

$$\bar{w} > w_m \qquad m = l + 1, l + s, \ldots, n,$$

in which w_m is the leading eigenvalue of the following combination of transmission-selection matrices:

$$\sum_{i=1}^{l} p_i T^{(im)}.$$

DISCUSSION

The phenotypic equilibria reflect the pressures of familial and contagious transmission and natural selection which distinguishes only between phenotypes. If the trait is efficiently transmitted among individuals between generations and if the trait does not greatly detract from the fitness of its carriers, then Type I equilibria, which are characterized by stable nonzero frequencies of the trait, are attained. Type I equilibria are descendants of the phenotypic equilibria found by Feldman and Cavalli-Sforza (9). Incorporation of the contagious transmission parameter h increases the range of phenotypes that may be maintained to include even deleterious traits. If the trait is severely disadvantageous or transmitted only at a low rate within and between generations, the trait is eliminated from the population, which reverts to the neutral Type 0 state. For moderately deleterious traits that are highly contagious, a balance is struck between the forces of removal and contagious spread, resulting in the threshold behavior associated with the Type II equilibria.

It is the dynamic behavior near Type I equilibria rather than that near Type II equilibria that is analogous to the threshold behavior often observed in epidemiological disease models. In the simplest deterministic epidemic models (see, e.g., ref. 12), differential equations such as the following describe the change in numbers of diseased individuals caused by removal of infected individuals and contagious spread to susceptible individuals:

$$dy/dt = (\beta x - \gamma)y, \quad [33]$$

in which y is the number of infected individuals, x is the number of susceptible individuals, β is the contact rate parameter representing the contagiousness of the disease, and γ is the removal rate. For initial increase of the disease ($dy/dt > 0$), the number of susceptible individuals must be sufficiently large:

$$\beta x_0 > \gamma, \quad [34]$$

in which x_0 is the initial number of susceptibles. In analogy with Eq. **33**, when $h_i = h$ and ν_i vary, within the $p = \hat{p}$ plane we have

$$K' - K = \Delta K = \frac{h\bar{\nu}(1 + s)K}{1 + sK}\left[1 - \frac{K\bar{\nu}(1 + s)}{1 + sK}\right] - \left[1 - \frac{\bar{\nu}(1 + s)}{1 + sK}\right]K. \quad [35]$$

For K near 0, condition [**34**] may be written in terms of Eq. **35** as $\bar{\nu}(1 + s)(1 + h) > 1$, which is the existence and stability condition [**15b**] for Type I equilibria. Condition [**15b**] represents a threshold in parameter values at which selection is balanced by phenotypic transmission. Type II threshold behavior involves a threshold in initial frequency of the phenotype (sufficiently *low* frequency of susceptible individuals) and represents a novel

epidemiological feature of the model examined in the present paper.

Within-generation transmission accelerates phenotypic evolution in the population and increases the nonzero equilibrium frequencies of the phenotype, which are given by the Type I and larger Type II root. One way to see this when $h_i = h$ and ν_i vary is to compute the difference in "mean fitness" of the population; namely, $(1 + sK') - (1 + sK)$ over a generation:

$$s(K' - K) = s[hK^*(1 - K^*) + K^* - K]. \quad [36]$$

If $s > 0$, and $\bar{\nu}$ is sufficiently large that $K^* > K$, there is clearly an acceleration of fitness change. With h_i varying and $\nu_i = \nu$, a similar argument works near the polymorphic equilibrium. In contrast to this phenotypic effect, by reducing the phenotypic variance between genotypes (usually called the "genetic" variance), contagious transmission in fact reduces the rate of genetic evolution. The rate of genetic evolution may be represented by the one-generation change in gene frequency from Eq. **1a**:

$$p' - p = spq(K_1 - K_2)/(1 + sK). \quad [37]$$

This relation suggests that the phenotypic marginal difference divided by the mean fitness, $(K_1 - K_2)/(1 + sK)$, controls the rate of change of p. Now from Eqs. **1** and **2** with $h_i = h$, ν_i varying, we have

$$(K_1' - K_2')/(1 + sK') = (K_1^* - K_2^*)(1 - hK^*)/[1 + sK^*(1 + h - hK^*)] \quad [38]$$

so that there is a reduction in the difference after familial transmission, $(K_1^* - K_2^*)/(1 + sK^*)$, due to nonzero h. When h_i vary and $\nu_i = \nu$, the same is true, at least in the neighborhood of the polymorphic gene frequency equilibrium.

Equilibria involving stable nonzero frequencies of the phenotype may be attained for deleterious as well as advantageous traits provided h is sufficiently large. Under such conditions, it can be seen from [**4**] and [**16**] that the underlying genetic configuration evolves in a direction that leads to the increase in mean fitness at equilibrium. A population will therefore evolve increased susceptibility to advantageous traits and increased resistance to deleterious traits such as contagious diseases. Increased resistance leads to elevation of the Type II threshold below which deleterious phenotypes cannot enter the population and also decreases the Type I and Type II frequencies at which the phenotype may be maintained in the population.

In the second model studied here, apart from vertical transmission from an affected transmitting parent, offspring may acquire the phenotype, at genotype-dependent rates, from some other source but in a frequency-independent manner. The results of the present analysis suggest that the phenogenotype will evolve toward higher mean fitness in the population. Transmission matrices such as Eq. **17** describe the pattern of acquisition of the trait for the three genotypes. The transmission matrix associated with a given genotype, together with the selection coefficients for the two phenotypes, specifies a phenotypic equilibrium that would obtain in a population consisting solely of that genotype. The equilibrium mean fitness in such populations corresponds to the leading eigenvalue of the transmission-selection matrix. These eigenvalues, w_A, w_B, and w_C, incorporating both selection and the transmission rules, assume roles analogous to genotypic fitness coefficients in traditional one-locus, two-allele models in which phenotype is strictly determined by genotype. Specifically, an internal genetic equilibrium exists only if $w_B > w_A, w_C$ or $w_B < w_A, w_C$. This internal genetic equilibrium is unique and is given by

$$\hat{p} = \frac{f_C(\bar{w}) - f_B(\bar{w})}{f_A(\bar{w}) + f_C(\bar{w}) - 2f_B(\bar{w})},$$

in which $\bar{w}$ is the mean fitness at equilibrium. In the case considered here, the generalization of the problem from one-dimensional genetic evolution to "two-dimensional" phenogenotypic evolution involves higher order expressions of fitness but preserves the structure of the system, including the maximization of mean fitness at equilibrium.

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