

A stochastic model of gene–culture coevolution suggested by the “culture historical hypothesis” for the evolution of adult lactose absorption in humans

(population genetics/autosomal dominant trait/culturally determined milk use/diffusion equation method)

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ABSTRACT A stochastic model of gene–culture coevolution, suggested by the “culture historical hypothesis” of Simoons and McCracken, is presented. According to this hypothesis, adult lactose absorption, believed to be an autosomal dominant trait, attained a high frequency in some human populations due to the positive selection pressure induced by culturally determined milk use in those populations. Two-dimensional Kolmogorov backward equations with appropriate boundary conditions are derived for the ultimate fixation probability of milk users, of the gene for adult lactose absorption, and of both jointly, and for the average time until fixation of the gene. These boundary value problems are solved numerically by the Gauss–Seidel method. I define a theoretical measure of the correlation between gene and culture in terms of the three ultimate fixation probabilities. Monte Carlo simulations are conducted to check and extend the numerical results and also to obtain the first arrival time at gene frequency 0.70, which is approximately the highest observed frequency in any population. Two results that pertain to the culture historical hypothesis are obtained. First, the incomplete correlation observed between adult lactose absorption and milk use does not necessarily constitute evidence against the hypothesis. Second, for the postulated genetic change to have occurred within the 6000-year period since the advent of dairying, either the effective population size was of the order of 100, or, if it was of larger order, the selection coefficient probably had to exceed 5%.

It has been proposed that the high frequency of adult humans able to digest and absorb the sugar lactose (adult lactose absorption, ALA) in some populations is the evolutionary consequence of a positive selection pressure induced by culturally determined milk use in those populations. Assuming a genetic basis for ALA, the “culture historical hypothesis,” independently proposed by Simoons and McCracken (1–3), stands mainly on the observed correlation between the degree to which adults in a population have traditionally consumed and been dependent on milk and the frequency of lactose absorbers in that population. It has also been pointed out, on the basis of deterministic calculations with a purely genetic model in which all lactose absorbers are tacitly assumed to be milk users, that there has been sufficient time for the genetic trait to have evolved since the advent of dairying some 6000 years ago (4, 5).

Unfortunately, a precise coevolutionary perspective is lacking in the arguments of Simoons and McCracken, thus eliciting some pertinent criticisms (6). By a coevolutionary perspective, I mean an interactive view of genetic and cultural variation, such that the evolutionary increase of a genetic variant and an associated cultural variant are mutu-

ally dependent. In this paper, I present and analyze a gene–culture coevolution model of ALA and milk use. This problem in “cultural genetics” (3) is very suitable for the interplay between theory and observation for the following reasons. First, present evidence strongly suggests an autosomal dominant mode of inheritance for ALA (7, 8). This justifies a simple monogenic model, and the predictions from such a model are realistic. Second, archaeological and zoological data exist delimiting the time available for genetic change (see ref. 9 for review). Third, there exist extensive data on the codistribution of the genetic trait and the cultural characteristic, as mentioned above.

The model is stochastic, including the effects of random sampling drift, to allow for the possibly small size of local human populations of prehistoric times. I address three questions pertaining to the culture historical hypothesis, although definite answers are, unfortunately, not forthcoming. The first question concerns the correlation expected between ALA and milk use. It is shown that the incompleteness of the observed correlation, sometimes adduced as evidence against the hypothesis (10), is actually to be expected on a stochastic model. The second question concerns the average time until fixation of the gene for ALA. When selection is induced by culture, the rate of gene frequency change may be slower than for a purely genetic trait (11, 12), and quantitative estimates of the retardation effect will be obtained. The third question concerns first arrival time. It should be noted that for populations from which large samples have been obtained, the estimated frequency of the gene for ALA lies mostly between 0.05 and 0.70 (2). The reason why the gene has not disappeared from some populations or approached fixation in others is not clear. The average time required for the gene initially at frequency 0.05 to reach frequency 0.70 for the first time (first arrival time) is compared with the 6000-year estimate of the time available (9) to test the consistency of the hypothesis.

THE MODEL

Assume two physical phenotypes, adult lactose absorption and malabsorption, determined by a single autosomal locus with two alleles A and a . A is completely dominant over a ; genotypes AA and Aa are lactose absorbers, and genotype aa is a malabsorber. Next, assume two cultural phenotypes, adult milk use and nonuse, corresponding to alternative “culturgens” of Lumsden and Wilson (12). Thus, four physical–cultural phenotypes exist. I assume that milk use confers a selective advantage only if the individual is a lactose absorber. Relative to a fitness of 1 for this phenotype, the other three phenotypes are assigned a selective value of $1 - s$ (Table 1).

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Abbreviation: ALA, adult lactose absorption.

Table 1. Fitness scheme for the four phenotypes

Physical phenotype	Cultural phenotype	
	Milk user	Milk nonuser
Lactose absorber	1	1 - s
Lactose malabsorber	1 - s	1 - s

The model life cycle, depicted in Fig. 1, has discrete generations with partial overlap to permit cultural transmission. The variables y , y' , and Y stand for the (relative) frequency of milk users; p , p' , and P for the frequency of the gene for ALA. An individual of the offspring generation adopts either of the two cultural phenotypes by observational learning from the adults of the parent generation ("oblique transmission," ref. 13). A lactose absorber becomes a milk user with probability $f(y)$, in which y is the frequency of milk users among the adults of the parent generation, and a nonuser with probability $1 - f(y)$. The corresponding probabilities for a malabsorber are $g(y)$ and $1 - g(y)$. Since malabsorbers may develop disagreeable symptoms upon drinking milk, it is reasonable to assume $f(y) \geq g(y)$. Although there are four phenotypes (and six pheno-genotypes, see Table 2), the assumption of oblique transmission permits us to describe the dynamics in terms of the two variables y and p (14).

Cultural transmission is followed by natural selection according to the scheme described previously. The deterministic equations for the change in y and p after random mating, cultural transmission, and natural selection are

$$\bar{W}y' = (1 - q^2)f(y) + (1 - s)q^2g(y) \quad [1a]$$

$$\bar{W}p' = p\{f(y) + (1 - s)[1 - f(y)]\}, \quad [1b]$$

where $q = 1 - p$, and \bar{W} is the mean fitness defined by

$$\bar{W} = 1 - s[1 - (1 - q^2)f(y)]. \quad [2]$$

Putting $\Delta y = y' - y$, $\Delta p = p' - p$, $a(y) = f(y) - y$, $b(y) = g(y) - y$, Eqs. 1a and 1b become

$$\begin{aligned} \bar{W}\Delta y &= (1 - q^2)a(y) + (1 - s)q^2b(y) \\ &\quad + s(1 - q^2)y[1 - y - a(y)] \end{aligned} \quad [3a]$$

$$\bar{W}\Delta p = spq^2[y + a(y)]. \quad [3b]$$

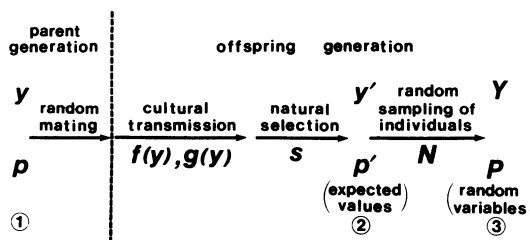


Fig. 1. Stage 1: Adults of parent generation of which there are N individuals. Frequency of milk users is y , that of the gene for ALA is p . The adults mate at random to produce an infinite number of offspring, who are enculturated by the adults with oblique transmission functions $f(y)$ and $g(y)$ and then subjected to viability selection with selection coefficient s . Stage 2: After these deterministic processes, the expected value of the frequency of milk users is y' and that of the gene for ALA is p' . Stage 3: N individuals are randomly sampled from among the survivors to produce the adults of the new generation. Y and P are random variables representing the frequencies of milk users and the gene for ALA, respectively.

Table 2. Multinomial probabilities for the stochastic model: Expected frequencies of the six pheno-genotypes

Genotype	Cultural phenotype	
	Milk user	Milk nonuser
Lactose absorber		
AA	$p^2f(y)/\bar{W}$	$p^2[1 - f(y)](1 - s)/\bar{W}$
Aa	$2pqf(y)/\bar{W}$	$2pq[1 - f(y)](1 - s)/\bar{W}$
Lactose malabsorber		
aa	$q^2g(y)(1 - s)/\bar{W}$	$q^2[1 - g(y)](1 - s)/\bar{W}$

The crucial assumption to be elaborated below is that $a(y)$ and $b(y)$ are both small in absolute value. In particular, the assumption on $a(y)$ implies that not all lactose absorbers are necessarily milk users. I also assume that the selection coefficient, s , is small. Thus the frequency of milk users and the gene change gradually over the generations. These assumptions are technically necessary to justify the diffusion approximation made below. Moreover, they are what make the model truly coevolutionary. Since $a(y)$ is assumed small, Eqs. 2 and 3b show that the rate of gene frequency change can be very slow when y is small.

After the deterministic processes just described, random sampling of N individuals occurs from among the survivors at stage 2. The sampling follows a multinomial distribution with probabilities given in Table 2. A Markov chain can be constructed on the two-dimensional state space of points (y, p) . However, this approach is in general tedious, and we proceed immediately to a stochastic treatment in terms of the two-dimensional Kolmogorov backward equation.

By standard techniques (ref. 15, p. 429; ref. 16, p. 171; ref. 17, p. 25; refs. 18 and 19) it can be shown that the appropriate differential operator L is

$$L = \frac{1}{2} V_{\delta y} \frac{\partial^2}{\partial y^2} + \frac{1}{2} V_{\delta p} \frac{\partial^2}{\partial p^2} + M_{\delta y} \frac{\partial}{\partial y} + M_{\delta p} \frac{\partial}{\partial p}, \quad [4]$$

where

$$V_{\delta y} = y(1 - y)/N, \quad V_{\delta p} = p(1 - p)/2N,$$

$$M_{\delta y} = a(y)(1 - q^2) + b(y)q^2 + s(1 - q^2)y(1 - y),$$

$$M_{\delta p} = spq^2y, \quad [5]$$

with $q = 1 - p$. $M_{\delta y}$ and $V_{\delta y}$ are the first and second moments of $Y - y$, and $M_{\delta p}$ and $V_{\delta p}$ are the first and second moments of $P - p$. Three properties of this operator are worth noticing. First, the denominator of $V_{\delta y}$ is N rather than $2N$ since individuals rather than genes are sampled. Second, the covariance term (ref. 16, p. 171) is missing. Third, whereas $M_{\delta y}$ contains s , $M_{\delta p}$ does not involve $a(y)$ and $b(y)$.

Two-dimensional diffusion occurs on the square domain of points (y, p) such that $0 \leq y \leq 1$ and $0 \leq p \leq 1$. I have neglected mutation since the time scale of interest is several hundred generations. The two boundaries $p = 0$ and 1 are therefore absorbing. In what follows, I assume that the form of $a(y)$ and $b(y)$ are such that the remaining two boundaries $y = 0$ and 1 are also absorbing. Thus, all sample paths eventually terminate in one of the four corners. I assume the same frequency-dependent cultural transmission function for lactose absorbers and malabsorbers:

$$a(y) = b(y) = cy(1 - y)(2y - 1), \quad [6]$$

with c nonnegative and small. This is an example of a "trend watching" function (12). When $c > 0$, Eq. 6 implies resistance to a "culturgene" when rare, with accelerated acceptance after it achieves a majority. The function does not include the effect of innovation, which is mathematically analogous to

mutation. Neither does it include the effect of cultural diffusion from neighboring populations, which most probably occurred as milk use spread from its primary origin.

ANALYSIS

Correlation. I define a correlation between ALA and milk use in terms of three ultimate fixation probabilities. Let $u_1(y, p)$ and $u_{11}(y, p)$ be the ultimate fixation probabilities of milk users and of the gene for ALA, respectively, and let $u_{11}(y, p)$ be their joint fixation probability. The arguments y and p stand for the initial frequency of milk users and of the gene, respectively. Then the correlation can be defined as

$$r = [u_{11} - u_1 u_{11}] / [u_1(1 - u_1)u_{11}(1 - u_{11})]^{1/2} \quad [7]$$

where the arguments have been suppressed. This is the correlation between two two-valued random variables assigned the values 0 or 1 corresponding to loss or fixation.

The partial differential equation satisfied by u_1 is

$$L[u_1] = 0 \quad [8]$$

where L is defined by Eqs. 4, 5, and 6. The same equation is also satisfied by u_1 and u_{11} . However, the boundary conditions differ. Let $G(y, s) = \exp\{-2[Ncy^2 + N(s - c)y]\}$ and $H(p, s) = \exp\{-2Nsp(2 - p)\}$. Then the appropriate boundary conditions on u_1 are

$$u_1(0, p) = 0, u_1(1, p) = 1 \quad [9a]$$

$$u_1(y, 0) = \int_0^y G(y, 0)dy / \int_0^1 G(y, 0)dy$$

and

$$u_1(y, 1) = \int_0^y G(y, s)dy / \int_0^1 G(y, s)dy. \quad [9b]$$

The boundary conditions on u_1 are

$$u_1(0, p) = p, u_1(1, p) = \int_0^p H(p, s)dp / \int_0^1 H(p, s)dp \quad [10a]$$

$$u_1(y, 0) = 0, u_1(y, 1) = 1. \quad [10b]$$

Finally, the boundary conditions on u_{11} are

$$u_{11}(0, p) = 0, u_{11}(1, p) = \int_0^p H(p, s)dp / \int_0^1 H(p, s)dp \quad [11a]$$

$$u_{11}(y, 0) = 0, u_{11}(y, 1) = \int_0^y G(y, s)dy / \int_0^1 G(y, s)dy. \quad [11b]$$

The integrals in the boundary conditions were evaluated numerically by Simpson's rule.

For each ultimate fixation probability, Eq. 8 subject to the appropriate boundary conditions was solved numerically by the Gauss-Seidel method (18-20). (To apply the Gauss-Seidel method, the domain $0 \leq y \leq 1, 0 \leq p \leq 1$ is covered by an $m \times m$ square lattice where each mesh has side length $h = 1/m$. Letting $y = hi$ and $p = hj$, where i and j are integers between 0 and m , the differential equation and boundary conditions are converted into a set of finite difference

equations. In the computations, m was usually taken to be 20.)

Average Time Until Fixation. Let $t_1(y, p)$ be the average time until fixation of the gene for ALA, excluding the cases of loss, when its initial frequency is p and when the initial frequency of milk users is y . Then, $t_1(y, p) = T_1(y, p)/u_1(y, p)$, where $T_1(y, p)$ satisfies

$$L[T_1] + u_1 = 0 \quad [12]$$

(ref. 16, p. 174) with L as in Eq. 8.

It is more convenient to solve for $z(y, p) = T_1(y, p)/N$, where the unit of time has been changed to N generations; z satisfies

$$\frac{y(1-y)}{2} \frac{\partial^2 z}{\partial y^2} + \frac{p(1-p)}{4} \frac{\partial^2 z}{\partial p^2} + y(1-y)[Nc(2y-1) + Ns(1-q^2)] \frac{\partial z}{\partial y} + Nspq^2y \frac{\partial z}{\partial p} + u_1 = 0. \quad [13]$$

The appropriate boundary conditions on z are

$$z(0, p) = -4(1-p)\log_e(1-p)$$

and

$$z(1, p) = u(p) \int_p^1 w(x)u(x)[1-u(x)]dx + [1-u(p)] \cdot \int_0^p w(x)[u(x)]^2 dx \quad [14a]$$

$$z(y, 0) = 0, z(y, 1) = 0 \quad [14b]$$

where $u(x) = u_1(1, x)$ and $w(x) = 4 \int_0^1 H(p, s)dp / [x(1-x)H(x, s)]$. The integrals in Eq. 14a were evaluated numerically by Simpson's rule.

In applying the Gauss-Seidel method to this boundary value problem, a striking discretization error occurs. It was found that the error could be made negligible by assuming the following ad hoc boundary condition at $p = 1$ (i.e., $j = m$). Letting $z_{ij} = z(hi, hj)$, put $z_{im} = 4(2\log_e 2 - 1)/m$ for $0 \leq i \leq m$ rather than the more natural $z_{im} = 0$. In fact, this ad hoc condition is a necessary condition for the analytical solution of the neutral case $Ns = Nc = 0$ to satisfy the corresponding finite difference equations at the interior points ($i, m - 1$) of the lattice. The validity of this correction factor was checked for some sets of parameter values by solving with $m = 100$ subject to the more natural boundary condition.

There are effectively two parameters Ns and Nc in the specific model defined by Eq. 6. The population size N does not occur independently. In applying the results from the idealized model to reality, it should be remembered that N is an effective population size, which is not equivalent to the census size. Although an effective size has not been rigorously defined in a gene-culture coevolution model, for our purposes it seems safe to say that it is about one-third the census size.

RESULTS

The main results are presented in Figs. 2 and 3. In both figures the initial frequency of the gene for ALA is 0.05. Partial justification for this choice is the aforementioned observation that the estimated allele frequencies lie between 0.05 and 0.70. The initial frequency of milk users was also taken to be 0.05. When milk use is first introduced into a population by either innovation or cultural diffusion, the frequency of users

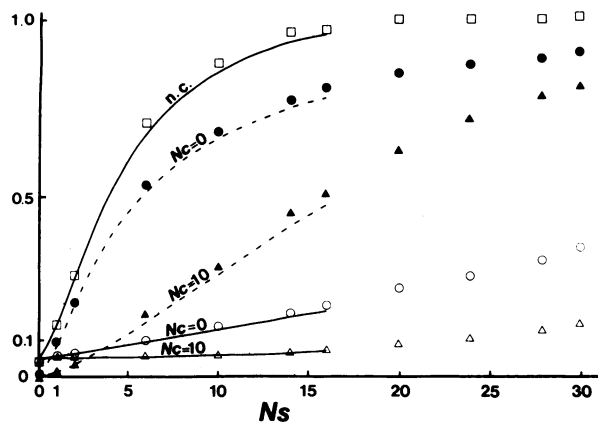


FIG. 2. Ultimate fixation probability of the gene for ALA, u_1 (continuous lines), and the correlation between gene and culture, r (broken lines). Initial frequencies of the gene and of milk users are both 0.05. Functional dependence on Ns is illustrated for the two cases $Nc = 0$ and $Nc = 10$. N , effective population size; s , selection coefficient; c , cultural transmission coefficient. For comparison, the ultimate fixation probability of a completely dominant gene with constant selective advantage is also given (top continuous line labeled n.c. = no culture). Results of Monte Carlo simulations are plotted as squares (n.c.), circles ($Nc = 0$), and triangles ($Nc = 10$). Ultimate fixation probability is given by open symbols and correlation by closed symbols.

is expected to be low. The particular choice was dictated by computer limitations and human patience.

In Fig. 2, the ultimate fixation probability of the gene $u_1(0.05, 0.05)$ is plotted as a function of Ns by continuous lines for the two cases $Nc = 0$ and $Nc = 10$. The correlation $r(0.05, 0.05)$ is plotted by broken lines for the same two cases. The accuracy of the numerical methods employed did not permit a solution beyond $Ns = 16$. In Fig. 3, the average time until fixation of the gene, in units of N generations, is plotted by continuous lines. Monte Carlo simulations were conducted as a check on numerically obtained values as well as to extend the solution to greater values of Ns . I used a population size of 100 in the simulations with a minimum of

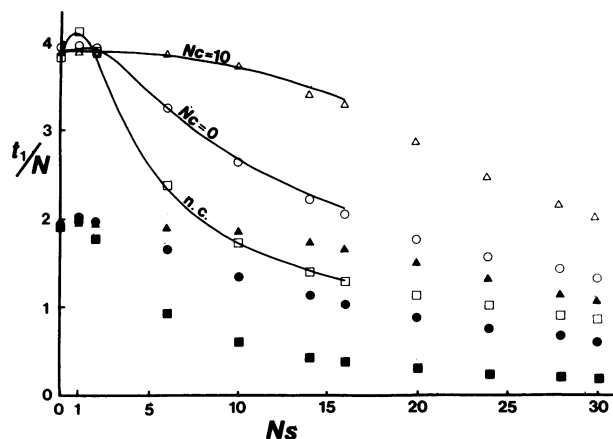


FIG. 3. Average time until fixation of the gene for ALA in units of N . Initial frequencies of the gene and of milk users are both 0.05. Relationship between the average time, t_1/N , and Ns is illustrated for the two cases, $Nc = 0$ and $Nc = 10$, and also for the case of a completely dominant gene with constant selective advantage, labeled n.c. N , effective population size; s , selection coefficient; c , cultural transmission coefficient. Results of Monte Carlo simulations are plotted as squares (n.c.), circles ($Nc = 0$), and triangles ($Nc = 10$). The open symbols verify and extend the numerical solution for the average time. The closed symbols give the first arrival time at gene frequency 0.70.

1000 replications for each point (cases of loss excluded for the average time). In Fig. 3, the results of simulations giving the first arrival time at gene frequency 0.70 are indicated by solid symbols.

To fully understand the implications of the results, let us consider in detail the particular case of $Ns = 10$ and $Nc = 10$. For example, this case would correspond to $N = 100$ with $s = c = 0.1$, or to $N = 500$ with $s = c = 0.02$. First, the ultimate fixation probability of the gene for ALA is 0.057, which is not much greater than the value of 0.050 for a selectively neutral allele. By contrast, a completely dominant allele with constant selective advantage is fixed with probability 0.850. One might argue that the maximum frequency of the gene in any human population is only about 0.70—i.e., that it is never fixed. According to the simulation, however, the gene should attain this frequency with probability 0.076, not much higher than the fixation probability.

Second, the correlation expected between ALA and milk use is 0.302. In fact, milk users and the gene for ALA are cofixed with probability 0.006, both are lost with probability 0.941, the former is fixed and the latter lost with probability 0.001, and the former is lost and the latter fixed with probability 0.052.

Third, the average time until fixation is $3.704N$ generations and the first arrival time is $1.841N$ generations. If $N = 100$, these values correspond to 370 and 184 generations, implying that there should have been sufficient time since the advent of dairying for the genetic change to have occurred. On the other hand, if $N = 500$, these values correspond to 1852 and 921 generations. If one human generation is 25 years, the first arrival time in the latter case becomes about 23,000 years, which seems too long. For a completely dominant gene with constant selective advantage, the average time until fixation is $1.723N$ generations and the first arrival time is $0.597N$ generations. Thus, the cultural retardation factor, defined as the ratio, is 2.15 for the average time until fixation and 3.08 for the first arrival time.

In the special case $a(y) = b(y) = 0$ (i.e., $c = 0$) with s small, a useful deterministic formula giving the time required for the gene frequency to increase from p_0 to p can be obtained from Eqs. 2, 3a, and 3b by approximating the difference equations by differential equations:

$$t = \int_{p_0}^p \{spq^2[1 - Kq\exp(-1/q)]\}^{-1} dp, \quad [15]$$

where $q = 1 - p$ and $K = (1 - y_0)\exp(-1/q_0)/q_0$ (y_0 and q_0 are initial values). For example, the number of generations required for the gene frequency to increase from 0.05 to 0.70, given an initial frequency of milk users of 0.05, turns out to be $19.67/s$ generations. The corresponding time for a completely dominant gene with constant selective advantage s is $6.07/s$ generations (ref. 15, equation 5.3.14). Thus, the cultural retardation factor is $19.67/6.07 = 3.24$. The retardation factor for the first arrival time in the stochastic model can be computed from the values plotted in Fig. 3. When $Nc = 0$, some values are given in Table 3. It appears that the deterministic value of 3.24 is an appropriate limiting value.

Table 3. Cultural retardation factor for the first arrival time ($c = 0$)

Ns	Retardation factor
0	1.00
10	2.25
20	2.93
30	3.11
∞	3.24

DISCUSSION

Using a stochastic model of gene-culture coevolution, I considered some theoretical questions raised by the culture historical hypothesis. The results suggest that an incomplete correlation between the frequency of lactose absorbers in a population and a traditional dependence on milk by that population does not necessarily constitute evidence against the hypothesis. However, for the genetic change to have occurred within the time available since the advent of dairying, Fig. 3 suggests that the effective population size must have been about 100, or if much larger, say even 500, that the selection coefficient in favor of the ALA milk use phenotype probably had to exceed 5%. It goes without saying that for smaller initial values of y and p , the time will be longer.

The maximum rate of gene frequency change is achieved when all lactose absorbers are milk users, and thus the retardation effect should be smaller if $a(y)$ and $b(y)$ are positive. However, although one may assume $a(y) > 0$, it seems realistic that $b(y) < 0$. That is, milk use may be attractive to lactose absorbers but not so to malabsorbers. Let $a(y) = ay(1 - y)$ and $b(y) = by(1 - y)$ with constant $a > 0$ and $b < 0$ (details of this attraction-repulsion model will be published elsewhere). Then, an equation analogous to Eq. 15 giving the deterministic time for genetic change can be obtained. Interestingly, if $a = 0.01$, $b = -0.01$, and $s = 0.1$, and if initially $y = p = 0.05$, the time required for the gene frequency to increase to 0.70 is 248 generations, giving a retardation factor of 4.09. The retardation effect is larger than if $a(y) = b(y) = 0$, which is the case considered in detail above.

Most likely, dairying and milk use originated in northern Mesopotamia (21). However, the gene for ALA probably existed in low frequencies in other areas as well. With the spread of culture (and genes) into Europe and elsewhere, coevolution of the type considered in this paper may have occurred in the local populations. Genetic and cultural migration, which I have ignored in this paper, should be taken into account in a more refined model. Furthermore, it is believed that the milk use culturgen spread to northern Europe within about 1000 years of its origin (9, 21), which seems to imply that it was attractive. This observation and my assumption 6 are apparently inconsistent, but recall the above discussion on the attraction-repulsion model. There

remain many unanswered questions, including the exact nature of the selection factor (8, 22, 23).

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1. Simoons, F. J. (1970) *Am. J. Dig. Dis.* **15**, 695-710.
2. Simoons, F. J. (1978) *Am. J. Dig. Dis.* **23**, 963-980.
3. McCracken, R. D. (1971) *Curr. Anthropol.* **12**, 479-517.
4. Cavalli-Sforza, L. L. (1972) *Proc. R. A. I.*, 15-25.
5. Heston, L. L. & Gottesman, I. I. (1973) in *Summary on the Conference on Lactose and Milk Intolerance*, eds. Gottesman, I. I. & Heston, L. L. (U.S. Dept. of Health, Washington, DC), pp. 1-49.
6. Omoto, K. (1971) *Curr. Anthropol.* **12**, 505.
7. Sahi, T., Isokoski, M., Jussila, J., Launiala, K. & Pyörälä, K. (1973) *Lancet*, 823-826.
8. Harrison, G. G. (1975) *Am. Anthropol.* **77**, 812-835.
9. Calder, N. (1983) *Timescale* (Viking, New York).
10. Vogel, F. & Motulsky, A. G. (1979) *Human Genetics* (Springer, Berlin).
11. Maynard Smith, J. & Warren, N. (1982) *Evolution* **36**, 620-627.
12. Lumsden, C. J. & Wilson, E. O. (1981) *Genes, Mind, and Culture* (Harvard Univ. Press, Cambridge, MA).
13. Cavalli-Sforza, L. L. & Feldman, M. W. (1981) *Cultural Transmission and Evolution* (Princeton Univ. Press, Princeton, NJ).
14. Aoki, K. (1984) *Proc. Jpn. Acad.* **60**, 310-313.
15. Crow, J. F. & Kimura, M. (1970) *An Introduction to Population Genetics Theory* (Harper & Row, New York).
16. Kimura, M. & Ohta, T. (1971) *Theoretical Aspects of Population Genetics* (Princeton Univ. Press, Princeton, NJ).
17. Maruyama, T. (1977) *Stochastic Problems in Population Genetics* (Springer, Berlin).
18. Kimura, M. & King, J. L. (1979) *Proc. Natl. Acad. Sci. USA* **76**, 2858-2861.
19. Kimura, M. (1985) in *Population Genetics and Molecular Evolution*, eds. Ohta, T. & Aoki, K. (Japan Sci. Soc. Press, Tokyo), pp. 19-39.
20. Smith, G. D. (1978) *Numerical Solution of Partial Differential Equations* (Clarendon Press, Oxford), 2nd Ed.
21. Sherratt, A. G. (1981) in *Pattern of the Past*, eds. Hodder, I., Isaac, G. & Hammond, N. (Cambridge Univ. Press, Cambridge), pp. 261-305.
22. Bayoumi, R. A. L., Flatz, S. D., Kühnau, W. & Flatz, G. (1982) *Am. J. Phys. Anthropol.* **58**, 173-178.
23. Flatz, G., Howell, J. N., Doench, J. & Flatz, S. D. (1982) *Hum. Genet.* **62**, 152-157.