The Decay of Genetic Variability in Geographically Structured Populations*

(population genetics/random drift/population structure/geographical structure/migration)

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ABSTRACT The geographical structure of a population distributed continuously and homogeneously along an infinite linear habitat is explored. The analysis is restricted to a single locus in the absence of selection, and every mutant is assumed to be new to the population. An explicit formula is derived for the probability that two homologous genes separated by a given distance at any time t are the same allele. The ultimate rate of approach to equilibrium is shown to be $t^{-1/2}e^{-2ut}$, where u is the mutation rate. An approximation is given for the stationary probability of allelism in an infinite two-dimensional population, which, unlike previous expressions, is finite everywhere. For a finite habitat of arbitrary shape and any number of dimensions, it is proved that if the population density is very high, then asymptotically the transient part of the probability of allelism is spatially uniform and decays at the rate $e^{-[2u+1/(2N)]t}$, where N is the total population size. Thus, in this respect the population behaves as if it were panmictic. The dependence of the amount of local gene frequency differentiation on population density and habitat size and dimensionality is discussed.

The rate of approach to homozygosity and the amount of genetic variability maintained by mutation are important classical problems in population genetics and evolutionary theory. Taking into account geographical structure makes the investigation of these questions richer in interest and more realistic for natural populations. A good review of this subject is given by Maruyama (1).

Let us write $e^{\lambda t}$ for the time dependence of the eigenfunctions describing the transient part of the probability of allelism. Then we know from the work of Maruyama (1, 2) that for various finite one- and two-dimensional habitats, if the population density is very high, the asymptotic rate of approach to equilibrium is given approximately by Wright's celebrated formula (extended to include mutation at rate u) $\lambda_0 = -2u - 1/(2N)$, where N is the population size. Indeed, we shall show that this result holds for any finite habitat. It seems, however, that frequently the limiting case of a population of fixed and not necessarily high density in a large habitat might be more appropriate. Under these conditions, the decrease of heterozygosity in different finite habitats will be qualitatively similar to the decay for a circle of circumference L (1-3), for which the eigenvalues are very close to

$$\lambda_n = -2u - 2(\pi\sigma/L)^2(n + 1/2)^2, \quad n = 0, 1, 2, \dots, \quad [1]$$

where σ is the standard deviation of the migration function r defined below in Sec. I.

As the habitat size increases, the eigenvalue spectrum given

by Eq. [1] tends to continuity on the halfline $\lambda \leq -2u$. Therefore, although $\lambda_0 \rightarrow -2u$, it does not follow that the ultimate rate of approach to the steady state is e^{-2ut} . To obtain the rate in this limit, one must calculate the probability of allelism at an arbitrary time t for an infinite linear habitat. The biological significance of this problem is greatly enhanced by the results of Malécot (4-6) and Weiss and Kimura (7), which show that at equilibrium in both one and two dimensions, even for infinite habitats, as the mutation rate tends to zero, so does the amount of genetic variability in the population.

The model treated in this paper is that of Malécot [5; 6, pp. 64-69], with the formulation of Maruyama (1, 2). We shall suppose that diploid monoecious individuals are distributed continuously and homogeneously in an habitat. They migrate in such a manner that the population density remains constant and uniform. Time is continuous and measured in units of generations. Zygotes are formed by the random union of proximate gametes. We shall confine ourselves to a single locus without selection, and assume very new mutant is of a type not preexisting in the population.

I. Infinite linear habitat

Let individuals be distributed along an infinite line with constant linear density ρ . We measure the distance x from an arbitrary origin on the line, positively in one direction and negatively in the other, and denote the probability that an individual migrates a distance between x and $x + \Delta x$ in time Δt by $m(\Delta t, x)\Delta x$. We do not assume m is symmetric in x . The homogeneity of the problem permits the use of a migration function depending only on displacement, rather than initial and final positions. Let $r(\Delta t, x)\Delta x$ designate the probability that the separation between two individuals changes by a distance between x and $x + \Delta x$ in time Δt . Then

$$r(\Delta t, x) = \int_{-\infty}^{\infty} m(\Delta t, y)m(\Delta t, x + y)dy. \quad [2]$$

From Eq. [2], it follows at once that r is symmetric in x (3).

Let $f(t, x)$ represent the probability that two homologous genes separated by a distance x are the same allele. Since r is symmetric in x , so is f (as is intuitively obvious), and therefore we may restrict our attention to the halfline $x \geq 0$. We put

$$f(t, x) = F(t, x) + f_{\infty}(x), \quad [3]$$

where $F(t, x) \rightarrow 0$ as $t \rightarrow \infty$. Thus, $F(t, x)$ and $f_{\infty}(x)$ are the transient and stationary parts of the probability of allelism. The corresponding components of the probability $h(t, x) = 1 - f(t, x)$ of nonallelism are evidently

$$H(t, x) = -F(t, x), \quad h_{\infty}(x) = 1 - f_{\infty}(x). \quad [4]$$

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We assume selection is absent, the mutation rate per generation for every gene is u , and each mutant is new to the population. Since r is symmetric, it clearly has mean zero. We posit that, as $\Delta t \rightarrow 0$,

$$\int_{-\infty}^{\infty} x^2 r(\Delta t, x) dx \sim \sigma^2 \Delta t, \quad [5]$$

$$\int_{-\infty}^{\infty} x^n r(\Delta t, x) dx \sim o(\Delta t), \quad n = 3, 4, \dots \quad [6]$$

Then (6, pp. 83, 84; Malécot uses the variance of m , which is one half that of r)

$$f_{\infty}(x) = \frac{\exp\left(-\frac{2\sqrt{u}}{\sigma}x\right)}{1 + 4\rho\sigma\sqrt{u}}, \quad [7]$$

and $H(t, x)$ satisfies the partial differential equation (2, 3)

$$\frac{\partial H}{\partial t} = -2uH + \frac{\sigma^2}{2} \frac{\partial^2 H}{\partial x^2}, \quad x > 0 \quad [8]$$

with the boundary condition (3)

$$a \frac{\partial H}{\partial x}(t, 0+) = H(t, 0), \quad [9]$$

where $a = 2\rho\sigma^2$ is a constant with dimensions of distance. If we suppose that we know the initial value $f(0, x)$, then $H(0, x)$ is given by

$$H(0, x) = f_{\infty}(x) - f(0, x), \quad [10]$$

and $H(t, x)$ is completely specified. We proceed with its calculation.

To find the eigenfunctions of Eqs. [8] and [9], let us substitute

$$H(t, x) = e^{\lambda t} \psi(x) \quad [11]$$

into these equations. This leads to

$$\frac{d^2 \psi}{dx^2} + \beta^2 \psi = 0, \quad x > 0 \quad [12]$$

$$a \frac{d\psi}{dx}(0+) = \psi(0), \quad [13]$$

with $\beta^2 = -2(\lambda + 2u)/\sigma^2$. Since $\psi(x)$ must be bounded as $x \rightarrow \infty$, it is easy to see that Eq. [13] requires that β^2 be real and nonnegative. Thus, λ is real and $\lambda \leq -2u$, as argued in the *Introduction*. The boundary value problem given by Eqs. [12] and [13] has the solution

$$\psi_{\beta}(x) = \sqrt{2/\pi}(1 + a^2\beta^2)^{-1/2}(a\beta \cos \beta x + \sin \beta x). \quad [14]$$

From the well-known relation (8, p. 97)

$$\int_{-\infty}^{\infty} e^{i\gamma x} dx = 2\pi\delta(\gamma) \quad [15]$$

obeyed by the Dirac delta function, with some manipulation we can prove that the eigenfunctions ψ_{β} are orthonormal:

$$\int_0^{\infty} \psi_{\beta}(x) \psi_{\gamma}(x) dx = \delta(\beta - \gamma). \quad [16]$$

Superposing the solutions Eq. [14] in accordance with Eq. [11], we find

$$H(t, x) = e^{-2ut} \int_0^{\infty} e^{-\sigma^2\beta^2 x/2} c_{\beta} \psi_{\beta}(x) d\beta. \quad [17]$$

Employing Eqs. [16] and [17], the constants c_{β} are immediately evaluated as

$$c_{\beta} = \int_0^{\infty} H(0, x) \psi_{\beta}(x) dx. \quad [18]$$

Substituting Eq. [18] into Eq. [17] yields the solution of the problem defined by Eqs. [8], [9], and [10]:

$$H(t, x) = \int_0^{\infty} H(0, x') G(t; x, x') dx', \quad [19]$$

where the Green's function G reads

$$G(t; x, x') = e^{-2ut} \int_0^{\infty} e^{-\sigma^2\beta^2 x/2} \psi_{\beta}(x) \psi_{\beta}(x') d\beta. \quad [20]$$

A slightly longer way to derive Eq. [20] is to calculate the Laplace transforms of Eqs. [8] and [9] in time, use the eigenfunction expansion of the Green's function (8, p. 256), and invert the transform of H . Inserting Eq. [14] into Eq. [20], the integral may be reduced to an elementary one and two other integrals given in (9, two top formulae on p. 497; these equations are not quite correct, however, and must be multiplied by $2/\sqrt{\pi}$). With the usual definition

$$\operatorname{erf} x = \frac{2}{\sqrt{\pi}} \int_0^x e^{-y^2} dy$$

of the error function, we get

$$\begin{aligned} G(t; x, x') = e^{-2ut} \left\{ (2\sqrt{\pi}b)^{-1} \left[\exp\left\{-\left(\frac{x+x'}{2b}\right)^2\right\} \right. \right. \\ \left. \left. + \exp\left\{-\left(\frac{x-x'}{2b}\right)^2\right\} \right] - a^{-1} \exp[(b/a)^2 + (x+x')/a] \right. \\ \left. \times \{1 - \operatorname{erf}[b/a + (x+x')/(2b)]\} \right\}, \quad [21] \end{aligned}$$

where $b = \sigma\sqrt{t/2}$ has the dimensions of length.

Equation [19] implies $G(0+; x, x') = \delta(x - x')$ and $G(t; x, x')$ satisfies Eqs. [8] and [9]. With some tedious calculation, one can demonstrate that Eq. [21] does agree with these three requirements, which determine it uniquely. Of course, to obtain the transient contribution to the heterozygosity of individuals in the population, we have merely to set $x = 0$ in Eq. [19].

Two limiting cases of our solution are of interest. First, we can fix t and let $x \rightarrow \infty$. From Eqs. [19] and [21] we obtain for $x \gg b$

$$\begin{aligned} H(t, x) \sim e^{-2ut} (2\sqrt{\pi}b)^{-1} \int_0^{\infty} H(0, x') \\ \times \exp\{-(x-x')/(2b)\}^2 dx'. \quad [22] \end{aligned}$$

It is a simple matter to verify that Eq. [22] is an asymptotic solution of Eq. [8]. The second limit, $t \rightarrow \infty$, with x constant, is of considerable biological importance. From Eqs. [19] and [21], we find now, for $b \gg a, x$,

$$\begin{aligned} H(t, x) \sim \sqrt{2/\pi} \sigma^{-3} t^{-3/2} e^{-2ut} (a+x) \\ \times \int_0^{\infty} H(0, x') (a+x') dx', \quad [23] \end{aligned}$$

making the reasonable assumption that the integral in Eq. [23] converges. Of course, it is independent of x and t . Equation [23] may be checked in two ways. First, it may be derived directly by computing the asymptotic behavior of the integral in Eq. [20]. According to standard asymptotic methods, this is accomplished by approximating $\psi_\beta(x)\psi_\beta(x')$ near $\beta = 0$. Second, we can verify trivially that Eq. [23] is an asymptotic solution of Eqs. [8] and [9].

Our result, Eq. [23], is a simple linear function of x , valid for $t \gg 8(\rho\sigma)^2, 2(x/\sigma)^2$. If there is no mutation, Eq. [7] shows that the population eventually becomes homozygous. Then $H(t, x)$ is the asymptotic probability of nonallelism, and this approaches zero rather rapidly at the rate $t^{-1/2}$. In particular, the ultimate probability that a randomly selected individual is heterozygous, $H(t, 0)$, tends to zero at the same rate.

II. Infinite two-dimensional habitat

It would be biologically highly desirable to solve the decay problem for an infinite population distributed over two spatial dimensions. Unfortunately, the two-dimensional formula given by Malécot (5) for the equilibrium probability of allelism diverges logarithmically as the separation between the two genes approaches zero. Not only is this pathology biologically unacceptable, but one can readily prove that it is inconsistent with the two-dimensional stationary analogue of Eq. [9]. As a first step toward an attack on the more difficult transient problem, we shall derive an approximation for the steady-state probability of allelism which is finite everywhere.

We generalize the formalism of Sec. I to two dimensions by employing vectors $\mathbf{x} = (x_1, x_2)$. We shall denote scalar products by $\mathbf{x} \cdot \mathbf{y}$ and the element of area by d^2x . Let $r(\mathbf{x})\Delta^2x$ designate the probability that the separation between two individuals changes by a vector in the interval $(\mathbf{x}, \mathbf{x} + \Delta\mathbf{x})$ in one generation. Since the proof in (3) clearly applies to any number of dimensions, we have $r(-\mathbf{x}) = r(\mathbf{x})$. The stationary probability of allelism, $f(\mathbf{x})$ satisfies the integral equation (1, 5)

$$f(\mathbf{x}) = (1 - u)^2 \left[\int r(\mathbf{y}) f(\mathbf{x} - \mathbf{y}) d^2y + sr(\mathbf{x}) \right], \quad [24]$$

where $s = [1 - f(0)]/(2\rho)$ and ρ is the number of individuals per unit area. Following (5), we solve Eq. [24] using Fourier transforms. The result reads

$$f(\mathbf{x}) = \frac{(1 - u)^2 s}{4\pi^2} \int \frac{e^{i\mathbf{k} \cdot \mathbf{x}} R(\mathbf{k})}{1 - (1 - u)^2 R(\mathbf{k})} d^2k, \quad [25]$$

where the Fourier transform of r is

$$R(\mathbf{k}) = \int e^{-i\mathbf{k} \cdot \mathbf{x}} r(\mathbf{x}) d^2x. \quad [26]$$

Since $r(-\mathbf{x}) = r(\mathbf{x})$,

$$\int x_j r(\mathbf{x}) d^2x = 0, \quad j = 1, 2, \quad [27]$$

and Eq. [26] may be expanded as

$$R(\mathbf{k}) \sim 1 - (1/2) \sum_{p,q=1}^2 k_p k_q \mu_{pq} + O(k^3), \quad [28]$$

where

$$\mu_{pq} = \int x_p x_q r(\mathbf{x}) d^2x. \quad [29]$$

We may suppose that the symmetric matrix μ is diagonal, $\mu_{pq} = \sigma_p^2 \delta_{pq}$, for if it is not, we can always diagonalize it by a rotation. Then Eq. [28] becomes

$$R(\mathbf{k}) \sim 1 - l^2/2 + O(l^3), \quad [30]$$

$$\sim (1 + l^2/2)^{-1} + O(l^3), \quad [31]$$

with $l_j = k_j \sigma_j$ and $l^2 = l_1^2 + l_2^2$.

We wish to approximate Eq. [25] for very small u . Equation [30] shows that the integral in Eq. [25] diverges at $\mathbf{k} = 0$ as $u \rightarrow 0$. This permits us to insert Eqs. [30] and [31] into Eq. [25]:

$$f(\mathbf{x}) \sim \frac{s}{\pi \sigma_1 \sigma_2} \left[\frac{1}{4\pi} \int \frac{e^{i\mathbf{l} \cdot \mathbf{x}} d^2l}{(1 + l^2/2)(2u + l^2/2)} + g(\mathbf{x}, u) \right], \quad [32]$$

where $\xi_i = x_i/\sigma_i$, and g is finite for all $u \geq 0$ and for all $\mathbf{x}$. Decomposing the denominator of the integral in Eq. [32] into partial fractions, we obtain two integrals of the type evaluated by Malécot (5). For $u \ll 1$, we find

$$f(\mathbf{x}) \sim \frac{1 - f(0)}{2\pi \rho \sigma_1 \sigma_2} [K_0(2\sqrt{u}\xi) - K_0(\sqrt{2}\xi) + g(\mathbf{x}, u)], \quad [33]$$

where $\xi^2 = \xi_1^2 + \xi_2^2$, and K_0 is the modified Bessel function of order zero. As $\mathbf{x} \rightarrow 0$, the bracket tends to $-(1/2)\ln 2u + g(0, u)$, of which the second term may be neglected for $u \ll 1$. Hence, Eq. [33] leads to

$$f(0) \sim [1 - 4\pi \rho \sigma_1 \sigma_2 / \ln 2u]^{-1}, \quad [34]$$

a slightly generalized form of Malécot's formula (5). Substituting Eq. [34] into Eq. [33], we obtain

$$f(\mathbf{x}) \sim -(2/\ln 2u) f(0) [K_0(2\sqrt{u}\xi) - K_0(\sqrt{2}\xi) + g(\mathbf{x}, u)]. \quad [35]$$

Finally, since $g(\mathbf{x}, 0)$ is finite for all $\mathbf{x}$, as $u \rightarrow 0$ we may drop it from Eq. [35] and write our final result

$$f(\xi) \sim -(2/\ln 2u) f(0) [K_0(2\sqrt{u}\xi) - K_0(\sqrt{2}\xi)]. \quad [36]$$

The first term in Eq. [36] generalizes Malécot's expression (5) to anisotropic migration, and displays explicitly the proportionality constant not computed by Weiss and Kimura (7; contrary to the assertions therein, the asymptotic analysis in this reference is valid for low mutation rate, not for large spatial separation. These authors' Eqs. [5.3] and the second of Eqs. [5.7] are incorrect, and the first of Eqs. [5.7] should be divided by 2.) One must keep in mind that neglecting g in Eq. [35] implies that any function which is finite everywhere and of $O[(\ln u)^{-1}]$ may be added to Eq. [36]. However, one can prove that Eq. [36] has the biologically very desirable property of being a monotonically nonincreasing function of ξ as long as $u < 1/2$, which will always be the case. In fact, the derivative of $f(\xi)$ vanishes at $\xi = 0$ and is negative for $\xi > 0$. Note that Eq. [36] correctly yields $f(\xi) \rightarrow f(0)$ as $\xi \rightarrow 0$. This consistency condition will always be violated if the second term in Eq. [36] is ignored. As $u \rightarrow 0$, for any ξ , Eqs. [34] and [36] show that $f(\xi) \rightarrow 1$, i.e., the population becomes homogeneous. Unless $\xi \ll 1$, $K_0(\sqrt{2}\xi)$ is negligible in Eq. [36]. In particular, if $2\sqrt{u}\xi \gg 1$, we recover the form of the previous (5, 7) asymptotic expression

$$f(\xi) \sim -[f(0)/\ln 2u] \sqrt{\pi/(\sqrt{u}\xi)} e^{-2\sqrt{u}\xi}. \quad [37]$$

III. Arbitrary densely populated finite habitat

In this section, we shall derive a simple, but very general, partial differential equation for the probability of allelism, and use it to prove that if the population density is very high, the asymptotic behavior of the transient component of the

probability of allelism is the same as for a panmictic population. We extend the vector notation of Sec. II to n dimensions, and employ continuous time, as in Sec. I. Since the habitat, S , now has a boundary, B , we cannot assume spatial homogeneity, and must define $f(t, \mathbf{x}, \mathbf{y})$ as the probability that two homologous genes, one at $\mathbf{x}$ and the other at $\mathbf{y}$, are the same allele. We denote the probability that an individual migrates in time Δt from $\mathbf{x}$ to a location in the interval $(\mathbf{y}, \mathbf{y} + \Delta \mathbf{y})$ by $m(\Delta t, \mathbf{x}, \mathbf{y}) \Delta^n \mathbf{y}$. For constant and uniform population density, ρ , one easily sees that m is the same as the probability density of initial positions, given final ones (6, p. 64). Then (1)

$$f(t + \Delta t, \mathbf{x}, \mathbf{y}) = (1 - u\Delta t)^2 \left\{ \int_S \int_S d^n \mathbf{x}' d^n \mathbf{y}' m(\Delta t, \mathbf{x}', \mathbf{x}) \right. \\ \times m(\Delta t, \mathbf{y}', \mathbf{y}) f(t, \mathbf{x}', \mathbf{y}') + \frac{\Delta t}{2\rho} \int_S d^n \mathbf{x}' m(\Delta t, \mathbf{x}', \mathbf{x}) \\ \times m(\Delta t, \mathbf{x}', \mathbf{y}) [1 - f(t, \mathbf{x}', \mathbf{x})] \left. \right\} \quad [38]$$

We take the limit $\Delta t \rightarrow 0$ by expanding $f(t, \mathbf{x}', \mathbf{y}')$ around $\mathbf{x}' = \mathbf{x}, \mathbf{y}' = \mathbf{y}$. We know

$$\int_S m(\Delta t, \mathbf{x}', \mathbf{x}) d^n \mathbf{x}' = 1, \quad [39]$$

and assume

$$\lim_{\Delta t \rightarrow 0} m(\Delta t, \mathbf{x}', \mathbf{x}) = \delta(\mathbf{x}' - \mathbf{x}), \quad [40]$$

the Dirac delta function in n dimensions, and

$$\int_S (x_i' - x_i) m(\Delta t, \mathbf{x}', \mathbf{x}) d^n \mathbf{x}' = o(\Delta t). \quad [41]$$

We suppose also that as $\Delta t \rightarrow 0$

$$\int_S (x_i' - x_i)(x_j' - x_j) m(\Delta t, \mathbf{x}', \mathbf{x}) d^n \mathbf{x}' \sim \mu_{ij} \Delta t \quad [42]$$

(for an homogeneous habitat, the covariance matrix of r , defined by Eq. [29], is twice that of m), and that terms of order higher than second contribute only to $o(\Delta t)$ in Eq. [38]. Using Eqs. [39] to [42] in Eq. [38] leads to

$$\frac{\partial f}{\partial t} = -2uf + (1/2) \sum_{ij} \mu_{ij} \left(\frac{\partial^2 f}{\partial x_i \partial x_j} + \frac{\partial^2 f}{\partial y_i \partial y_j} \right) \\ + \left[\frac{1 - f(t, \mathbf{x}, \mathbf{x})}{2\rho} \right] \delta(\mathbf{x} - \mathbf{y}). \quad [43]$$

The symmetric matrix μ may be diagonalized by a rotation, so we shall assume $\mu_{ij} = \sigma_i^2 \delta_{ij}$. Finally, we introduce scaled coordinates $\xi_i = x_i/\sigma_i$ and $\eta_i = y_i/\sigma_i$ to obtain the basic equation

$$\frac{\partial f}{\partial t} = -2uf + (1/2)(\nabla_{\xi}^2 + \nabla_{\eta}^2)f \\ + \left[\frac{1 - f(t, \xi, \xi)}{2\rho c} \right] \delta(\xi - \eta), \quad [44]$$

where the Laplacian reads, as usual,

$$\nabla_{\xi}^2 = \sum_i \frac{\partial^2}{\partial \xi_i^2}, \quad [45]$$

and $c = \prod_{i=1}^n \sigma_i$, the "migration volume." Equation [44] is more general and compact than the equilibrium equation of Malécot (6, p. 69). We carry over the decomposition given by Eqs. [3] and [4] in an obvious way, and, subtracting the equation satisfied by $f_{\infty}(\xi, \eta)$ from Eq. [44], find for $H = H(t; \xi, \eta)$

$$\frac{\partial H}{\partial t} = -2uH + (1/2)(\nabla_{\xi}^2 + \nabla_{\eta}^2)H - \frac{H(t; \xi, \eta)}{2\rho c} \\ \times \delta(\xi - \eta). \quad [46]$$

Writing $H(t; \xi, \eta) = e^{(\kappa - 2u)t} \psi(\xi, \eta)$, we obtain

$$[(1/2)(\nabla_{\xi}^2 + \nabla_{\eta}^2) + Q]\psi(\xi, \eta) = \kappa \psi(\xi, \eta), \quad [47]$$

where $Q = -\delta(\xi - \eta)/(2\rho c)$.

If we fix the time t , f changes only due to migration. Since there is no migration normal to the boundary B , we expect the normal derivative of f to vanish on B . Hence, we supplement Eq. [47] with the boundary conditions

$$\left(\frac{\partial \psi}{\partial n_{\xi}} \right)_{\xi \text{ on } B} = \left(\frac{\partial \psi}{\partial n_{\eta}} \right)_{\eta \text{ on } B} = 0, \quad [48]$$

where the notation means normal derivative. The conditions specified by Eq. [48] were recently given and discussed for a line segment by W. Fleming and C. Su (Brown University preprint, 1973). Green's Second Identity yields for any functions $\phi(\xi, \eta)$, $\chi(\xi, \eta)$ satisfying Eq. [48],

$$\int_S (\chi \nabla_{\xi}^2 \phi - \phi \nabla_{\xi}^2 \chi) d^n \xi \\ = \oint_B \left(\chi \frac{\partial \phi}{\partial n_{\xi}} - \phi \frac{\partial \chi}{\partial n_{\xi}} \right) da = 0, \quad [49]$$

where da is the element of "area" in $n - 1$ dimensions. We conclude that the Laplacians in Eq. [47] are selfadjoint, allowing us, as $\rho \rightarrow \infty$, to treat Q as a small perturbation with standard theory (8, Ch. 10).

As $\rho \rightarrow \infty$, we expect the leading eigenvalue $\kappa_0 = 0$ for an infinite population. From Eqs. [47] and [48], the corresponding eigenfunction $\psi_0(\xi, \eta)$ is constant. We take $\psi_0 = c/V$, where V is the "volume" of the habitat, in order to have

$$\int_S \int_S \psi_0^2 d^n \xi d^n \eta = 1. \quad [50]$$

Then to $O(Q)$ the corrected eigenvalue is given by (8, Ch. 10)

$$\kappa_0 \approx \bar{\kappa}_0 + \int_S \int_S \psi_0 Q \psi_0 d^n \xi d^n \eta \\ = -1/(2\rho V) = -1/(2N), \quad [51]$$

where N is the total population size. This proves that the ultimate approach to equilibrium for a very densely populated finite habitat is close to that for a panmictic population of the same total size. In particular, if $u = 0$, the ultimate probability of nonallelism, and hence the heterozygosity, decay at the rate $e^{-t/(2N)}$.

If the habitat has a typical linear dimension L , and the characteristic migration standard deviation is σ , we expect our panmictic result to hold when the ratio of the characteristic dimension of Q to that of the Laplacian, α_n , is much less than one. Writing $M = \rho c$ for the number of individuals in a "migration volume," we have $\alpha_n = (\sigma/L)^n M^{-1}/(\sigma/L)^2 =$

$(\sigma/L)^{n-2}/M$. If α_n is close to or greater than unity, there ought to be significant local differentiation of gene frequencies. Therefore, if a linear habitat is sufficiently large, the population occupying it will be ultimately strongly differentiated. For a two-dimensional habitat, only the number of individuals in a local mating unit, M , matters, and if this is much greater than one, the population will be essentially panmictic. These statements agree with the work of Wright (10, Ch. 12) and Maruyama (1, 2). A population in a very large three-dimensional habitat is asymptotically necessarily panmictic.

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