

ON THE FISHER AND THE CUBIC-POLYNOMIAL EQUATIONS FOR THE PROPAGATION OF SPECIES PROPERTIES

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For precise boundary conditions of biological relevance, it is proved that the steadily propagating plane-wave solution to the Fisher equation requires the unique (eigenvalue) velocity of advance $2(Df)^{1/2}$, where D is the diffusivity of the mutant species and f is the frequency of selection in favor of the mutant. This rigorous result shows that a so-called "wrong equation", i.e. one which differs from Fisher's by a term that is seemingly inconsequential for certain initial conditions, cannot be employed readily to obtain approximate solutions to Fisher's, for the two equations will often have qualitatively different manifolds of exact solutions. It is noted that the Fisher equation itself may be inappropriate in certain biological contexts owing to the manifest instability of the lower-concentration uniform equilibrium state (UES). Depicting the persistence of a mutant-deficient spatial pocket, an exact steady-state solution to the Fisher equation is presented. As an alternative and perhaps more faithful model equation for the propagation of certain species properties through a homogeneous population, we consider a reaction-diffusion equation that features a cubic-polynomial rate expression in the species concentration, with two stable UES and one intermediate unstable UES. This equation admits a remarkably simple exact analytical solution to the steadily propagating plane-wave eigenvalue problem. In the latter solution, the sign of the eigenvelocity is such that the wave propagates to yield the "preferred" stable UES (namely, the one further removed from the unstable intermediate UES) at all spatial points as $t \rightarrow \infty$. The cubic-polynomial equation also admits an exact steady-state solution for a mutant-deficient or mutant-isolated spatial pocket. Finally, the perpetuating growth of a mutant population from an arbitrary localized initial distribution, a mathematical problem analogous to that for ignition in laminar flame theory, is studied by applying differential inequality analysis, and rigorous sufficient conditions for extinction are derived here.

1. *Introduction.* Let $c=c(\mathbf{x},t)$ denote the concentration (3-dimensional cases) or density. (2- and 1-dimensional cases) of a mutant in the population of a biological species, or, more generally, the concentration or density of a subpopulation of species with a particular distinguishing

property. Then the time development of c can often be modeled quantitatively by solutions to a reaction-diffusion equation of the form (Fisher, 1937; Montroll, 1968; Cohen, 1971; Rosen, 1974 a-c, 1975, 1977 a, b; Testa, 1975; Horgan, 1975; Larson, 1978; Williams and Chow, 1978)

$$\partial c/\partial t = D\nabla^2 c + Q(c), \quad (1)$$

where $D(>0)$ is the constant diffusivity or motility of the mutant, and $Q(c)$ is the local rate of growth of the mutant concentration due to biological reproduction. On the basis of the simplest biological assumptions (e.g., Fisher, 1937), the latter function of c might be prescribed as

$$Q(c) = (\text{positive const})(c - \bar{c}^{(1)})(\bar{c}^{(2)} - c), \quad (2)$$

in which the constants $\bar{c}^{(1)}(<)\bar{c}^{(2)}$ are the concentration values for two uniform equilibrium states (UES) with the mutant concentration increasing locally by reproduction for c in the *beneficial range* $\bar{c}^{(1)} < c < \bar{c}^{(2)}$. Putting (2) into (1) and introducing the dimensionless variable

$$\theta \equiv (c - \bar{c}^{(1)})/(\bar{c}^{(2)} - \bar{c}^{(1)}), \quad (3)$$

we obtain the Fisher (1937) equation,

$$\partial \theta/\partial t = D\nabla^2 \theta + f(\theta - \theta^2), \quad (4)$$

where the constant $f(>0)$ is the frequency of selection in favor of the mutant in the beneficial range, the maximum local rate of reproductive growth of the mutant concentration being equal to $(1/4)f(\bar{c}^{(2)} - \bar{c}^{(1)})$ (implicit mathematical definition of f).

It is proved in Section 2 that the steadily propagating plane-wave solution to (4) requires the unique (eigenvalue) velocity of advance $2(Df)^{1/2}$, the extremal case actually calculated numerically by Fisher in his 1937 paper, if one imposes boundary conditions of essential biological relevance. This rigorous result shows that a so-called "wrong equation" (Montroll, 1968; Ames, 1972), i.e., one which differs from Fisher's by a term that is seemingly inconsequential for certain initial conditions, cannot be employed readily to obtain approximate solutions to Fisher's, for the two equations will often have qualitatively different manifolds and associated eigenvalue spectrums for allowable exact solutions. The uniqueness of the steadily propagating plane-wave eigenvelocity is a subtle,

important feature of Fisher's equation that has antecedents in the recent work of McKean (1975) and Kametaka (1976); the former author has shown that a step-function initial-distribution for θ evolves dynamically into a steadily propagating plane-wave solution to (4) with the unique velocity of advance $2(Df)^{1/2}$, while the latter author has reconfirmed Fisher's original observation that steadily propagating plane-wave solutions to (4) exist for all eigenvelocities greater or equal to $2(Df)^{1/2}$ with less stringent (pre-reaction) boundary conditions.

Since $\theta \doteq 0$ or $c \doteq \bar{c}^{(1)}$ throughout the spatial region in front of a Fisher wave, the solution is patently unstable with respect to concentration perturbations of suitably long wave-length (e.g., Benjamin, 1972; Rosen, 1977a). Such a manifest instability of the lower-concentration UES $\bar{c}^{(1)}$ may be a serious shortcoming of the Fisher equation in certain biological contexts. Stability questions notwithstanding, for $\bar{c}^{(2)} \leq 3\bar{c}^{(1)}$ the Fisher equation admits the exact steady-state (time-independent) solution displayed in (15) below, which depicts the persistence of a mutant-deficient spatial pocket for a concentration distribution governed by the Fisher equation.

As an alternative and perhaps more faithful model equation for the propagation of a species property through a homogeneous population, one is led to consider a reaction-diffusion equation of the form (1) with

$$Q(c) = (\text{positive const})(c - \bar{c}^{(1)})(c - \bar{c}^{(2)})(\bar{c}^{(3)} - c), \quad (5)$$

in which the constants $\bar{c}^{(1)}(<)\bar{c}^{(3)}(<)\bar{c}^{(2)}$ are the concentration values for three UES. The structure of (5) is such that c increases locally by reproduction in either of the two beneficial ranges $0 \leq c < \bar{c}^{(1)}$ and $\bar{c}^{(3)} < c < \bar{c}^{(2)}$; both $\bar{c}^{(1)}$ and $\bar{c}^{(2)}$ are stable UES, while the intermediate $\bar{c}^{(3)}$ is unstable. Substituting (5) into (1) and again employing the dimensionless variable (3), we obtain the model propagation equation of special interest in neurophysiology (Cohen, 1971; Aronson and Weinberger, 1975; Fife and McLeod, 1977):

$$\partial\theta/\partial t = D\nabla^2\theta + f(\theta - \theta^2)(\theta - \alpha), \quad (6)$$

where $f(>0)$ is a reproductive growth frequency constant, and the dimensionless constant parameter

$$\alpha \equiv (\bar{c}^{(3)} - \bar{c}^{(1)})/(\bar{c}^{(2)} - \bar{c}^{(1)}), \quad (7)$$

is positive but less than unity. In Section 3 it is shown that the reaction-diffusion equation (6) admits a remarkably simple exact analytical solution to the steadily propagating plane-wave eigenvalue problem. The sign of the (unique) eigenvelocity (19) is such that the wave (18) propagates to yield the "preferred" stable UES, i.e. $\bar{c}^{(1)}$ for $\alpha > 1/2$, $\bar{c}^{(2)}$ for $\alpha < 1/2$, at all spatial points as $t \rightarrow \infty$. In contrast to the steadily propagating plane-wave solution to the Fisher equation, both terminal UES in the wave solution to (6) given by (18) are stable, and hence it follows that the overall form of the solution is absolutely stable with respect to general perturbations in the concentration distribution (Benjamin, 1972). The cubic-polynomial reaction-diffusion equation (6) also admits the exact steady-state solution (20) for a mutant-deficient or mutant-isolated spatial pocket.

In connection with the application of (6) to the propagation of biological species properties, there arises a mathematical problem analogous to that for ignition in laminar flame theory (Rosen, 1959; Williams, 1965), namely, the perpetuating growth and expansion (by steadily propagating plane-waves or otherwise) of a localized mutant subpopulation from an arbitrary initial distribution. The latter problem is studied in detail in Section 4 by applying differential inequality analysis to (6), and rigorous extinction criteria are derived here.

2. Uniqueness of the Fisher Eigenvelocity and the Persistence of a Mutant-Deficient Spatial Pocket. Consider a steadily propagating wave solution to (4) with θ depending exclusively on the dimensionless phase variable,

$$\eta \equiv 2\lambda ft \pm (f/D)^{1/2}(x - x_0), \quad (8)$$

in which the constant parameter $\lambda (> 0)$ is proportional to the wave-propagation velocity ($= \mp 2\lambda(fD)^{1/2}$, according to (8)), and x_0 is a disposable constant. Putting $\theta = w(\eta)$ into (4), we obtain:

$$2\lambda \frac{dw}{d\eta} = \frac{d^2w}{d\eta^2} + w - w^2. \quad (9)$$

For the boundary conditions $c = \bar{c}^{(1)}$, $\bar{c}^{(2)}$ at $x = \pm \infty$, (3) implies that $w(-\infty) = 0$ and $w(+\infty) = 1$ with an appropriate choice of sign in (8). As $\eta \rightarrow -\infty$, the asymptotic solution to the linear correspondent of (9) is

$$w = (\text{const})[\exp(\lambda + \sqrt{\lambda^2 - 1})\eta] + (\text{const})[\exp(\lambda - \sqrt{\lambda^2 - 1})\eta],$$

requiring $\lambda \geq 1$ for a solution of biological interest with w decreasing monotonically to zero as $\eta \rightarrow -\infty$. Observe that the second term in this asymptotic solution to (9) depicts mutants through a distance of the order $(D/f)^{1/2}(\lambda - \sqrt{\lambda^2 - 1})^{-1} \geq (D/f)^{1/2}$ in front of the body of the Fisher wave. Now in an actual biological system there is a limiting velocity associated with species motility, and mutants cannot travel a distance greater than $(D/f)^{1/2}$ in the characteristic time for their reproduction f^{-1} . Thus, the biologically relevant solution to (9) takes the asymptotic form $w = (\text{const})[\exp(\lambda + \sqrt{\lambda^2 - 1})\eta]$ as $\eta \rightarrow -\infty$, with the more slowly decaying term precluded, and the boundary conditions for admissible solutions to (9) are:

$$\left. \begin{aligned} w=0 \\ w^{-1} dw/d\eta = \lambda + \sqrt{\lambda^2 - 1} \end{aligned} \right\} \text{ for } \eta = -\infty, \\
 \left. \begin{aligned} w=1 \\ dw/d\eta = 0 \end{aligned} \right\} \text{ for } \eta = +\infty. \quad (10)$$

The dimensionless dependent variable w increases monotonically from the (asymptotically) constant value zero to the (asymptotically) constant value unity for a solution of biological interest. Equation (9) subject to the boundary conditions (10) is in the class of eigenvalue problems encountered in laminar flame theory with Lewis number equal to unity (Rosen, 1959; Williams, 1965). As in the latter theory, the eigenvalue λ in (9) must take on a unique value for the solution that satisfies (10). We prove that $\lambda = 1$ by working with the Fisher (1939) variable

$$z \equiv (w - w^2)^{-1} (dw/d\eta), \quad (11)$$

which, as a consequence of (9), obeys the equation

$$(w - w^2) \frac{dz}{dw} = 2\lambda - z - z^{-1} + 2wz \quad (12)$$

when viewed as a function of w . From the asymptotic (exponential) forms of $w(\eta)$ as $\eta \rightarrow \pm \infty$ implied by (9) and (10), we find that (11) has the initial and final values

$$\begin{aligned} z = z_0 &\equiv \lambda + \sqrt{\lambda^2 - 1} \text{ for } w = 0 \text{ (i.e., } \eta = -\infty) \\ z = z_1 &\equiv \sqrt{\lambda^2 + 1} - \lambda \text{ for } w = 1 \text{ (i.e., } \eta = +\infty). \end{aligned} \quad (13)$$

So far these results correspond closely to those of Fisher's, with the first member of (13) requiring $\lambda \geq 1$. But now we note that z must decrease from z_0 to the smaller positive value z_1 as w increases from zero to unity, while (12) implies that

$$(w - w^2) \frac{dz}{dw} \geq 2\lambda - z - z^{-1} \geq 0 \quad (14)$$

for $z_0 \geq z \geq \lambda - \sqrt{\lambda^2 - 1} (> z_1)$. Hence, z cannot decrease through the latter range of values if $\lambda > 1$. We are thus left with the unique eigenvalue $\lambda = 1$, the extremal case for which Fisher argued to be "biological" and performed a numerical computation of the associated eigenfunction $w(\eta)$ satisfying (9).

It is easy to verify that (4) also admits the steady-state solution

$$\theta = 1 - \frac{3}{2} \left\{ \cosh \left[\frac{1}{2} (f/D)^{1/2} (x - x_0) \right] \right\}^{-2}, \quad (15)$$

which is admissible according to (3) for $\bar{c}^{(2)} \leq 3\bar{c}^{(1)}$. The concentration distribution (15) depicts a mutant-deficient spatial pocket centered at x_0 that does not change its shape or evolve in any way with time. In this interesting steady-state solution, the overall death-rate of mutants in the pocket is just compensated by the rate at which fresh mutants diffuse into the pocket.

3. Exact Wave Solution to the Cubic-Polynomial Equation. Let us now consider a steadily propagating plane-wave solution to (6), depending exclusively on the dimensionless phase variable (8). Putting $\theta = w(\eta)$ into (6), we obtain

$$2\lambda \frac{dw}{d\eta} = \frac{d^2w}{d\eta^2} + (w - w^2)(w - \alpha) \quad (16)$$

as the governing ordinary differential equation for the wave profile. Subject to the boundary conditions (10), the unique eigenfunction solution to (16) is given exactly by the remarkably simple closed-form expression,

$$w = \frac{1}{2} [1 + \tanh(\eta/2\sqrt{2})] \quad (17)$$

with the eigenvalue $\lambda = ((1/2) - \alpha)/\sqrt{2}$, as verified directly by substituting (17) into (16). From the full form of the solution with (8) and (17),

$$\theta = \frac{1}{2} \left\{ 1 + \tanh \left[\frac{1}{2} \left(\frac{1}{2} - \alpha \right) f t \pm \frac{1}{2} (f/2D)^{1/2} (x - x_0) \right] \right\}, \quad (18)$$

it follows that the wave velocity is:

$$(dx/dt)_{\theta=\text{const}} = \mp \left(\frac{1}{2} - \alpha \right) (2fD)^{1/2}. \quad (19)$$

The latter result shows that the wave propagates in the direction which yields the UES $\bar{c}^{(1)}$ (i.e., $\theta=0$) for $\alpha > 1/2$ or the UES $\bar{c}^{(2)}$ (i.e., $\theta=1$) for $\alpha < 1/2$ at all spatial points as $t \rightarrow \infty$, with the tanh term in (18) tending to -1 or $+1$, respectively. This direction of propagation of the wave suggests the notion of a "preferred" UES, $\bar{c}^{(1)}$ for $\alpha > 1/2$, $\bar{c}^{(2)}$ for $\alpha < 1/2$, i.e., the one further removed from unstable intermediate UES. The critical case $\alpha = 1/2$ corresponds to a steady-state (time-independent) solution which embodies neutrality of preference between the stable UES, according to (7).

In analogy to the exact solution (15) to the Fisher equation, the cubic-polynomial equation (6) also admits an exact steady-state solution for a mutant-deficient or mutant-isolated spatial pocket, namely

$$\theta = 3\alpha \left\{ 1 + \alpha + \left(1 - \frac{1}{2}\alpha \right)^{1/2} (1 - 2\alpha)^{1/2} \cosh[(\alpha f/D)^{1/2} (x - x_0)] \right\}^{-1}$$

for $\alpha < \frac{1}{2}$ (20)

$$\theta = 1 - 3(1 - \alpha) \left\{ 2 - \alpha + (1 + \alpha)^{1/2} \left(\alpha - \frac{1}{2} \right)^{1/2} \cosh[(1 - \alpha)^{1/2} (f/D)^{1/2} (x - x_0)] \right\}^{-1}, \quad \text{for } \alpha > \frac{1}{2}.$$

It should be noted that (18) and (20) reflect a general symmetry property of exact solutions to (6): *If $\theta(\mathbf{x}, t; \alpha)$ is a solution, then so is $[1 - \theta(\mathbf{x}, t; 1 - \alpha)]$.* The proof is immediate.

4. *Sufficient Condition for Extinction of a Mutant Distribution Governed by the Cubic-Polynomial Equation.* Consider an arbitrary initial distribution $c(x, 0)$ of mutants around the plane $x=0$ with both $N_1(0)$ and $N_2(0)$ finite, where

$$N_k = N_k(t) \equiv \int_{-\infty}^{\infty} [\theta(x, t)]^k dx, \quad \text{for } k=1, 2, \dots \quad (21)$$

As t increases, the initial distribution evolves according to (6) either with perpetuating growth ($N_1(t), N_2(t) \rightarrow \infty$) or suffers eventual extinction ($N_1(t), N_2(t) \rightarrow 0$). Sufficient conditions for extinction of the initial mutant population are derived as follows by applying differential inequality analysis (Rosen, 1974a; Rosen and Fizell, 1975; Horgan, 1977).

Multiplying (6) by θ , integrating the resulting equation from $x = -\infty$ to $x = +\infty$, using the definition (21) for $k=2, 3, 4$, and finally employing the Appendix A Sobolev-type inequality (A5) for θ at any instant of t , we find the differential inequality

$$\frac{1}{2} dN_2/dt \leq -3D(N_4)^2(N_2)^{-3} + f(-N_4 + (\alpha + 1)N_3 - \alpha N_2). \quad (22)$$

By virtue of the Schwarz inequality $N_3 \leq (N_2 N_4)^{1/2}$ (valid automatically for N_3 negative), (22) implies that:

$$\frac{1}{2} N_2 dN_2/dt < -3D\bar{\theta}^4 + fN_2^2(\bar{\theta} - \alpha)(1 - \bar{\theta}), \quad (23)$$

where $\bar{\theta} = \bar{\theta}(t) \equiv (N_4/N_2)^{1/2}$ and strict inequality holds (because the special cases for equality of the Sobolev and Schwarz inequalities are mutually exclusive). Patently negative for either $\bar{\theta} \leq \alpha$ or $\bar{\theta} \geq 1$, the right side of (23) is also non-positive if

$$N_2^2 \leq 3Df^{-1}\bar{\theta}^4(\bar{\theta} - \alpha)^{-1}(1 - \bar{\theta})^{-1} \quad (24)$$

for $\alpha < \bar{\theta} < 1$. Now the right side of (24) is a minimum for

$$\bar{\theta} = \beta \equiv \frac{3}{4} \left\{ 1 + \alpha - [(1 + \alpha)^2 - \frac{32}{9}\alpha]^{1/2} \right\}, \quad (25)$$

and hence if

$$N_2 \leq N_2^* \equiv (3Df^{-1})^{1/2} \beta^2 (\beta - \alpha)^{-1/2} (1 - \beta)^{-1/2} \tag{26}$$

at any instant of time, then it follows from (23) that $dN_2/dt < 0$ at the instant of time, independent of the value of $\bar{\theta}$. Thus, if (26) holds at $t=0$, N_2 must decrease monotonically for all $t > 0$. This means that $\lim_{t \rightarrow \infty} \theta(x, t) = 0$ for all x if

$$\int_{-\infty}^{\infty} [\theta(x, 0)]^2 dx \leq N_2^*. \tag{27}$$

Owing to the dependence of β on α in (25), N_2^* defined in (26) is asymptotic to $(16/3) (Df^{-1})^{1/2} \alpha^{3/2}$ for small α , and therefore (27) is a stringent condition for guaranteed extinction if $\alpha \ll 1$. On the other hand, it follows from (25) that N_2^* is asymptotic to $2(3Df^{-1})^{1/2} (1 - \alpha)^{-1}$ as $\alpha \rightarrow 1$, and therefore (27) is a practical condition for guaranteed extinction (which can preclude the perpetuating growth and expansion of the mutant population) if α is close to unity. The sufficient condition for extinction given by (27) harmonizes with the form of the exact solution (18), which shows that steadily propagating plane-waves cannot eventually develop and propagate outward toward $x = \pm \infty$ if α is greater or equal to 1/2. A supplementary sufficient condition for extinction of a distribution governed by (6) is derived in Appendix B.

APPENDIX A:
PROOF OF A SOBOLEV-TYPE INEQUALITY

Consider the functional

$$\Lambda[u] \equiv \left(\int_{-\infty}^{\infty} (du/dx)^2 dx \right) \left(\int_{-\infty}^{\infty} u^2 dx \right)^3 \left(\int_{-\infty}^{\infty} u^4 dx \right)^{-2}, \tag{A1}$$

defined on the class of continuous piecewise C^1 real functions $u = u(x)$ for which the three integrals in (A1) are finite. For this analytical functional to be a minimum at $u = \hat{u}$, we must have $\delta\Lambda \equiv \Lambda[\hat{u} + \delta u] - \Lambda[\hat{u}] = 0$ for arbitrary variations δu with both $(\hat{u} + \delta u)$ and \hat{u} in the domain of Λ . Calculating the variation of (A1), we obtain the equation for the minimizing function,

$$\frac{d^2 \hat{u}}{dx^2} - a^2 \hat{u} + 2b^2 \hat{u}^3 = 0, \tag{A2}$$

in which

$$a^2 \equiv 3 \int_{-\infty}^{\infty} (d\hat{u}/dx)^2 dx / \int_{-\infty}^{\infty} \hat{u}^2 dx, \quad b^2 \equiv 2 \int_{-\infty}^{\infty} (d\hat{u}/dx)^2 dx / \int_{-\infty}^{\infty} \hat{u}^4 dx. \tag{A3}$$

With the first constant of integration fixed to give \hat{u} in the domain of Λ (i.e., $\hat{u}(\pm\infty)=0$), the desired solution to (A2) is

$$\hat{u} = ab^{-1}[\cosh a(x - x_0)]^{-1}, \tag{A4}$$

where x_0 is a disposable constant of integration. Putting (A4) into (A1) and making use of (A3), we find that $\Lambda[\hat{u}]=3$, and thus the minimizing condition $\Lambda[u] \geq \Lambda[\hat{u}]$ yields the Sobolev-type inequality (Rosen, 1974a; Rosen and Fizell, 1975, and works cited therein)

$$\int_{-\infty}^{\infty} (du/dx)^2 dx \geq 3 \left(\int_{-\infty}^{\infty} u^4 dx \right)^2 \left(\int_{-\infty}^{\infty} u^2 dx \right)^{-3}, \tag{A5}$$

for all real continuous piecewise $C^1 u = u(x)$ such that the three integrals are finite. That \hat{u} satisfies sufficient conditions for the *global minimum value* of $\Lambda[u]$, or equivalently, that the 3 in (A5) is the maximum permissible value for the prefactor constant, can be established by employing the method for Talenti (1976).

APPENDIX B:
SUPPLEMENTARY SUFFICIENT CONDITION FOR EXTINCTION
OF A MUTANT DISTRIBUTION GOVERNED BY THE
CUBIC-POLYNOMIAL EQUATION

By integrating (6) from $x = -\infty$ to $x = +\infty$ and making use of the definition (21) for $k=1, 2, 3$, we obtain

$$dN_1/dt = f(-N_3 + (1 + \alpha)N_2 - \alpha N_1). \tag{B1}$$

In view of (B1) and (22), the time-derivative of $N \equiv (1 + \alpha)N_1 + (1/2)N_2$ has the upper bound

$$dN/dt \leq -3D(N_4)^2(N_2)^{-3} + f(-N_4 + (1 + \alpha + \alpha^2)N_2 - (\alpha + \alpha^2)N_1). \tag{B2}$$

Now for $\theta(x, 0) \geq 0$ for all x , (6) implies that $\theta(x, t) \geq 0$ for all x and $t \geq 0$ (e.g., Testa, 1975). Thus, assuming that the initial distribution is non-negative, we have $N_k \geq 0$ for odd (as well as even) k , and the Hölder inequality $N_4 \geq (N_2)^3(N_1)^{-2}$ can then be used to eliminate N_4 from (B2), yielding

$$dN/dt < -3D\bar{\theta}^3 N_1^{-1} + fN_1(\bar{\theta} - \alpha)(1 - \bar{\theta})(\bar{\theta} + 1 + \alpha), \tag{B3}$$

where $\bar{\theta} = \bar{\theta}(t) \equiv N_2/N_1$ and strict inequality holds (because the special cases for equality of the Sobolev and Hölder inequalities are mutually exclusive). Manifestly negative for either $\bar{\theta} \leq \alpha$ or $\bar{\theta} \geq 1$, the right side of (B3) is also non-positive if

$$N_1^2 \leq 3Df^{-1}\bar{\theta}^3[(\bar{\theta} - \alpha)(1 - \bar{\theta})(\bar{\theta} + 1 + \alpha)]^{-1}, \tag{B4}$$

for $\alpha < \bar{\theta} < 1$. But the right side of (B4) is a minimum for $\bar{\theta} = 3(\alpha + \alpha^2)/2(1 + \alpha + \alpha^2)$, and hence if

$$N_1 \leq N_1^* \equiv (3Df^{-1})^{1/2} \left[\frac{4(1 + \alpha + \alpha^2)^3}{27(\alpha + \alpha^2)^2} - 1 \right]^{-1/2} \tag{B5}$$

at any instant of time, then it follows from (B3) that $dN/dt < 0$ at the instant of time, independent of the value of $\bar{\theta}$. Moreover, we have $dN/dt < 0$ at any instant of time for which

$$N = (1 + \alpha + \frac{1}{2}\bar{\theta})N_1 \leq \left(1 + \frac{3\alpha}{2} \right) N_1^*, \tag{B6}$$

since the latter inequality implies that either $N_1 \leq N_1^*$ or $\bar{\theta} < \alpha$. Hence, N must decrease monotonically for all $t > 0$ and $\lim_{t \rightarrow \infty} \theta(x, t) = 0$ for all x if (B6) is satisfied at $t = 0$, i.e.

$$\int_{-\infty}^{\infty} [(1 + \alpha)\theta(x, 0) + \frac{1}{2}\theta(x, 0)^2] dx \leq \left(1 + \frac{3\alpha}{2} \right) N_1^* \tag{B7}$$

is a sufficient condition for extinction of a mutant distribution with $\theta(x, 0) \geq 0$. The quantity N_1^* defined by (B5) is asymptotic to $(9/2)(Df^{-1})^{1/2}\alpha$ for small α and approaches $2(Df^{-1})^{1/2}(1 - \alpha)^{-1}$ as $\alpha \rightarrow 1$, with the right side of (27) less than the right side of (B7) for all admissible values of α . Thus, the latter condition for guaranteed extinction applies in certain cases for which (27) does not, as illustrated by considering (27) and (B7) with the numerical values for $\alpha = 1/2$: $N_2^* = (3.112)(Df^{-1})^{1/2}$ and $(1 + 3\alpha/2)N_1^* = (4.725)(Df^{-1})^{1/2}$.

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