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Comptetition in a Spatially Heterogeneous Environment: Modelling the Risk of Spread of a Genetically Engineered Population

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In recent years regulations have been developed to address the risks of releasing genetically engineered organisms into the natural environment. These risks are generally considered to be proportional to the exposure multiplied by the hazard. Exposure is, in part, determined by the spatial spread of the organisms, a component of risk suited to mathematical analysis. In this paper we exampine a mathematical model describing the spread of organisms introduced into a hetereogeneous environment, focusing on the risk of spread and plausibility of containment strategies. Two competing populations are assumed, one the natural species and the other an engineered species or strain, both of which move randomly in a spatially heterogenous environment consisting of alternating favourable and unfavourable patches. The classical Lotka–Volterra competition model with diffusion is used. Analyses of the possible spread and invasion of engineered organisms are thus reduced to finding periodic travelling wave solutions to the model equations. We focus on whether a very small number of engineerd organisms can spatially invade a natural population. Initially we investigate the problem for spatially periodic diffusion coefficients and demonstrate that, under the right circumstances and a large enough unfavourable patch, invasion does not succeed. However, if spatially periodic carrying capacities are assumed along with spatially varying diffusion rates, the situation is far more complex. In this case containment of the engineered species is

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no longer only a simple function of the unfavourable patch length. By using perturbation solutions to the nonuniform steady states, approximate invasion conditions are obtained.

1. Introduction

Through recombinant DNA technology it is now practical to modify plants and animals to perform special agricultural or ecosystem functions. However, concerns regarding the disruption of the ecosystem and even the climatic system, by the release of such genetically engineerd organisms, have been raised (see, for example, Tiedje *et al*., 1989; Andow *et al*., 1986). A study of the spatio-temporal dynamics of genetically engineered organisms in the natural environment has therefore become increasingly important. Indeed no genetically engineered microbe has yet been approved for widespread use, because scientists have not reached a consensus regarding risks or containment.

The main concerns regarding the release of engineered organisms are how far and how rapidly are they likely to spread, assuming different ecological scenarios and management plans (Office of Technology Assessment, 1988; Anderson and Betz, 1991). Ultimately an assessment of risk associated with release should lead to strategies for the effective containment of an outbreak. To date there is no good quantitive basis for estimating spread rates and analysing possible containment strategies.

Genetically engineered microbes are especially amenable to mathematical analyses because they are continuously reproducing, lack complex behaviours, and exhibit population dynamics well-described by simple models. One example of such a microbe is *Pseudomonas syringae* (ice minus bacteria), which can reduce frost damage to crops by occupying crop foliage to the exclusion of *Pseudomonas syringae* strains that do cause frost (Lindow, 1987).

With the aid of a theoretical model we obtain quantitative results on the spatio-temporal spread of genetically engineered organisms in a spatially heterogeneous environment. In doing this we generate information regarding the risk of outbreak of an engineered population from its release site in terms of its dispersal and growth rates as well as those of a competing species. As shown below, the nature of the environment plays a key role in the spread of the organisms. We focus specifically on whether containment can be ensured by the use of geographical barriers, for example water, a different crop, or, day, barren land.

One of the most successful ways of modelling the spread of a growing population is by using Fisher's equation, pioneered by Fisher (1937), in which it is assumed that spatial spread is only due to diffusion and logistic growth. Applications of this model include the spread of waves of advantageous genes, pests, epidemics and exotic organisms (see, for example, Murray, 1989; Murray *et al*., 1986; Andow *et al*., 1990; Fife, 1979).

This basic model can be extended to a more involved system of two competing and diffusing species, yielding the Lotka–Volterra competition model with diffusion (see, for example, Murray, 1989). This system has been successfully used by Okubo *et al.* (1990) for modelling the spatial spread of the grey squirrel in Britain. With this model they were able to provide an explanation why the externally introduced grey squirrel invaded at the cost of the indigenous red squirrel.

Such models deal with invasion, only as travelling waves propagating in a homogeneous environment. However, in practice, because of the geographical, geological, and human-made variations in the environment, this is almost never the case. Not only is spatial heterogeneity one of the most obvious features in the natural world, but it is very likely one of the most important factor influencing population dynamics.

A first analysis of propagating frontal waves in a heterogeneous unbounded habitat was carried out by Shigesada *et al.* (1986) for Fisher's equation which describes a single species with logistic population growth and dispersal. The condition for linear stability of the steady states and the travelling wave speed were obtained.

Here we use the Lotka–Volterra competition model with diffusion to model the population dyncamics of natural microbes and competing engineered microbes. We, however, adapt this model to account for a spatially heterogeneous environment by assuming a periodically varying domain consisting of *good* and *bad* patches. The good patches signify the favourable regions in which the microbes are released, while the bad patches model the unfavourable barriers for inhibiting the spread of the microbes. We give special attention to the invasion and/or containment conditions for the genetically engineered population.

Although the motivation for this work is to determine the conditions for the spread of genetically engineered organisms, the models and analyses also apply to the introduction of other exotic species where containment, or in some cases deliberate propagation is the goal.

2. The Model Equations

Our approach is to write reaction-diffusion equations that specify the spatio-temporal dynamics of both engineered microbes, whose density at time t and position x is $E(x, t)$, and unmodified microbes similarly represented by $N(x, t)$. We use classical Lotka–Volterra dynamics to describe competition between our engineered and natural microbes. Our innovation is to allow key model parameters to vary spatially, reflecting habitat heterogeneity.

Specifically the dynamics of the system is described by

$$\frac{\partial E}{\partial t} = \frac{\partial}{\partial x}\left(D(x)\,\frac{\partial E}{\partial x}\right) + r_E E(G(x) - a_E E - b_E N), \tag{2.1a}$$

$$\frac{\partial N}{\partial t} = \frac{\partial}{\partial x}\left(d(x)\,\frac{\partial N}{\partial x}\right) + r_N N(g(x) - a_N N - b_N E), \tag{2.1b}$$

which is the Lotka–Volterra competition model with difusion; see, for example, Murray (1989). The functions $D(x)$ and $d(x)$ measure the diffusion rates. The intrinsic growth rates of the organisms are reflected by the positive parameters r_E and r_N. These are scaled so that the maximum values of the functions $G(x)$ and $g(x)$, reflecting the respective carrying capacities, are unity. The positive parameters a_E and a_N measure the effects of intraspecific competition, while b_E and b_N are the interspecific competition coefficients.

As a first step in describing environmental heterogeneity we focus on a model in which it is the dispersal and carrying capacity that vary (i.e., the functions $D(x)$, $d(x)$, $G(x)$, and $g(x)$ are spatially periodic). We assume that l is the periodicity of the environmental variation and accordingly define

$$D(x) = D(x+l), \qquad d(x) = d(x+l), \qquad G(x) = G(x+l),$$
$$g(x) = g(x+l).$$

We further assume that there are no engineered microbes initially; that is $E(x, 0) \equiv 0$. So, the natural microbes, $N(x, 0)$, satisfy the equation

$$\frac{\partial}{\partial x}\left(d(x)\,\frac{\partial N}{\partial x}\right) + r_N N(g(x) - a_N N) = 0.$$

The engineered organisms are then introduced at a release site, which in our case we shall take as the origin. This initial distribution in $E(x, t)$ is represented by the initial conditions

$$E(x, 0) = \begin{cases} H(x) > 0 & \text{if } \ |x| \leqslant x_c \\ 0 & \text{if } \ |x| > x_c, \end{cases} \tag{2.2}$$

where $H(x)$ is a one-humped continuous function of x and x_c is a positive constant, typically as used in Fig. 1.

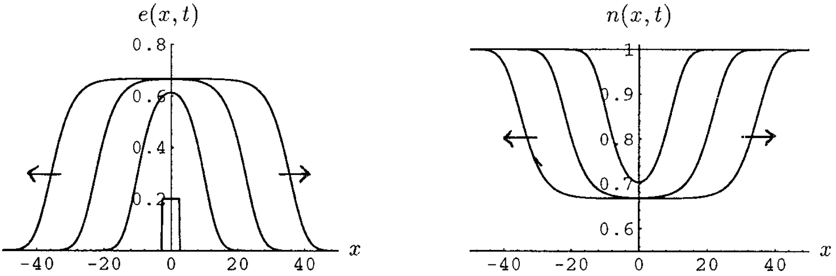


FIG. 1. A travelling wave solution connecting the native-dominant steady state to the coexistence steady state in a spatially uniform environment. Parameter values used were $\gamma_e = \gamma_n = 0.5$, $D(x) = d(x) = G(x) = g(x) = 1$, and $r = 2$, so that the coexistence state is the only stable state.

We further assume that the environment consists of two kinds of homogeneous patches, say Patch 1 of length l_1 and Patch 2 of length l_2, connected alternately along the x-axis. These patches are such that $l = l_1 + l_2$. We take Patch 1 as the favourable patch and Patch 2 as the unfavourable patch. In the unfavourable patches the diffusion and carrying capacity of the organisms are less than in the favourable patches. Biologically this could occur because the unfavourable patch is a hostile environment that either limits a population or interferes with its dispersal. Correspondingly, the functions $D(x)$, $d(x)$, $G(x)$, and $g(x)$ are periodic functions of x. In Patch 1, where $ml < x < ml + l_1$ for $m = 0, \pm 1, \pm 2, ...,$

$$\begin{aligned} D(x) &= D_1 > 0, \qquad & d(x) &= d_1 > 0; \\ G(x) &= 1, & g(x) &= 1. \end{aligned} \tag{2.3}$$

In Patch 2, where $ml - l_2 < x < ml$ for $m = 0, \pm 1, \pm 2, ...,$

$$\begin{aligned} D(x) &= D_2 > 0, \qquad & d(x) &= d_2 > 0; \\ G(x) &= G_2, & g(x) &= g_2; \end{aligned} \tag{2.4}$$

Since Patch 1 is favourable,

$$\begin{aligned} D_1 &\geqslant D_2, \qquad & d_1 &\geqslant d_2; \\ 1 &\geqslant G_2, & 1 &\geqslant g_2. \end{aligned}$$

In Fig. 2 we show, an example, of how the diffusion of the engineered microbes could vary in space.

At the boundaries between the patches, say $x = x_i$, with

$$x_{2m} = ml, \qquad x_{2m+1} = ml + l_1 \qquad \text{for} \quad m = 0, \pm 1, \pm 2, ...,$$

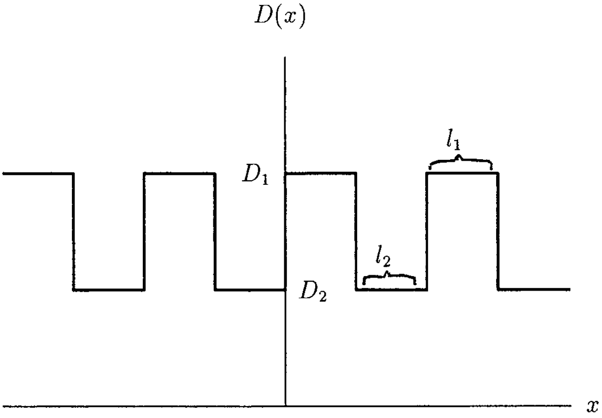


FIG. 2. The spatial pattern in the diffusion coefficient of the genetically engineered microbes, $D(x)$, in the periodic environment. There are two patch types. Diffusion is higher in the favourable patch, Patch 1, of length l_1, than the unfavourable patch, Patch 2, of length l_2.

the population densities $E(x, t)$ and $N(x, t)$ must be conserved, so

$$\lim_{x \to x_i^+} E(x, t) = \lim_{x \to x_i^-} E(x, t),$$

$$\lim_{x \to x_i^+} N(x, t) = \lim_{x \to x_i^-} N(x, t),$$

and since the flux most also be conserved,

$$\lim_{x \to x_i^+} D(x) \frac{\partial E(x, t)}{\partial x} = \lim_{x \to x_i^-} D(x) \frac{\partial E(x, t)}{\partial x},$$

$$\lim_{x \to x_i^+} d(x) \frac{\partial N(x, t)}{\partial x} = \lim_{x \to x_i^-} d(x) \frac{\partial N(x, t)}{\partial x}.$$

The system of equations for modelling the problem has now been defined completely. Using this, the key questions we attempt to answer below are: (1) Under which conditions will the engineered organisms invade successfully when rare? and (2) If invasion succeeds, will the engineered species drive the natural population to invader-dominant or will a coexistant state be reached?

Pacala and Roughgarden (1982) used a similar Lotka–Volterra competition model with diffusion in a two patch finite domain for describing two general competing species. They, however, only assumed spatially varying death rates and competition effects. They examined these equations for conditions of invasion and, apart for one very special case, all their results were obtained from numerical experimentation. In contrast, we follow

Shigesada *et al.* (1986) by studying the problem on the inifinite domain and by assuming that the diffusion and carrying capacities vary among the different patch types.

Our focus throughout this paper is upon the stability of the system to invasions initiated by a very small number of individuals. Mathematically this corresponds with linear analysis of steady state solutions to perturbations with a spatial component. Except where otherwise noted, our numerical results indicate that the predictions from our linear analysis hold true even if the number of invading organisms is not small.

3. NONDIMENSIONALISATION

We can nondimensionlise our equations by introducing

$$\begin{gathered} e=a_E E, \qquad n=a_N N, \qquad t^*=r_E t, \qquad x^*=x\left(\frac{r_E}{D_1}\right)^{1/2}, \\ d^*(x)=\frac{d(x)}{D_1}, \qquad D^*(x)=\frac{D(x)}{D_1}, \qquad r=\frac{r_N}{r_E}, \qquad \gamma_e=\frac{b_E}{a_N}, \qquad \gamma_n=\frac{b_N}{a_E}, \end{gathered} \tag{3.1}$$

and so

$$l^*=l\left(\frac{r_E}{D_1}\right)^{1/2}, \qquad l_1^*=l_1\left(\frac{r_E}{D_1}\right)^{1/2}, \qquad l_2^*=l_2\left(\frac{r_E}{D_1}\right)^{1/2}. \tag{3.2}$$

The nondimensional model equations, where we have dropped the asterisks for convenience, are now

$$\frac{\partial e}{\partial t}=\frac{\partial}{\partial x}\left(D(x)\frac{\partial e}{\partial x}\right)+e(G(x)-e-\gamma_e n), \tag{3.3a}$$

$$\frac{\partial n}{\partial t}=\frac{\partial}{\partial x}\left(d(x)\frac{\partial n}{\partial x}\right)+rn(g(x)-n-\gamma_n e), \tag{3.3b}$$

where

$$D(x)=\begin{cases}1 & \text{if} \quad ml<x<ml+l_1 \\ D_2 & \text{if} \quad ml-l_2<x<ml,\end{cases} \tag{3.4}$$

$$d(x)=\begin{cases}d_1 & \text{if} \quad ml<x<ml+l_1 \\ d_2 & \text{if} \quad ml-l_2<x<ml,\end{cases} \tag{3.5}$$

and the functions $G(x)$ and $g(x)$ are as before (see (2.3) and (2.4)). The values of d_1, d_2, and D_2 in (3.4) and (3.5) are as given by the nondimensionalization in (3.1).

At the boundaries between the patches, $x = x_i$, where $x_i = ml$ for $i = 2m$ and $x_i = ml + l_1$ for $i = 2m + 1$ ($m = 0, \pm 1, \pm 2, \ldots$) the nondimensional conditions are now,

$$\lim_{x \to x_i^+} e(x, t) = \lim_{x \to x_i^-} e(x, t), \tag{3.6a}$$

$$\lim_{x \to x_i^+} n(x, t) = \lim_{x \to x_i^-} n(x, t), \tag{3.6b}$$

and also

$$\lim_{x \to x_i^+} D(x) \frac{\partial e(x, t)}{\partial x} = \lim_{x \to x_i^-} D(x) \frac{\partial e(x, t)}{\partial x}, \tag{3.7a}$$

$$\lim_{x \to x_i^+} d(x) \frac{\partial n(x, t)}{\partial x} = \lim_{x \to x_i^-} d(x) \frac{\partial n(x, t)}{\partial x}, \tag{3.7b}$$

for all integer i.

4. No Patchiness

We begin by examining the behaviour of our model equations in the absence of patchiness. Hence we assume that the whole domain is favourable and thus the unfavourable patch has zero length, $l_2 = 0$. So $D(x) = 1$, $d(x) = d_1$. $G(x) = 1$, and $g(x) = 1$ everywhere. This results in the classical Lotka–Volterra competition model with diffusion.

The initial steady state condition reduces to $e_1 = 0$, $n_1 = 1$. We shall refer to this steady state as the *native-dominant* steady state further on. There are two other relevant steady states. The *invader-dominant* steady state, where the engineered organisms have driven the natural organisms to invader-dominant; that is $e_2 = 1$, $n_2 = 0$, and the *coexistence* steady state

$$e_3 = \frac{\gamma_n - 1}{\gamma_n \gamma_e - 1}, \qquad n_3 = \frac{\gamma_e - 1}{\gamma_n \gamma_e - 1}. \tag{4.1}$$

The latter is only relevant if it is positive, which means that either $\gamma_e < 1$ and $\gamma_n < 1$, thus weak interspecific competition for both spieces, or $\gamma_e > 1$ and $\gamma_n > 1$, thus strong interspecific competition for both species. The trivial steady state, given by $e_0 = n_0 = 0$, is not of any significance here.

It has been shown formally (see, for example, Grusa, 1988) that the Lotka–Volterra competition model with diffusion does not have any other steady state solutions, for example patterned solutions, apart from the above uniform steady states when zero-flux boundary conditions are imposed. Furthermore, all solutions are bounded and always nonnegative for nonnegative initial conditions such as (2.2).

We are now interested in the existence of travelling wave solutions to (3.3) connecting the native-dominant steady state, (e_1, n_1), to the existence steady state, (e_2, n_2), or the invader-dominant steady state, (e_3, n_3). Such solutions would correspond to waves of microbial invasion, either driving the natural species to invader-dominant or to a new, but lower, steady state.

By performing a linear stability analysis about the initial native-dominant steady state, (e_1, n_1), we can determine under which conditions invasion succeeds. By looking for solutions of the form $e^{ikx+\lambda t}$ in the linearised system we obtain the linear dispersion relationship

$$\lambda(k^2) = \frac{-b(k^2) \pm \sqrt{b^2(k^2) - 4c(k^2)}}{2},$$

where

$$b(k^2) = k^2(d_1 + 1) + (\gamma_e - 1) + r,$$
$$c(k^2) = d_1 k^4 + [\gamma_e - 1 + r]\, k^2 + r(\gamma_e - 1).$$

The native-dominant steady state is linearly unstable if there exists a k^2 so that $\lambda(k^2) > 0$. From the dispersion relationship it can be seen that if $\gamma_e > 1$ then the initial steady state will always be linearly stable, since $b(k^2)$ is always positive. However if $\gamma_e < 1$ then there are values of k for which the steady state is unstable and the invasion of the engineered species, e, will succeed.

By similarly linearising about the other steady states we can also determine their stability. The invader-dominant steady state, (e_2, n_2), is stable if $\gamma_n > 1$, and unstable if $\gamma_n < 1$. On the other hand the coexistence steady state (e_3, n_3) is stable if $\gamma_e < 1$ and $\gamma_n < 1$, and unstable if $\gamma_e > 1$ and $\gamma_n > 1$. Note that if $\gamma_e < 1 < \gamma_n$ or $\gamma_n < 1 < \gamma_e$, the coexistence steady state is no longer relevant, since either e_3 or n_3 becomes negative.

It is furthermore easy to show that the trivial steady state is always linearly unstable; in the absence of an indigenous species either the natural strain, the engineered strain, or both, would invade.

We begin by examining numerically whether travelling wave solutions can exist when the native-dominant steady state is unstable. Indeed, when $\gamma_e < 1$, a travelling wave connecting the native-dominant steady state to the invader-dominant steady state results, but only if $\gamma_n > 1$, On the other hand, a travelling wave connecting the native-dominant steady state to the coexistence steady state results only if $\gamma_n < 1$. In Fig. 1 we illustrate the numerical solutions for the case when $\gamma_e < 1$ and $\gamma_n < 1$.

The requirement, $\gamma_e < 1$, for the native-dominant steady state to be unstable, implies, in terms of our original dimensional variables (see (3.1)), that the interspecific competitive effect of the natural organisms, n, on the engineered species, e, is dominated by the intraspecific competition of the natural species.

If $\gamma_n > 1$ the natural species is driven to invader-dominant and in terms of our original dimensional parameters, this happens when increases in density of the engineered species reduce the population growth of the natural species more than they reduce their own population's growth rate. When $\gamma_n < 1$ the situation is just reversed; again refer to (3.1).

If, on the other hand, the native-dominant state is stable, $\gamma_e > 1$, we can, simultaneously, have the invader-dominant steady state stable if $\gamma_n > 1$. This is also the conditions for the coexistence steady state to be unstable. In this case the stability of the native-dominant steady state depends on the initial conditions (2.2). If $H(x)$ represents a small perturbations about $e = 0$ then the native-dominant steady state remains the final steady state solution. However, we found from numerical experimentation, that for very large perturbations, corresponding to a very large initial release of e, a travelling wave solution results and the invader-dominant steady state becomes the final solution. Conley and Gardner (1989) proved the existence of such a travelling solution under these circumstances. Thus, containment can be only ensured for all initial release strategies if $\gamma_e > 1$ and $\gamma_n < 1$.

Note that if we consider the whole domain as *unfavourable*, instead of favourable, by setting $l_1 = 0$ instead of $l_2 = 0$, then we obtain analogous results. However, our nonzero steady states are different now. The native-dominant steady state is $e_1 = 0$, $n_1 = g_2$, the invader-dominant steady state is $e_2 = G_2$, $n_2 = 0$, while the coexistence steady state is

$$e_3 = \frac{\gamma_n G_2 - g_2}{\gamma_e \gamma_n - 1}, \qquad n_3 = \frac{\gamma_e g_2 - G_2}{\gamma_e \gamma_n - 1}.$$

The stability conditions are now determined from whether γ_e and γ_n are respectively larger or smaller than G_2/g_2 and $\gamma_n < g_2/G_2$ the coexistence steady state is stable, and all other steady states are unstable.

5. SPATIALLY VARYING DIFFUSION

As above we perform here a linear stability analysis about the various steady states when the patchiness only affects the diffusion functions. In the first part of this section we investigate how spatially varying diffusion coefficients affect the ability of the engineered species to invade. In the second part we determine the conditions necessary for reaching a specific invasion steady state.

5.1. *Conditions for Invasion*

The initial native-dominant steady state is (e_1, n_1), where again $e_1 = 0$ and, depending on the function $g(x)$, either $n_1 = 1$ or n_1 is a periodic function of x with period related to the length of the patches.

In this section, as a first case, we assume, however, that $g(x) = 1$ so that n_1 is thus independent of x. As we shall see below, this simplifies the problem considerably. We consider the much more involved problem when $g(x)$ is a periodic function in x in Section 6.

To determine the stability of the initial native-dominant steady state we linearise about $(e_1, n_1) = (0, 1)$ to obtain

$$\frac{\partial e}{\partial t} = \frac{\partial}{\partial x}\left(D(x)\frac{\partial e}{\partial x}\right) + e[G(x) - \gamma_e], \tag{5.1a}$$

$$\frac{\partial n}{\partial t} = \frac{\partial}{\partial x}\left(d(x)\frac{\partial n}{\partial x}\right) + r[-n - \gamma_n e], \tag{5.1b}$$

where e and n now represent perturbations away from the steady state (n_1, e_1) and $|e| \ll 1$ and $|n| \ll 1$.

The stability of this system can be determined by looking only at the equation for the engineered species (5.1a), since it is independent of n. This reduces the linear stability problem to

$$\frac{\partial e}{\partial t} = \frac{\partial^2 e}{\partial x^2} + e[1 - \gamma_e] \qquad \text{in} \quad \text{Patch 1}, \tag{5.2a}$$

$$\frac{\partial e}{\partial t} = D_2\frac{\partial^2 e}{\partial x^2} + e[G_2 - \gamma_e] \qquad \text{in} \quad \text{Patch 2}. \tag{5.2b}$$

By substituting $e(x, t) = e^{-\lambda t} f(x)$ into (5.2) we obtain the characteristic equation

$$\frac{\partial}{\partial x}\left(D(x)\frac{\partial f}{\partial x}\right) + [G(x) - \gamma_e + \lambda] f = 0, \tag{5.3}$$

which is generally known as Hill's equation. Here, according to our definition, $G(x) - \gamma_e$ and $D(x)$ are both periodic functions of period l; see Section 3.

It is known from the theory of Hill's equation with period coefficients, that there exists a monotonically increasing infinite sequence of real eigenvalues λ,

$$-\infty < \lambda_0 < \tilde{\lambda}_1 \leqslant \tilde{\lambda}_2 < \lambda_1 \leqslant \lambda_2 \leqslant \tilde{\lambda}_3 \leqslant \tilde{\lambda}_4 < \cdots,$$

associated with (5.3), for which it has nonzero solutions. The solutions are of period l if and only if $\lambda = \lambda_i$ and of period $2l$ if and only if $\lambda = \tilde{\lambda}_i$. Furthermore, the solution associated with $\lambda = \lambda_0$ has no zeros and is globally unstable (in the spatial sense) in that $f \to \infty$ as $|x| \to \infty$; refer to Shigesada *et al.* (1986). For the detailed theory see Coddington and Levinson (1972) or Magnus and Winkler (1966).

So, the stability of the native-dominant steady state of the partial differential equation system (5.1) is determined by the sign of λ_0. If $\lambda_0 < 0$ the trivial solution $e_0 = 0$ of (5.1) is dynamically unstable and if $\lambda_0 > 0$ this solution is dynamically stable.

By extending a result of Borg (1946) it is possible to obtain a bound on λ_0 (see Appendix A).

By defining the function

$$Q(x) = G(x) - \frac{l_1 + G_2 l_2}{l},$$

we can write Eq. (5.3) in the form

$$\frac{\partial}{\partial x}\left(D(x)\frac{\partial f}{\partial x}\right) + \left[Q(x) + \frac{l_1 + G_2 l_2}{l} - \gamma_e + \lambda\right] f = 0. \tag{5.4}$$

Since

$$\int_{\zeta l}^{(\zeta+1)l} Q(x)\,dx = 0 \qquad \text{for arbitrary} \quad \zeta \in \Re,$$

it follows from the result in Appendix A that

$$\frac{l_1 + G_2 l_2}{l} - \gamma_e + \lambda_0 < 0.$$

Thus a sufficient condition for $\lambda_0 < 0$ and for the system of Eq. (5.1) to be unstable is

$$(1 - \gamma_e)\, l_1 \geqslant (\gamma_e - G_2)\, l_2. \tag{5.5}$$

There are now three relevant cases to consider. Recall that $G_2 < 1$.

In the case when $\gamma_e > 1 > G_2$ the native-dominant steady state is stable in both the favourable and unfavourable patches if they are considered in isolation. Refer again to Section 4 for the detailed discussion of the stability conditions for either the favourable or unfavourable patches (note that $g_2 = 1$ here). However, although it seems reasonable, we cannot conclude from (5.5) that the native-dominant steady state will be stable for the full problem, since this is only a sufficient condition for instability.

On the other hand, when $1 > G_2 > \gamma_e$ the native-dominant steady state is unstable in both patches if they are considered in isolation. Moreover, as expected, it follows from (5.5) that the native-dominant steady state is also unstable for the problem on the full domain considered here. Thus, if the carrying capacity of the engineered microbes in the unfavourable patch, Patch 2 (reflected by G_2) exceeds their loss, due to the interspecific competitive effect of the natural organisms (reflected by γ_e), the engineered organisms always invade.

However, if $1 > \gamma_e > G_2$, the native-dominant steady state is unstable in the favourable patch but stable in the unfavourable patch when considered in isolation. Which of these patches dominates the actual stability of the native-dominant steady state depends on the relative sizes of these patches, as can be seen from inequality (5.5). By increasing the favourable patch length, l_1, and/or decreasing the unfavourable pach length, l_2, the native-dominant steady state will become unstable so that invasion does occur. The above condition (5.5) is not a necessary condition for instability and so does not provide exact conditions for ensuring the stability of the native-dominant steady state.

We begin by obtaining separable solutions for the above equation (5.2) for each of the two types of patches. Since we expect periodic solutions we use Fourier series expansions to find the solutions.

In Patch 1 we obtain the solution

$$e(x, t) = \sum_{i=0}^{\infty} A_i e^{-\lambda_i t} \cos\left[\left(x - \frac{l_1}{2} - ml\right)\sqrt{1 - \gamma_e + \lambda_i}\right], \tag{5.6}$$

while in Patch 2 we have

$$e(x, t) = \sum_{i=0}^{\infty} B_i e^{-\lambda_i t} \cos\left[\left(x + \frac{l_2}{2} - (m+1)\, l\right)\sqrt{\frac{G_2 - \gamma_e + \lambda_i}{D_2}}\right], \tag{5.7}$$

with A_i and B_i constants.

Applying the continuity conditions (3.6) and (3.7) the following series of equalities must hold

$$\sqrt{1-\gamma_e+\lambda_i}\tan\left(\frac{l_1}{2}\sqrt{1-\gamma_e+\lambda_i}\right)$$
$$=-D_2\sqrt{\frac{G_2-\gamma_e+\lambda_i}{D_2}}\tan\left(\frac{l_2}{2}\sqrt{\frac{G_2-\gamma_e+\lambda_i}{D_2}}\right),$$

for $i=0, 1, 2, \ldots$ Note that if the expressions inside the above square roots become negative identities

$$\tan iz = i\tanh z, \qquad \text{arc}\tan iz = i\,\text{arc}\tanh z, \tag{5.8}$$

should be used.

We are, of course, interested in the sign of the smallest eigenvalue, $\lambda=\lambda_0$, satisfying the above equality. It is not difficult to show that λ_0 will be negative if and only if the expressions $1-\gamma_e+\lambda_0$ and $G_2-\gamma_e+\lambda_0$ appearing under the square roots have opposite signs.

Since, by definition $G_2<1$, this can occur only if $\gamma_e<1$. Thus, as is the case in the problem with spatially uniform coefficients, a necessary condition for the native-dominant steady state to be unstable, thus permitting engineered microbes to invade is that the competitive effect b_E, of the natural species on the engineered species is smaller than the intraspecific competition effect, a_N, of the natural species; refer to (3.1).

If $G_2\geqslant\gamma_e$ then λ_0 is negative and invasion will succeed regardless of the other parameters and the patch sizes, as we have discussed above.

However, if $G_2<\gamma_e<1$, then depending on the various parameter values, λ_0 can either be negative or positive. We shall now consider this case, in which the native-dominant steady state is unstable in the favourable patch, but stable in the unfavourable patch, in further detail. As we have seen above the relative sizes of the patches now become important.

At critical value, $\lambda_0=0$, the following inequality holds:

$$\sqrt{1-\gamma_e}\tan\left[\frac{l_1}{2}\sqrt{1-\gamma_e}\right]=D_2\sqrt{\frac{\gamma_e-G_2}{D_2}}\tanh\left[\frac{l_2}{2}\sqrt{\frac{\gamma_e-G_2}{D_2}}\right], \tag{5.9}$$

from which we find the critical length, l_1^*, of Patch 1 as

$$l_1^*=\frac{2}{\sqrt{1-\gamma_e}}\,\text{arc}\tan\left[\sqrt{\frac{D_2(\gamma_e-G_2)}{1-\gamma_e}}\tanh\left\{\frac{l_2}{2}\sqrt{\frac{\gamma_e-G_2}{D_2}}\right\}\right].$$

For $l_1<l_1^*$ the native-dominant steady state would be stable, since λ_0 would be positive, while for $l_1>l_1^*$, λ_0 would be negative and the native-dominant steady state unstable. So, as shown earlier in this section, invasion will succeed if the favourable patch is large enough compared to the unfavourable patch.

Note that as l_2 increases towards infinity the boundary curve approaches an asymptote

$$\lim_{l_2 \to \infty} l_1(l_2) = l_1^c = \frac{2}{\sqrt{1-\gamma_e}} \arctan \sqrt{\frac{D_2(\gamma_e - G_2)}{1-\gamma_e}}. \tag{5.10}$$

Thus invasion will always succeed, regardless of the unfavourable patch size, if $l_1 \geqslant l_1^c$. Furthermore, since

$$l_1^c > l_1^m = \frac{2 \arctan \infty}{\sqrt{1-\gamma_e}} = \frac{\pi}{\sqrt{1-\gamma_e}},$$

invasion will succeed regardless of the values of l_2, G_2 ($<\gamma_e$) and D_2 if $l \geqslant l_1^m$. The stability region in terms of l_1 and l_2, for the case when $G_2 < \gamma_e$, is shown in Fig. 3(a).

Likewise we can draw a stability curve for γ_e versus l_2. We have shown that if $\gamma_e < G_2$ invasion will always succeed independent of the length of Patch 2 (l_2). However, as γ_e increases beyond G_2 a stability curve appears from infinity at some critical value $\gamma_e = \gamma_e^c$. The asymptote of the curve, γ_e^c can be obtained from the following nonlinear relationship

$$\frac{D_2(\gamma_e^c - G_2)}{1-\gamma_e^c} = \tan^2\left(\frac{l_1}{2}\sqrt{1-\gamma_e^c}\right).$$

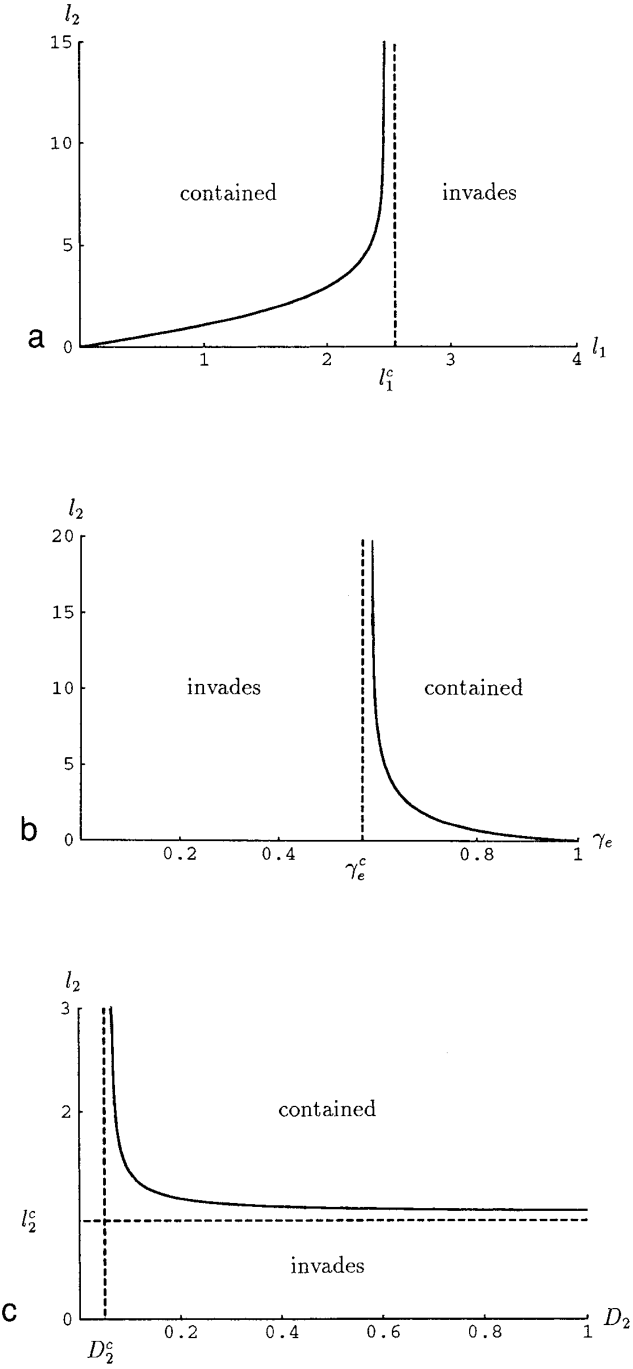
The stability region is shown in Fig. 3b. Note that, as l_1 increases towards l_1^c, the stability curve would appear for increasingly larger values of γ_e^c, while for $l_1 \geqslant l_1^c$, the stability curve would not appear at all.

The properties of the stability graph of G_2 versus l_2 is similar to that of γ_e versus l_2. For $G_2 > \gamma_e$ invasion is successful, however, as the value of G_2 decreases beyond γ_e, a stability curve appears from infinity at the asymptote

$$G_2^c = \gamma_e + \frac{\gamma_e - 1}{D_2} \tan^2\left(\frac{l_1}{2}\sqrt{1-\gamma_\varepsilon}\right).$$

The diffusion rate of the engineered species in the unfavourable patch, Patch 2, also plays an important role in determining the stability of the native-dominant steady state if $l_1 < l_1^*$. For sufficiently small values of D_2 invasion succeeds regardless of the value of l_2. Biologically this implies that the diffusion rate is so small in the unfavourable patch that the effect on the favourable patch is minimal. However, as D_2 increases, a stability curve appears from infinity at the critical asymptotic value $D_2 = D_2^c$, with

$$D_2^c = \frac{1-\gamma_e}{\gamma_e - G_2} \tan^2\left(\frac{l_1}{2}\sqrt{1-\gamma_e}\right).$$


l_2
15
10
5
0
contained
invades
a
1
2
3
4
l_1
l_1^c
l_2
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15
10
5
0
invades
contained
b
0.2
0.4
0.8
1
γ_e
γ_e^c
l_2
3
2
l_2^c
0
contained
invades
c
0.2
0.4
0.6
0.8
1
D_2
D_2^c

On the other hand, as $D_2 \to \infty$ the stability curve approaches an asymptote at l_2^c. Since from (5.9)

$$l_2 = 2\sqrt{\frac{D_2}{\gamma_e - G_2}}\,\text{arc tanh}\left[\sqrt{\frac{1-\gamma_e}{D_2(\gamma_e - G_2)}}\tan\left(\frac{l_1}{2}\sqrt{1-\gamma_e}\right)\right],$$

and, after applying L'Hopital's rule, we obtain

$$\lim_{D_2 \to \infty} l_2(D_2) = l_2^c = \frac{2\sqrt{1-\gamma_e}}{\gamma_e - G_2}\tan\left(\frac{l_1}{2}\sqrt{1-\gamma_e}\right).$$

Thus $l_2 < l_2^c$ the engineered microbes invade for any diffusion rate. In Fig. 3c, the graph showing the D_2 versus l_2 stability curve, is shown.

We can conclude that for $\gamma_e < 1$ necessary conditions for containment are $G_2 < \gamma_e$, and

$$l_1 < l_1^c, \qquad l_2 > l_2^c, \qquad \gamma_e > \gamma_e^c, \qquad G_2 < G_2^c, \qquad D_2 > D_2^c.$$

These inequalities point out that containment can be ensured either by decreasing l_1 or G_2, or by increasing γ_e, D_2, or l_2. Note that $\gamma_e < 1$ implies, in the context of Section 4, that the native-dominant steady state is unstable in the favourable patch, while, on the other hand, $G_2 < \gamma_e$ implies that it is stable in the unfavourable patch. The simplest strategy for ensuring the stability of the native-dominant steady state is, however, to have $\gamma_e > 1$ as discussed above.

It is important to note here that linear stability has been discussed in this section for the patchy domain as a whole. Even though invasion succeeds somewhere in the whole domain, it might be the case that, depending on initial conditions, invasion is only local and, in effect, contained in a certain patch. This could be the case when $1 > \gamma_e > G_2$. Although the native-dominant steady state can be stable for the full problem it is locally unstable in the favourable patch. Local invasion in a favourable patch, resulting from small nonzero initial perturbations for e in that patch, might thus occur in some cases. We shall consider such an example in more detail in Section 6.4.

FIG. 3. The stability diagram for the native-dominant steady state, obtained from (5.9), when we have spatially periodic diffusion coefficients and a spatially periodic carrying capacity for the engineered population. The boundary curves are indicated by the solid line, while the asymptotes are indicated by the dotted lines: (a) The (l_1, l_2) plane for $D_2 = 0.5$, $\gamma_e = 0.75$, and $G_2 = 0.5$. (b) The (γ_e, l_2) plane for $D_2 = 0.5$, $l_1 = 1.0$, and $G_2 = 0.5$. (c) The (D_2, l_2) plane for $\gamma_e = 0.75$, $l_1 = 1.0$, and $G_2 = 0.5$. The algebraic expressions for the asymptotes are given in the text; see Section 5.1.

5.2. *Invasion Steady States*

In the previous section we have obtained stability conditions for the native-dominant steady state, (e_1, n_1). As there are three other possible steady states, the zero steady state (e_0, n_0), the invader-dominant steady state (e_2, n_2), and the coexistence steady state (e_3, n_3) (see Section 3), we must now determine whether, and under which conditions, our solution would evolve into any of these steady states. Naturally in these cases, travelling wave solutions, connecting the unstable native-dominant steady state to non-native-dominant steady states, are expected.

We begin by examining the stability of zero steady state $(e_0, n_0) = (0, 0)$. Application of methods from the previous section indicates that the zero steady state is always dynamically unstable. Thus we would not expect a stable travelling wave solution connecting the zero steady state with the unstable native-dominant state.

Examination of the invader-dominant steady state, (e_2, n_2) with a spatially varying capacity function, $G(x)$, yields a spatially varying steady state solution, e_2. However, since are unable to obtain the exact solution for e_2 it is therefore not possible to examine its stability. We shall therefore assume, in the remainder of this section, that $G_2 = 1$, leaving the more involved case for the next section. The invader-dominant steady state now becomes $(e_2, n_2) = (1, 0)$.

Due to the symmetry of the model equations we can obtain, in complete analogy with the previous section, the linear stability conditions for the invader-dominant steady state. The initial sufficient condition for instability, similar to that in (5.5), is

$$(1-\gamma_n)\, l_1 \geqslant (\gamma_n - g_2)\, l_2.$$

Also, as before, a more exact stability boundary can be obtained, by applying the boundary conditions (3.6) and (3.7) to the separable solutions of (5.1). This gives as stability boundary

$$\sqrt{rd_1(1-\gamma_n)}\, \tan\left(\frac{l_1}{2}\sqrt{\frac{r(1-\gamma_n)}{d_1}}\right) = -\sqrt{rd_2(g_2-\gamma_n)}\, \tan\left(\frac{l_2}{2}\sqrt{\frac{r(g_2-\gamma_n)}{d_2}}\right)$$

and, as before, we can find a critical l_1^*,

$$l_1^* = 2\sqrt{\frac{d_1}{1-\gamma_n}}\, \text{arc tan}\left\{\sqrt{\frac{d_2(\gamma_n - g_2)}{d_1(1-\gamma_n)}}\, \tanh\left[\frac{l_2}{2}\sqrt{\frac{r(\gamma_n - g_2)}{d_2}}\right]\right\}.$$

Stability curves similar to those in Figs. 3 can be obtained, where G_2 is now replaced by g_2, γ_e is replaced by γ_n, and D_2 is replaced by d_2.

Again there are three cases to consider.

When $\gamma_n > 1 > g_2$, so that the invader-dominant steady state is stable in both patch types when considered in isolation (refer to Section 3), then the invader-dominant state is indeed stable for the full problem. On the other hand, if $1 > g_2 > \gamma_n$, so that the invader-dominant state is unstable in both the favourable and unfavourable patches when considered independently, it is unstable on the patchy domain.

The critical situations occurs when $1 > \gamma_n > g_2$ so that the invader-dominant steady state is unstable in the favourable patch and stable in the unfavourable patch. As was the case for the native-dominant state the stability of the global problem now depends on the parameter values. For example, the instability of the invader-dominant state on the full domain can be ensured by having the relative length of the favourable Patch 1, l_1, much larger than the unfavourable Patch 2, l_2.

We would, however, like to consider this stability curve in conjunction with the stability of the native-dominat steady state, (e_1, n_1). To obtain the stability boundary for (e_1, n_1) we assumed that $g_2 = 1$ and so we have to extend this assumption to this section as well. Similarly, since we have assumed here that $G_2 = 1$, this has to be extended to the results of Section 5.1.

With this in mind, we, third, consider the stability of the coexistence steady state when $G_2 = g_2 = 1$, so that (e_3, n_3) is as in (4.1). By linearising about (e_3, n_3), two coupled linear equations are obtained. Looking for solutions proportional to $e^{-\lambda t}$ gives a set of two ordinary differential equations in which the sign of λ determines the dynamics stability of the coexistence steady state. We again obtain two separable solutions for this sect of equations, each valid for one of the two types of patches. Introducing the continuity conditions (3.6) and (3.7) leads to a set of eight linear equations. From the solvability condition we can determine the sign of the smallest eigenvalue $\lambda = \lambda_0$. This is obtained by setting the determinant of the following matrix equal to zero,

$$\begin{bmatrix} \cosh(l_1\theta_+) & \cosh(l_1\theta_-) & -\cosh(l_2\beta_+) & -\cosh(l_2\beta_-) \\ k_{\theta_+}\cosh(l_1\theta_+) & k_{\theta_-}\cosh(l_1\theta_-) & -k_{\beta_+}\text{-}\cosh(l_2\beta_+) & -k_{\beta_-}\cosh(l_2\beta_-) \\ \theta_+\sinh(l_1\theta_+) & \theta_-\sinh(l_1\theta_-) & D_2\beta_+\sinh(l_2\beta_+) & D_2\beta_-\sinh(l_2\beta_-) \\ d_1\theta_+k_{\theta_+}\sinh(l_1\theta_+) & d_1\theta_-k_{\theta_-}\sinh(l_1\theta_-) & d_2\beta_+k_{\beta_+}\sinh(l_2\beta_+) & d_2\beta_-k_{\beta_-}\sinh(l_2\beta_-) \end{bmatrix},$$

where the expresions for $\theta_\pm$, $\beta_\pm$, $k_{\theta_\pm}$, and $k_{\beta_\pm}$ are given in Appendix B.

As can be seen from these the solvability condition is extremely involved in terms of the model parameters, and it is impossible to determine the role of the various model parameters in the stability of the coexistence steady state. Its stability has to examined separately for each set of parameter values.

Recall that a positive coexistence steady state can only exist if $\gamma_e < 1$ and $\gamma_n < 1$, or if $\gamma_e > 1$ and $\gamma_n > 1$. We are thus unable to demonstrate conclusively that the coexistence steady is stable if and only if $\gamma_e < 1$ and $\gamma_n < 1$, and unstable if and only if $\gamma_e > 1$ and $\gamma_n > 1$, as in the case for constant diffusion. However, detailed numerical experimentation, provides strong evidence in support of this.

We now examine our system for travelling wave solutions connecting the unstable native-dominant steady state to any of these other three steady states. We assume that there are no other steady states apart from the four uniform states and that all the solutions are bounded and nonnegative. Although we are considering spatially varying diffusion here these assumptions still seem reasonable in the light of the results of Grusa (1988) as discussed in Section 4.

When $G_2 = g_2 = 1$ everywhere and the native-dominant steady state (e_1, n_1) is unstable (i.e., $\gamma_e < G_2 = 1$), we can conclude that if the invader-dominant steady state (e_2, n_2) is unstable (i.e., $\gamma_n < g_2 = 1$) the coexistence steady state (e_3, n_3) is stable. A travelling wave of invasion could thus result connecting the native-dominant steady state (e_1, n_1) to the coexistence steady state (e_3, n_3).

On the other hand, when the invader-dominant steady state (e_2, n_2) is stable (i.e., $\gamma_n > g_2 = 1$) then the coexistence steady state is negative. Since all biologically reasonable solutions are nonnegative a travelling wave solution connecting the native-dominant steady state (e_1, n_1) to the invader-dominant steady state (e_3, n_3) is indicated.

However, as before, when the native-dominant and the invader-dominant steady states are linearly stable (i.e., $\gamma_e > 1$ and $\gamma_n > 1$) then invasion depends on the density of the engineered organisms introduced initially, that is $H(x)$ in (2.2). If the initial release is relatively small, containment is ensured.

So, in the light of the above analyses, $\gamma_e > 1$ and $\gamma_n < 1$ is the only strategy for containment that is safe for any initial microbe release density. Comparing this with the result of Section 4 we see that varying diffusion does not affect the stability conditions at all.

6. SPATIALLY VARYING CARRYING CAPACITIES AND DIFFUSION

In Section 5.1, because $g(x)$ is assumed to be a constant, the initial native-dominant steady state (e_1, n_1) is spatially uniform. However, to address carrying capacities that differ among the favourable and unfavourable patches for both populations, we assume now that $g(x)$ and $G(x)$ are spatially periodic functions, which means all three nonzero steady states have spatially periodic solutions. Because it is impossible to obtain exact expression for these spatially nonuniform steady state solutions it is difficult to determine their stability. However, by using regular perturbation solutions to the nonuniform steady states, approximate stability conditions can be found, as is shown below.

6.1. *Perturbation Solutions*

Here we obtain a regular perturbation solution to the initial native-dominant steady state, (e_1, n_1), when the carrying capacity of n in the unfavourable patch, $g(x) = g_2$, is different, but close to its carrying capacity in the favourable patch, $g(x) = 1$. In some types of environments this could indeed be the case and the perturbation solution would thus be in very close agreement with the exact solution.

As before, at the initial native-dominant steady state the density of the genetically engineered population, e_1 is zero everywhere. The initial steady state distribution of the natural population, n_1, is described by the equation

$$\frac{\partial}{\partial x}\left[d(x)\frac{\partial n_1}{\partial x}\right] + rn_1[g(x) - n_1] = 0. \tag{6.1}$$

To obtain an approximate solution to this equation we solve it in each of the respective patches before introducing the continuity conditions. We define a small perturbation parameter, ε, as the difference between the carrying capacities in the favourable and unfavourable patches,

$$\varepsilon = 1 - g_2, \qquad |\varepsilon| \ll 1.$$

To avoid notational ambiguity we shall represent the natural species, n_1, in Patch 1 by v and in Patch 2 by η.

In Patch 1 we assume a power series expansion of the form

$$v = 1 + \varepsilon v_1 + \varepsilon^2 v_2 + O(\varepsilon^3), \tag{6.2}$$

while in Patch 2 we assume

$$\eta = g_2 + \varepsilon\eta_1 + \varepsilon^2\eta_2 + O(\varepsilon^3). \tag{6.3}$$

We substitute these into the steady state equations coefficients of the same order of ε.

The equation for Patch 1 at $O(\varepsilon)$ is

$$d_2\frac{d^2 v_1}{dx^2} - rg_2 v_1 = 0,$$

which has the general solution

$$v_1 = A_1 \cosh\{\sqrt{(r/d_2)}\,(x - l_1/2 - ml)\} + B_1 \sinh\{\sqrt{(r/d_2)}\,(x - l_1/2 - ml)\},$$

where A_1 and B_1 are constants to be determined from the boundary conditions and $m = 0, \pm 1, \pm 2, \ldots$. Similarly, for Patch 2, we find

$$\begin{aligned}\eta_1 = {} & A_2 \cosh\{\sqrt{(rg_2/d_2)}\,(x + l_2/2 - (m+1)\,l)\} \\ & + B_2 \sinh\{\sqrt{(rg_2/d_2)}\,(x + l_2/2 - (m+1)\,l)\},\end{aligned}$$

with A_2 and B_2 constants and $m = 0, \pm 1, \pm 2, \ldots$.

By matching the continuity conditions (3.6) and (3.7) we find that both B_1 and B_2 are zero. The expressions for A_1 and A_2 are, however, nonzero and are given in Appendix C.

The equation for Patch 1 at $O(\varepsilon^2)$ is

$$d_1 \frac{d^2 v_2}{dx^2} - r v_2 = r v_1^2.$$

By adding the general and particular solutions we obtain a solution to this equation,

$$\begin{aligned}v_2 = {} & C_1 \cosh\left\{\sqrt{\frac{r}{d_1}}\left(x - \frac{l_1}{2} - ml\right)\right\} + F_1 \sinh\left\{\sqrt{\frac{r}{d_1}}\left(x - \frac{l_1}{2} - ml\right)\right\} \\ & - A_1^2 \cosh^2\left\{\sqrt{\frac{r}{d_1}}\left(x - \frac{l_1}{2} - ml\right)\right\} + A_1^2 \sinh^2\left\{\sqrt{\frac{r}{d_1}}\left(x - \frac{l_1}{2} - ml\right)\right\},\end{aligned}$$

where the constants C_1 and F_1 are to be determined from the continuity conditions. We obtain a similar solution in Patch 2, that is,

$$\begin{aligned}\eta_2 = {} & C_2 \cosh\left\{\sqrt{\frac{rg_2}{d_2}}\left(x + \frac{l_2}{2} - (m+1)\,l\right)\right\} \\ & + F_2 \sinh\left\{\sqrt{\frac{rg_2}{d_2}}\left(x + \frac{l_2}{2} - (m+1)\,l\right)\right\} \\ & - A_2^2 \cosh^2\left\{\sqrt{\frac{rg_2}{d_2}}\left(x + \frac{l_2}{2} - (m+1)\,l\right)\right\} \\ & + A_1^2 \sinh^2\left\{\sqrt{\frac{rg_2}{d_2}}\left(x + \frac{l_2}{2} - (m+1)\,l\right)\right\},\end{aligned}$$

with C_2 and F_2 constants.

By again using the boundary conditions we find that F_1 and F_2 are zero. The expressions for C_1 and C_2 are given in Appendix C.

We now have the Patch 1 perturbation solution

$$\begin{aligned} v = 1 + \varepsilon \left[A_1 \cosh \left\{ \sqrt{\frac{r}{d_2}}\,(x - l_1/2 - ml) \right\} \right] \\ + \varepsilon^2 \left[C_1 \cosh \left\{ \sqrt{\frac{r}{d_1}} \left(x - \frac{l_1}{2} - ml \right) \right\} \right. \\ - A_1^2 \cosh^2 \left\{ \sqrt{\frac{r}{d_1}} \left(x - \frac{l_1}{2} - ml \right) \right\} \\ \left. + A_1^2 \sinh^2 \left\{ \sqrt{\frac{r}{d_1}} \left(x - \frac{l_1}{2} - ml \right) \right\} \right] + O(\varepsilon^3), \end{aligned} \tag{6.4}$$

which matches with the Patch 2 perturbation solution,

$$\begin{aligned} \eta = g_2 + \varepsilon \left[A_2 \cosh \left\{ \sqrt{\frac{rg_2}{d_2}}\,(x - l_1/2 - ml) \right\} \right] \\ + \varepsilon^2 \left[C_2 \cosh \left\{ \sqrt{\frac{rg_2}{d_2}} \left(x + \frac{l_2}{2} - (m+1)\,l \right) \right\} \right. \\ - A_2^2 \cosh^2 \left\{ \sqrt{\frac{rg_2}{d_2}} \left(x + \frac{l_2}{2} - (m+1)\,l \right) \right\} \\ \left. + A_1^2 \sinh^2 \left\{ \sqrt{\frac{rg_2}{d_2}} \left(x + \frac{l_2}{2} - (m+1)\,l \right) \right\} \right] + O(\varepsilon^3). \end{aligned} \tag{6.5}$$

These perturbation solutions were compared with the numerical solutions and we found that even when ε is relatively large, which means the carrying capacity in the unfavourable patch $g(x) = g_2$ is much smaller than the carrying capacity in the favourable patch, $g(x) = 1$, they agree remarkably well with our the numerical calculated result (see Figs. 4 and 5).

6.2. *Conditions for Invasion*

Using the above perturbation solution we can determine the approximate stability boundaries of the, now spatially periodic, native-dominant steady state (e_1, n_1). As before it is sufficient to consider only the equation

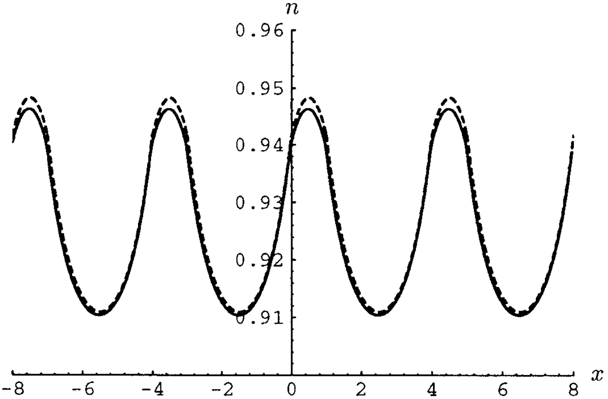

FIG. 4. A comparison of the perturbation solution (see (6.4) and (6.5)) to the numerically calculated solution for the native-dominant steady state. The perturbation solution is taken to $O(\varepsilon)$, with $\varepsilon = 0.1$, while the other parameters are $g_2 = 0.9$, $d_2 = 0.5$, $r = 1.0$, $l_1 = 1.0$, and $l_2 = 3.0$.

for the engineered microbial population which in its linearised form about the native-dominant steady state (e_1, n_1) is

$$\frac{\partial e}{\partial t} = \frac{\partial^2 e}{\partial x^2} + e[1 - \gamma_e v] \qquad \text{in Patch 1,} \tag{6.6a}$$

$$\frac{\partial e}{\partial t} = D_2 \frac{\partial^2 e}{\partial x^2} + e[G_2 - \gamma_e \eta] \qquad \text{in Patch 2,} \tag{6.6b}$$

where v and η are the perturbation solutions to n_1 in Patch 1 and Patch 2, respectively; see (6.4) and (6.5).

- The corresponding characteristic equation is

$$\frac{\partial}{\partial x}\left(D(x)\frac{\partial e}{\partial x}\right) + [G(x) - \gamma_e n_1 + \lambda]\, e = 0, \tag{6.7}$$

which is valid for $|e| \ll 1$.

Since the functions $G(x) - \gamma_e n_1(x)$ and $D(x)$ are periodic in l,

$$D(x) = D(x + l), \qquad G(x) - \gamma_e n_1(x) = G(x + l) - \gamma_e n_1(x + l), \tag{6.8}$$

we can use results of Hill's equation to examine the stability of the native-dominant steady state.

As in Section 5.1 we again employ the results of Appendix A, but now in conjunction with the perturbation solution for n_1 (6.3). For illustrative purposes we consider here the perturbation solution only to $O(\varepsilon)$. This

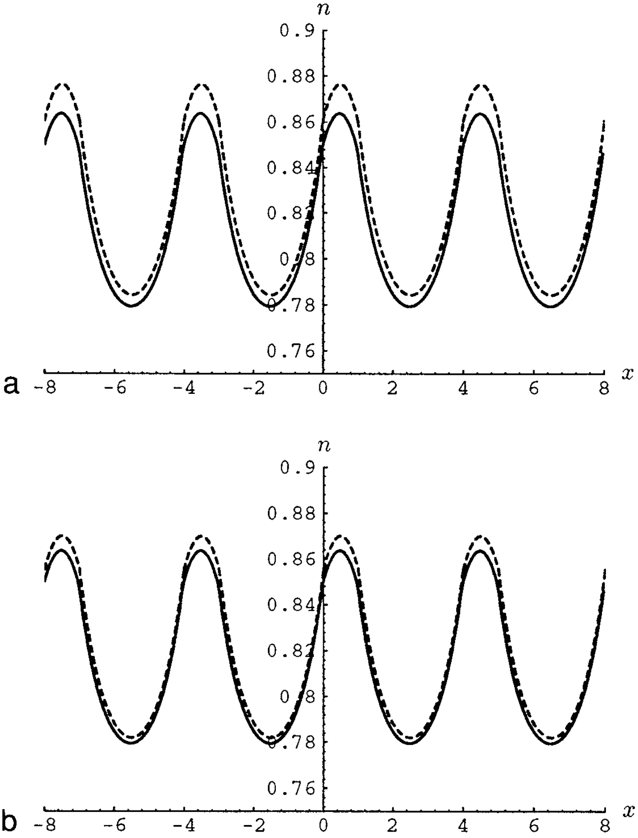

FIG. 5. Here we compare the native-dominant steady state perturbation solution (see (6.4) and (6.5)) to the numerically calculated solution for a relatively large $\varepsilon = 0.25$. The parameter values are $g_2 = 0.75$, $d_2 = 0.5$, $r = 0.1$, $l_1 = 1.0$, and $l_2 = 3.0$. In (a) the perturbation solution is taken to $O(\varepsilon)$, while in (b) it is taken to $O(\varepsilon^2)$.

gives a good approximation to the actual solution for small enough values of ε as we have seen in Figs. 6 and 7.

We begin by rewriting (6.7) as

$$\frac{\partial}{\partial x}\left(D(x)\,\frac{\partial e}{\partial x}\right) + [\,Q(x) + \lambda + S\,]\,e = 0, \tag{6.9}$$

where S is a constant and

$$Q(x) = G(x) - \gamma_e n_1 - S.$$

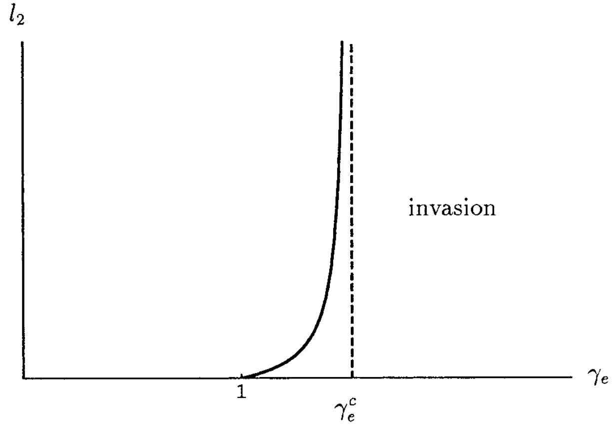

FIG. 6. The (γ_e, l_2) stability diagram for the native-dominant steady state, as obtained from (6.11), when $G_2 < g_2$ and we have spatially periodic diffusion coefficients and carrying capacities for both populations. The boundary curve is indicated by the solid line, while the asymptote $\gamma_e^c = G_2/g_2$ is indicated by the dotted line. Refer to cases (i) and (ii) in Section 6.4.

The constant S is chosen such that

$$\int_{\zeta}^{(\zeta+1)\,l} Q(x)\,dx = 0, \qquad \zeta \in \Re.$$

Using our perturbation solution to $O(\varepsilon)$, it can be shown that

$$S = (1-\gamma_e)\,l_1 + (G_2 - \gamma_e g_2)\,l_2 + \frac{2\gamma_e \varepsilon}{l}\left[A_1\sqrt{\frac{d_1}{r}}\sinh\left(\sqrt{\frac{r}{d_1}}\frac{l_1}{2}\right) - A_2\sqrt{\frac{d_2}{rg_2}}\sinh\left(\sqrt{\frac{rg_2}{d_2}}\frac{l_2}{2}\right)\right]$$

with A_1 and A_2 as in Appendix C.

As before there exists a series of monotonically increasing values $\lambda_i + S$, $i = 0, 1, 2, \ldots$, for which Eq. (6.9) has nonzero solutions. From the result in Appendix A it now follows that the smallest value in this series satisfies

$$\lambda_0 + S < 0.$$

A dynamically unstable solution to (6.6) corresponds to a nonzero solution of (6.7) for which $\lambda_0 < 0$. So, a sufficient condition for this to hold is that $S \geqslant 0$.

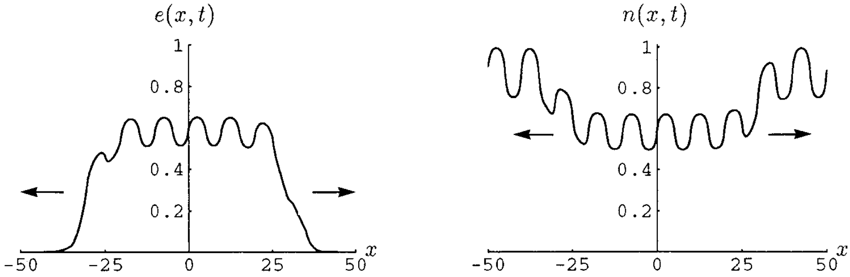

FIG. 7. A numerical solution of the model equations when parameters are such that coexistence is predicted for both the favourable and unfavourable patches, so $\gamma_e < \min\{1, G_2/g_2\}$ and $\gamma_n < \min\{1, g_2/G_2\}$. As expected invasion occurs via a travelling wave connecting the native-dominant steady state to the coexistence steady state. The parameters used in this example are $l_1 = l_2 = 5.0$, $D_2 = d_2 = 0.5$, $G_2 = g_2 = 0.75$, $\gamma_e = \gamma_n = 0.5$, and $r = 2.0$.

By substituting the expressions for A_1 and A_2 into S this inequality becomes

$$\left[\sqrt{\frac{rg_2}{d_2}}\coth\left(\sqrt{\frac{rg_2}{d_2}}\frac{l_2}{2}\right) + g_2\sqrt{\frac{r}{d_1}}\coth\left(\sqrt{\frac{r}{d_2}}\frac{l_1}{2}\right)\right]$$
$$\times\left[(1-\gamma_e)\,l_1 + (G_2 - \gamma_e g_2)\,l_2\right] \geqslant 2\gamma_e(g_2-1)^2. \tag{6.10}$$

Note, however, that the right-hand side of this inequality is $O(\varepsilon^2)$, since, by definition, $\varepsilon = 1 - g_2$. So, because the first factor of the expression on the left-hand side of the inequality is always positive, as a first approximation, we can replace the above condition by

$$(1-\gamma_e)\,l_1 > (\gamma_e g_2 - G_2)\,l_2, \tag{6.11}$$

which is a sufficient condition for the native-dominant steady state to the linearly unstable.

From the above we see that if the carrying capacities are equal in Patches 1 and 2, thus $g_2 = 1$, the inequality (6.10) reduces to the one we obtained for the case when there is no patchiness in the natural population's carrying capacity; see (5.5).

The full implications of this condition (6.11) will be discussed in Section 6.4 after the stability conditions for the other steady states have been examined.

6.3. *Invasion Steady States*

In the last section we determined an approximate sufficient condition for which the native-dominant steady state, (e_1, n_1), would be unstable. Here we examine the linear stability of the other steady state solution so as to determine the new solution, given that the native-dominant steady state is unstable.

As in Section 5.2 it is easy to show that the trivial steady state $(0, 0)$ is unstable for all relevant parameter ranges.

To determine the stability of the invader-dominant steady state, (e_2, n_2), we first obtain its perturbation solution, using as small parameter $\varepsilon = 1 - G_2$. In Patch 1 we then find

$$e = 1 + \varepsilon \left[\tilde{A}_1 \cosh\left(x - \frac{l_1}{2} - ml\right)\right] + \varepsilon^2 \left[\tilde{C}_1 \cosh\left(x - \frac{l_1}{2} - ml\right) - \tilde{A}_1^2 \cosh^2\left(x - \frac{l_1}{2} - ml\right) + \tilde{A}_1^2 \sinh^2\left(x - \frac{l_1}{2} - ml\right)\right] + O(\varepsilon^3),$$

while in Patch 2,

$$\begin{aligned} e = G_2 + \varepsilon &\left[\tilde{A}_2 \cosh\left\{\sqrt{\frac{G_2}{D_2}}\,(x + l_2/2 - (m+1)\,l)\right\}\right] \\ &+ \varepsilon^2 \left[\tilde{C}_2 \cosh\left\{\sqrt{\frac{G_2}{D_2}}\left(x + \frac{l_2}{2} - (m+1)\,l\right)\right\} \right. \\ &- \tilde{A}_2^2 \cosh^2\left\{\sqrt{\frac{G_2}{D_2}}\left(x + \frac{l_2}{2} - (m+1)\,l\right)\right\} \\ &\left. + \tilde{A}_1^2 \sinh^2\left\{\sqrt{\frac{G_2}{D_2}}\left(x + \frac{l_2}{2} - (m+1)\,l\right)\right\}\right] + O(\varepsilon^3), \end{aligned}$$

where the expressions for $\tilde{A}_1$, $\tilde{A}_2$, $\tilde{C}_1$, and $\tilde{C}_2$ are given in Appendix C.

As before we can obtain approximate stability curves for this steady state by using the result in Appendix A. From this we find that the sufficient approximate condition for the invader-dominant steady state (e_2, n_2) to be unstable is

$$\left[\sqrt{\frac{G_2}{D_2}} \coth\left(\sqrt{\frac{G_2}{D_2}}\,\frac{l_2}{2}\right) + G_2 \coth\left(\frac{l_1}{2}\right)\right] \times \left[(1 - \gamma_n)\, l_1 + (g_2 - \gamma_n G_2)\, l_2\right] \geqslant \frac{2r\gamma_n}{d_1}\,(1 - G_2)^2.$$

Again, since $1 - G_2 = \varepsilon$ we can approximate this condition by

$$(1 - \gamma_n)\, l_1 > (G_2 \gamma_n - g_2)\, l_2. \tag{6.12}$$

Now as before we can draw stability curves to determine the parameter values for which this steady state is unstable.

Unfortunately, although one could in principle find a regular perturbation solution to the coexistence steady state (e_3, n_3), the calculations are so involved as to be impractical. Furthermore, even with these perturbation solutions, it does not seem possible to do a stability analysis of the steady state as in the case with the invader-dominant and native-dominant steady states. However, it is possible to get bounds on the coexistence steady state for each species since the steady state values would always lie between the coexistence steady state value would always lie between the coexistence steady state values for Patch 1 and Patch 2 when considered in isolation. Thus,

$$\min\left\{\frac{\gamma_e g_2 - G_2}{\gamma_e\gamma_n - 1}, \frac{\gamma_e - 1}{\gamma_e\gamma_n - 1}\right\} \leqslant e_3 \leqslant \max\left\{\frac{\gamma_e g_2 - G_2}{\gamma_e\gamma_n - 1}, \frac{\gamma_e - 1}{\gamma_e\gamma_n - 1}\right\}, \qquad (6.13a)$$

$$\min\left\{\frac{\gamma_n G_2 - g_2}{\gamma_e\gamma_n - 1}, \frac{\gamma_n - 1}{\gamma_e\gamma_n - 1}\right\} \leqslant n_3 \leqslant \max\left\{\frac{\gamma_n G_2 - g_2}{\gamma_e\gamma_n - 1}, \frac{\gamma_n - 1}{\gamma_e\gamma_n - 1}\right\}. \qquad (6.13b)$$

6.4. *Discussion of Implications for Containment*

Using the results obtained above we discuss here the global behaviour of the model in the case of spatially varying carrying capacities. First, from inequalities (6.11) and (6.12) we see that varying carrying capacities determine the stability properties of the native-dominant and invader-dominant steady states, but that the diffusion parameters $d(x)$ and $D(x)$ are not involved in the stability conditions. Note that this does not mean diffusion rates are irrelevant to rates of spread when microbes escape—only that whether or not containment is possible is dominated by local habitat dynamics and the pattern of spatial variation in habitats. We summarize the results in Table I.

There are altogether four cases to consider. We begin by examining the stability of the native-dominant steady state when $0 < \gamma_e < 1$. For the favourable patch, considered in isolation, this means that either the engineered species, *e*, wins or the engineered and natural species, *e* and *n*, coexist; refer to Section 4. Under these two circumstances the inequality (6.11) will always be satisfied if $\gamma_e < G_2/g_2$, while a stability curve results if $\gamma_e > G_2/g_2$; see Fig. 6. This gives rise to the first two cases:

(i) When $\gamma_e < \min\{1, G_2/g_2\}$, then, depending on the value of γ_n, either the two species, *e* and *n*, coexist or the engineered species, *e* wins in the unfavourable patch when considered in isolation; again refer to Section 4. Since the native-dominant steady state is linearly unstable, invasion always succeeds. Intuitively this is to be expected, since *e* invades in both the favourable and unfavourable patch types.

TABLE I

Approximate Predictions of Coexistence and Extention and Invasion for Genetically Engineered Microbes Competing with a Wild-Type Strain

Predictions for isolated patch		Coexist in GOOD	GEM wins in GOOD	Wild type wins in GOOD	Either wins in GOOD
	Parameter ranges	$\gamma_e < 1, \gamma_n < 1$	$\gamma_e < 1, \gamma_n > 1$	$\gamma_e > 1, \gamma_n < 1$	$\gamma_e > 1, \gamma_n > 1$
Coexist in Bad	$\gamma_e < G_2/g_2$, $\gamma_n < g_2/G_2$	Coexist everywhere	GOOD: coexist if (6.12); otherwise GEM wins BAD: coexist	GOOD: coexist if (6.11); otherwise wild type wins BAD: coexist	Inconclusive
GEM wins in BAD	$\gamma_e < G_2/g_2$, $\gamma_n > g_2/G_2$	GOOD: coexist BAD: coexist if (6.12); otherwise GEM wins	GEM wins everywhere	GOOD: coexist if (6.11); otherwise wild type wins BAD: coexist if (6.12); otherwise GEM wins	Inconclusive
Wild type wins in BAD	$\gamma_e > G_2/g_2$, $\gamma_n < g_2/G_2$	GOOD: coexist BAD: coexist if (6.11); otherwise wild type wins	GOOD: coexist if (6.12); otherwise GEM wins BAD: coecist if (6.11); otherwise wild type wins	Wild type wins everywhere	Inconclusive
Either wins in BAD	$\gamma_e > G_2/g_2$, $\gamma_n > g_2/G_2$	Inconclusive	Inconclusive	Inconclusive	Inconclusive

Note. Here it is assumed that the environment consists of alternating “good” patches of length l_1 and “bad” patches of length l_2. We assume that both strains of microbes grow and disperse in this heterogeneous environment according to Eq. (3.3). The constants g_2 and G_2 scale the growth rates in the bad patch, as described in Eq. (2.4). The relative effects of inter-strain vs, intrastrain competition are characterized by the variables γ_e and γ_n, as described in Eq. (3.3). The predictions for an isolated “good” patch are shown in the top row, and predictions for an isolated “bad” patch are shown in the left column. The parameter spaces corresponding to the possible outcomes are shown in the adjacent row and column. Finally, the lower right section of the table shows the predicted outcome for alternating adjacent “good” and “bad” patches which are connected together. If a given strains “wins” this means that it invades and drives the competing strain extinct.

Crucially, the relative patch sizes do not play any role in determining the approximate stability of the native-dominant steady state.

We now examine which steady state would be reached on invasion. When $\gamma_n < 1$ and $\gamma_n < g_2/G_2$, so that n and e coexist in both patch types, it follows from (6.12) that the invader-dominant steady state is unstable. As expected the only possible stable steady state is, thus, the coexistence one. Recall that the zero steady state is always unstable. In this case, as is shown in Fig. 7, a travelling wave of invasion connects the native-dominant steady state to the coexistence steady state. On the other hand, when e wins in both the favourable and unfavourable patches, which implies $\gamma_n > 1$ and $\gamma_n > g_2/G_2$, then, as expected, e wins overall. This follows from the fact that the coexistence steady state is negative (see (6.13)), which, in turn, means that the invader-dominant steady state is the only relevant stable steady state.

However, when $G_2 > g_2$ and either e wins in Patch 1 or Patch 2 and coexists with n in the other patch (thus either $1 < \gamma_n < g_2/G_2$ or $g_2/G_2 < \gamma_n < 1$), the resulting invasion steady state is determined by the invader-dominant state stability condition (6.12). As is expected, the larger the patches in which coexistence is indicated, the more likely is the invader-dominant state to be unstable, in which case the only stable steady state could be coexistence state.

(ii) When the carrying capacity of the engineered population is smaller than that of the natural poplation in the unfavourable patches, $G_2 < g_2$, then γ_e could satisfy the inequality $G_2/g_2 < \gamma_e < 1$. Here, as in case (i), e either wins, or it coexists with n in Patch 1. However, the fact that n now wins in Patch 2, or, depending on the initial conditions, either n or e wins in Patch 2, complicates the situation considerabley. According to (6.11), for invasion the unfavourable patch, l_2, must be sufficiently small relative to the favourable patch, l_1, so that the effect of the natural species winning in the unfavourable patches is relatively small (Fig. 6).

When n wins in the unfavourable patch (i.e., $\gamma_n < g_2/G_2$) and coexistence is indicated in the favourable patch (i.e., $\gamma_n < 1$) then, according to (6.12), the invader-dominant state is unstable and so the coexistence steady state is reached on invasion. However, if e wins in the favourable patch (i.e., $1 < \gamma_n < g_2/G_2$) then either an invader-dominant steady state or a coexistence steady state is possible depending on whether (6.12) is satisfied. However, when the winner in the unfavourable pathc depends on the initial conditions (i.e., $\gamma_n > g_2/G_2$) our above analysis does not indicate the resulting steady state.

Next we assume that $\gamma_e > 1$, which implies either the natural species wins in the favourable patches or the winner in the favourably patches depends on the initial conditions. In the previous sections we saw, for spatially uniform carrying capacities, that containment is ensured when $\gamma_e > 1$. However, as we shall see below, when we have spatially varying carrying capacities, this no longer holds. Inequality (6.12) gives rise to a stability curve if $G_2 > g_2$ and $1 < \gamma_e < G_2/g_2$ (see Fig. 8), thus giving rise to two separate cases.

(iii) We begin by examining the case when $G_2 > g_2$ and γ_e is such that $1 < \gamma_e < G_2/g_2$. Under these conditions either e wins in the unfavourable patch or the winner depends on the initial conditions. From (6.11) we see that invasion now occurs only if the length of the *unfavourable* patch, l_2, is *large* in relation to the length of the favourable patch, l_1. As is illustrated in Fig. 8, this is especially true for values of γ_e close to $\gamma_e^c = G_2/g_2$. However, for a fixed Patch 1 length, as γ_e increases towards 1, a progressively smaller l_2 is required for ensuring ensuring invasion. Given that invasion succeeds, the next question is which steady state will be reached.

If n wins in the favourable patch (i.e., $\gamma_n < 1$) and the species coexist in Patch 2 (i.e., $\gamma_n < g_2/G_2$) then, according to (6.12), the invader-dominant state is always unstable and so the only stable steady state is the coexistence steady state. If, however, e wins in Patch 2 (i.e., $g_2/G_2 < \gamma_n < 1$) then the stability of the invader-dominant state depends on (6.12). If it is satisfied a coexistence state would develop; otherwise the engineered species could win.

The only other possibility to consider is when the winner in the favourable patch depends on the initial conditions and e wins in the unfavourable patch

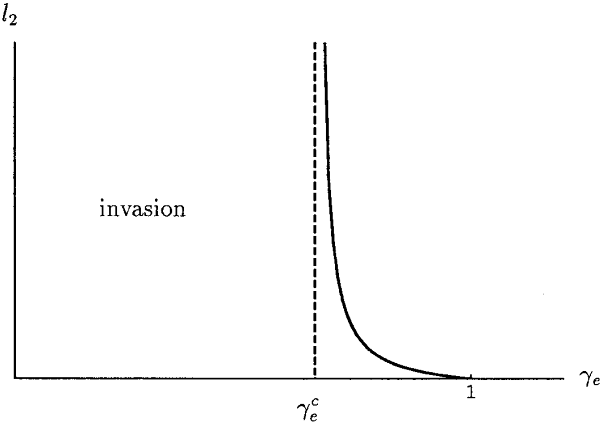

FIG. 8. The (γ_e, l_2) stability diagram for the native-dominant steady state, as obtained from (6.11), when we have spatially periodic diffusion coefficients and carrying capacities for the both populations. The boundary curve is indicated by the solid line, while the asymptote $\gamma_e^c = g_2/G_2$ is indicated by the dotted line. Refer to cases (iii) and (iv) in Section 6.4.

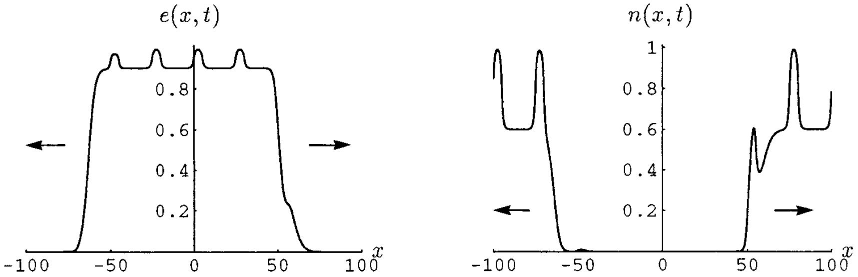

FIG. 9. A numerical solution of the model system when the parameters are such that the winner depends on the initial conditions for the favourable patch and the engineered species wins in the unfavourable patch, so $G_2 > g_2$, $1 < \gamma_e < G_2/g_2$ and $\gamma_n > \max\{1, g_2/G_2\}$. Now invasion occurs only if the unfavourable patch length, l_2, is large enough relative to the favourable patch length. This is indeed the case inour example and as a result the invader-dominant steady state is reached. The parameter used are $l_1 = 5$, $l_2 = 20$, $D_2 = d_2 = 0.75$, $G_2 = 0.9$, $g_2 = 0.6$, $\gamma_e = \gamma_n = 1.25$, and $r = 2.0$.

(i.e., $\gamma_n > 1 > g_2/G_2$). For this case it is not possible to predict the resulting steady state. In our numerical example we portray this situation using a case in which an invader-dominant steady state is reached on invasion (see Fig. 9; notice how large l_2 is relative to the other parameters).

(iv) The last case to consider is when $\gamma_e > \max\{1, g_2/G_2\}$. Under these conditions either the natural species wins or the winner depends on the initial conditions for both the favourable and unfavourable patches. If n wins in both patches, $\gamma_n < \min\{1, g_2/G_2\}$, then as is expected, n also wins overall.

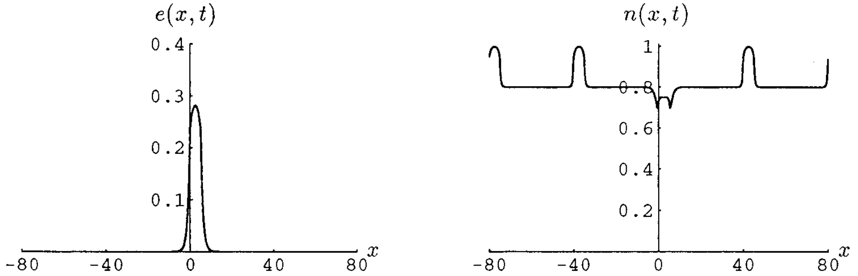

FIG. 10. A numerical solution of the model system when only localised invasion occurs. The parameters are such that the species coexist in the favourable patches and the natural population wins in the unfavourable patch, so $G_2 < g_2$, $G_2/g_2 < \gamma_e < 1$, and $\gamma_n < \min\{1, g_2/G_2\}$. The unfavourable patch is too large for the engineered species to cross, and invasion occurs only in the favourable patch into which it was introduced. Here it coexists with the natural species. The parameters used are $l_1 = 5$, $l_2 = 35$, $D_2 = d_2 = 0.25$, $G_2 = 0.5$, $g_2 = 0.8$, $\gamma_e = \gamma_n = 0.9$, and $r = 2.0$.

When n wins in either of the patch types and the winner depends on the initial conditions in the other patch type (i.e., either $1 < \gamma_n < g_2/G_2$ with $G_2 < g_2$ or $g_2/G_2 < \gamma_n < 1$, with $G_2 > g_2$), it is not evident from our analysis whether invasion succeeds or not. In both cases the stability condition (6.12) comes into play; see Fig. 10.

7. CONCLUSION

Although our model is too simple to be realistic, it identifies several key scenarios for the effect of a heterogeneous environment on invasion in competitive systems. First, although invasion is less likely to occur for large unfavorable "moats" surrounding an interior suitable habitat island, once the interior island get sufficiently large, no size of the surrounding hostile region can prevent an invasion. In general, a decrease in the relative size of patch type in which the native species dominates increases the chances that the exotic species can invade. The most interesting scenario involves a situation in which an invasion can succeed locally (within one patch) but fail globally. This is the situation in which results are not intuitively clear and the mathematical model is particularly helpful.

We suspect that the most important avenue for further theory is the examination of models that include convective transport as well as a possible distinction of sedentary and mobile classes into the model (Lewis *et al.*, 1995). This would account for the fact that microbes enter different mobile and immobile compartments, such as the roots of plants, various hosts, ground water, or wind. Finally, an absolutely crucial aspect of this study and extension of the basic model is the associated field studies to estimate the interspecific competition parameters.

APPENDIX A

We extend here a result found by Borg (1946) concerning the sign of the smallest eigenvalue of Hill's equation for the case when we have a periodic diffusion function. Our proof is a generalisation of that of Ungar (1961).

Consider the equation

$$\frac{\partial}{\partial x}\left(D(x)\frac{\partial u}{\partial x}\right) + [\sigma + Q(x)]\, u = 0,$$

where $D(x)$ and $Q(x)$ are periodic with period l and $D(x) > 0$.

We know from the theory on Hill's equation (refer to Section 3) that the periodic solution $u(x) = u_0(x)$ of period l corresponding to the smallest eigenvalue $\sigma = \sigma_0$ has no zeros. We may assume that $u_0(x) > 0$ for all x and, therefore, define the integrating factor $h(x)$ as

$$h(x) = \frac{d}{dx}(\ln u_0(x)).$$

Thus $h(x)$ is periodic with period l and is a solution to the equation

$$\frac{\partial}{\partial x}(D(x)\,h(x)) + D(x)\,h^2(x) = -\sigma_0 - Q(x).$$

Integrating this relationship over one period of length l yields

$$\int_{\zeta l}^{(\zeta+1)\,l} D(x)\,h^2(x)\,dx = -l\sigma_0, \qquad \zeta \in \Re,$$

since $D(x)$, $h(x)$, and $Q(x)$ are periodic. So $\sigma_0 = 0$ if the integral over $h^2(x)$ vanishes; otherwise $\sigma_0 < 0$ because $D(x) > 0$.

APPENDIX B

The expressions for $\theta_\pm$, $\beta_\pm$, $k_{\theta_\pm}$, and $k_{\beta_\pm}$, as used in Section 5.2, are

$$\theta_\pm = \frac{1}{2}\left[\frac{-b_\theta \pm \sqrt{b_\theta^2 - 4d_1 c_\theta}}{2d_1}\right]^{1/2},$$

$$\beta_\pm = \frac{1}{2}\left[\frac{-b_\beta \pm \sqrt{b_\beta^2 - 4D_2 d_2 c_\beta}}{2D_2 d_2}\right]^{1/2},$$

where

$$b_\theta = \frac{d_1(1-\gamma_e) + r(1-\gamma_n)}{\gamma_e\gamma_n - 1} + \lambda(1+d_1),$$

$$c_\theta = \frac{r(1-\gamma_e)(1-\gamma_n)}{1-\gamma_e\gamma_n} + \left(\frac{r(1-\gamma_n) + 1 - \gamma_e}{\gamma_e\gamma_n - 1}\right)\lambda + \lambda^2,$$

$$b_\beta = \frac{d_2(1-\gamma_e) + rD_2(1-\gamma_n)}{\gamma_e\gamma_n - 1} + \lambda(d_2 + D_2),$$

$$c_\beta = \frac{r(1-\gamma_e)(1-\gamma_n)}{1-\gamma_e\gamma_n} + \left(\frac{r(1-\gamma_n) + (1-\gamma_e)}{\gamma_e\gamma_n - 1}\right)\lambda + \lambda^2,$$

and

$$k_{\theta_+} = -\frac{(\lambda + \theta_+^2)(\gamma_e \gamma_n - 1) + (1 - \gamma_e)}{\gamma_e (1 - \gamma_e)},$$

$$k_{\theta_-} = -\frac{(\lambda + \theta_-^2)(\gamma_e \gamma_n - 1) + (1 - \gamma_e)}{\gamma_e (1 - \gamma_e)},$$

$$k_{\beta_+} = -\frac{(\lambda + D_2 \beta_+^2)(\gamma_e \gamma_n - 1) + (1 - \gamma_e)}{\gamma_e (1 - \gamma_e)},$$

$$k_{\beta_-} = -\frac{(\lambda + D_2 \beta_-^2)(\gamma_e \gamma_n - 1) + (1 - \gamma_e)}{\gamma_e (1 - \gamma_e)}.$$

APPENDIX C

The expressions for A_1, A_2, C_1, and C_2 as they appear in the perturbation solution for the native-dominant steady state in Section 6.1 are

$$A_1 = \frac{-\operatorname{cosech}\left(\sqrt{\frac{r}{d_1}}\frac{l_1}{2}\right)}{\frac{d_1}{g_2 d_2}\coth\left(\sqrt{\frac{r g_2}{d_2}}\frac{l_2}{2}\right) + \coth\left(\sqrt{\frac{r}{d_1}}\frac{l_1}{2}\right)},$$

$$A_2 = \frac{-\operatorname{cosech}\left(\sqrt{\frac{r g_2}{d_2}}\frac{l_2}{2}\right)}{\coth\left(\sqrt{\frac{r g_2}{d_2}}\frac{l_2}{2}\right) + \frac{g_2 d_2}{d_1}\coth\left(\sqrt{\frac{r}{d_1}}\frac{l_1}{2}\right)},$$

$$C_1 = \frac{(A_1^2 - A_2^2)\operatorname{cosech}\left[\sqrt{\frac{r}{d_1}}\frac{l_1}{2}\right]}{\frac{d_2}{g_2 d_1}\coth\left(\sqrt{\frac{r g_2}{d_2}}\frac{l_2}{2}\right) + \coth\left(\sqrt{\frac{r}{d_1}}\frac{l_1}{2},\right)},$$

$$C_2 = \frac{(A_2^2 - A_1^2)\operatorname{cosech}\left[\sqrt{\frac{r g_2}{d_2}}\frac{l_2}{2}\right]}{\coth\left(\sqrt{\frac{r g_2}{d_2}}\frac{l_2}{2}\right) + \sqrt{\frac{g_2 d_1}{d_2}}\coth\left(\sqrt{\frac{r}{d_1}}\frac{l_1}{2}\right)}.$$

The expressions for $\tilde{A}_1$, $\tilde{A}_2$, $\tilde{C}_1$ and $\tilde{C}_2$ as they appear in the perturbation solution for the invader-dominant steady state in Section 6.2 are

$$\tilde{A}_1 = \frac{-\operatorname{cosech}\left(\frac{l_1}{2}\right)}{\frac{1}{G_2 D_2}\coth\left(\sqrt{\frac{G_2}{D_2}}\frac{l_2}{2}\right) + \coth\left(\frac{l_1}{2}\right)},$$

$$\tilde{A}_2 = \frac{-\operatorname{cosech}\left(\sqrt{\frac{G_2}{D_2}}\frac{l_2}{2}\right)}{\coth\left(\sqrt{\frac{G_2}{D_2}}\frac{l_2}{2}\right) + \sqrt{G_2 D_2}\coth\left(\frac{l_1}{2}\right)},$$

$$\tilde{C}_1 = \frac{(A_1^2 - A_2^2)\operatorname{cosech}\left(\frac{l_1}{2}\right)}{\frac{D_2}{G_2}\coth\left(\sqrt{\frac{G_2}{D_2}}\frac{l_2}{2}\right) + \coth\left(\frac{l_1}{2}\right)},$$

$$\tilde{C}_2 = \frac{(A_2^2 - A_1^2)\operatorname{cosech}\left(\sqrt{\frac{G_2}{D_2}}\frac{l_2}{2}\right)}{\coth\left(\sqrt{\frac{G_2}{D_2}}\frac{l_2}{2}\right) + \sqrt{\frac{G_2}{D_2}}\coth\left(\frac{l_1}{2}\right)}.$$

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