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GENE FLOW AND THE COEVOLUTION OF PARASITE RANGE

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Abstract.—The geographic range of many parasites is restricted relative to that of their hosts. We study possible evolutionary mechanisms for this observation using a simple model that couples coevolution and demography. The model assumes that the environment consists of two habitats connected by movement and that coevolution is governed by quantitative traits. Our results demonstrate that host gene flow is an important determinant of parasite geographic range. Fluctuations in the rate of host gene flow cause shifts in parasite population densities and associated range expansions or contractions. In extreme cases, changing the rate of host gene flow can lead to global extinction of the parasite. Through a process we term demographic compensation, these shifts in parasite density may occur with little or no change in parasite adaptation to the host. As a consequence, reciprocal adaptation between host and parasite can become uncoupled from the rate of host gene flow.

Key words.—Demographic compensation, geographic, local adaptation, predator, prey, range evolution.

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The geographic ranges of many parasite or predator species are restricted relative to that of their host or prey. Few individuals, for instance, worry about contracting malaria in most of the world's temperate regions (Kiple 1993). Similar patterns emerge within a broad range of natural and agricultural systems, including lodgepole pine and pine squirrels (Benkman 1999), magpies and cuckoos (Soler et al. 1999), salamanders and predatory fish (Storfer and Sih 1998), and powdery mildew and wheat (Paillard et al. 2000). Often, good proximate explanations are available for these patterns. With malaria for instance, it is argued that the geographic range of *Plasmodium* is restricted by the absence of the appropriate *Anophiline* vectors (Kiple 1993). Although this is certainly true in the short term, it leaves unanswered the more ultimate question of why some parasites or predators do not adapt to novel environments or hosts at the periphery of their geographic ranges.

Two evolutionary explanations have drawn the majority of experimental and theoretical attention. One of these, put forward verbally by Haldane (1956), suggested that adaptation at the periphery of a species range may be swamped by gene flow from the range center. Empirical work has since provided broad support for the role of gene flow in impeding local adaptation (Camin and Ehrlich 1958; Stearns and Sage 1980; Dias et al. 1996; Stanton and Galen 1997; Storfer and Sih 1998). Theoretical investigations have also demonstrated the efficacy of this mechanism and clarified its dependence on mechanisms of density regulation (Holt 1996; Holt and Gomulkiewicz 1997) and rates of environmental change and gene flow (Garcia-Ramos and Kirkpatrick 1997; Kirkpatrick and Barton 1997). Another possibility, originally suggested by Darwin (1859), is that species borders are largely determined by interspecific competition. Recent theory developed to address this possibility demonstrated that competition alone is insufficient to limit species geographic ranges (Case and Taper 2000). When environmental gradients were also incorporated in this model, however, competition contributed to limiting species ranges. While Case and Taper sketched out a general framework for understanding range evolution in single species and coevolving competitors, no similar theoretical results are available for host-parasite or predator-prey interactions.

The importance of antagonistic coevolution to parasite or predator geographic range evolution is suggested by both empirical and theoretical results. Of particular interest are empirical studies demonstrating that parasites generally perform better on sympatric hosts (e.g., Ballabeni and Ward 1993; Lively and Jokela 1996; Mopper et al. 2000; McCoy et al. 2002). As a consequence, gene flow between spatially separated parasite populations should frequently lead to local maladaptation (Thompson 1994; Thompson et al. 2002). Empirical studies demonstrating local maladaptation in parasites or predators have often implicated gene flow as a potential cause, suggesting that this may frequently be the case (e.g., Storfer and Sih 1998; Kaltz et al. 1999; Oppliger et al. 1999). Theoretical work provides additional support that gene flow can lead to observed patterns of parasite or predator local maladaptation (e.g., Gandon et al. 1996; Lively 1999; Gomulkiewicz et al. 2000; Nuismer et al. 2000). Particularly intriguing are results suggesting that parasite maladaptation depends on the relative rates of host and parasite gene flow (Gandon et al. 1996; Gandon 2002). Together, this work suggests that there is ample opportunity for the geographic range of a parasite or predator to be directly affected by the rate of gene flow in another interacting species.

Our goal is to investigate exactly this type of possibility. We would like to know whether antagonistic coevolution, in conjunction with gene flow, can limit a parasite's geographic range. To this end, we use the framework developed by Kirkpatrick and Barton (1997) to study host-parasite and predator-prey coevolution. To the extent that this framework couples demography and evolution, our model will be similar to several existing models of spatially structured coevolution (Gandon et al. 1996; Hochberg and van Baalen 1998; Burdon and Thrall 1999; Thrall and Burdon 1999; Case and Taper 2000). Where our model will be quite different is in the genetic assumptions and the availability of analytical results. By assuming that coevolution is governed by quantitative traits and limiting our consideration to only two coupled communities, we will be able to generate analytical predictions

for the conditions favoring the evolution of restricted parasite range.

In addition to the question of parasite range evolution, we anticipate that our model will provide insight into several predictions made by the geographic mosaic theory of coevolution (Thompson 1994, 1997). Specifically, we are interested in evaluating whether the predicted patterns of local maladaptation and spatial heterogeneity in coevolved traits arise in our model. These predictions have been verified by several population genetic models that lack demography (Gomulkiewicz et al. 2000; Nuismer et al. 2000). The results of our model will help to evaluate how robust these predictions are to specific genetic and demographic assumptions.

The Model

Coevolution is mediated by a single quantitative trait in each species whose value in the parasite is denoted as p and in the host as h. The mean values of the traits in patch i are written $\bar{p}_i$ and $\bar{h}_i$, respectively. The breeding values for both traits are assumed to follow Gaussian distributions. Their additive genetic variances, denoted G_P and G_H, respectively, are initially assumed to be constant in time and space. (We relax this assumption in a later section of the paper.) The phenotypic variance for the parasite trait is written V_P. We assume that both species grow continuously and have overlapping generations.

The fitness of an individual parasite is determined by two factors: its interaction with hosts and stabilizing selection caused by other factors (which, for convenience, we will refer to as abiotic causes of selection). The intrinsic rate of increase of a parasite with phenotype p in patch i is

$$r_i^P(p) = r_0 + \int \delta_i^P(p, h)\phi_i^H(h)\, dh - \gamma_P p^2. \quad (1)$$

The parameter r_0 represents a baseline population growth rate for the parasite, which we assume is identical in the two patches. For a parasite species that is obligate on the host, r_0 will be negative; in other cases, it may be positive. The integral accounts for the fitness effects of interacting with hosts in patch i. The function $\delta_i^P(p, h)$ describes the effects on the fitness of parasites with phenotype p when they interact with hosts of phenotype h, and the function $\phi_i^H(h)$ is the density of hosts with phenotype h in patch i. This assumes random encounters between parasite and host. The parameter γ_P measures the intensity of abiotic stabilizing selection on the parasite, with larger (positive) values corresponding to stronger selection. The optimal value of the parasite trait is assumed to be the same in both patches, and we have scaled the measurement of the trait so that this optimum is at $p = 0$.

The host also experiences selection resulting from the coevolutionary interaction and from abiotic sources. In contrast to the parasite, however, we assume that the demographic effects of selection are weak and that host population density is maintained at a fixed level by density dependence. This assumption is reasonable for many plant and animal species whose density is limited by access to space (Hubbell 2001), but not for hosts whose densities are strongly impacted by parasites. The intrinsic rate of increase of an individual with phenotype h in patch i results from the combined action of these forces

$$r_i^H(h) = \Gamma(N_i^H) + \int \delta_i^H(p, h)\phi_i^P(p)\, dp - \gamma_H(\theta_i - h)^2. \quad (2)$$

The function $\Gamma(N_i^H)$ represents density dependence in the host and maintains population density at a constant and equal level in both patches. For convenience (and without loss of generality), we scale the measurement of host density such that its value is one. The integral accounts for the fitness effects of interacting with parasites in patch i. Here $\delta_i^H(p, h)$ is the fitness effect on a host with phenotype h interacting with a parasite of phenotype p in patch i, and $\phi_i^P(p)$ is the density of parasites with that phenotype in that patch. This assumes random encounters between host and parasite. Abiotic selection is captured by the third term on the right hand side, where γ_H is the intensity of abiotic stabilizing selection that favors an optimal host trait value of $h = \theta_i$ in patch i.

Although equations (1, 2) are quite general with respect to the functional relationship between species, this paper will focus specifically on a scenario of ''coevolutionary escalation'' (e.g., Saloniemi 1993; Abrams and Matsuda 1997; Brodie and Brodie 1999). Our interest in this situation is motivated by its demonstrated importance in interactions between plants and herbivores such as that seen with the moth *Depressaria pastinacella* and the wild parsnip *Pastinaca sativa* (Berenbaum and Zangerl 1998). In this interaction, plants with greater concentrations of furanocoumarins are more resistant to moth attack. Similarly, moths with greater concentrations of detoxifying enzymes are better able to attack well-defended host plants (Berenbaum et al. 1986; Berenbaum and Zangerl 1992). For this type of coevolutionary interaction, the fitness consequences of an encounter between a host and parasite can be represented by

$$\delta_i^P(p, h) = \alpha_P(p - h) \quad \text{and} \quad (3a)$$

$$\delta_i^H(p, h) = -\alpha_H(p - h). \quad (3b)$$

The parameters α_P and α_H (both positive) determine the fitness effects of an encounter between a host with phenotype h and a parasite with phenotype p, for the parasite and host, respectively. Equations (3a, b) are mathematically convenient, but they can also be viewed as linear approximations to more realistic interaction functions. Although equation (3b) may seem to imply that a host could benefit through interacting with the parasite when $h > p$, this is not the case. Because we assume that host density is fixed, (3b) implies that hosts with larger phenotypic values are relatively more resistant to parasite attack, not that they actual do better when attacked.

The last assumption needed regards movement. Parasites and hosts move between the patches at constant rates, which we denote as m_P and m_H, respectively. The effects of movement between the habitat patches are twofold. First, movement homogenizes population densities and population mean phenotypes. Second, movement may cause changes in the genetic variances. For the moment, we ignore this latter effect and assume that movement does not alter variances. We later evaluate the validity of this assumption through numerical simulations.

Under these assumptions, the total parasite density in patch i changes at a rate

$$\frac{dN_i^{\mathrm{P}}}{dt} = \int r_i^{\mathrm{P}}(p)\phi_i^{\mathrm{P}}\,dp + m_{\mathrm{P}}(N_j^{\mathrm{P}} - N_i^{\mathrm{P}})$$
$$= [r + \alpha_{\mathrm{P}}(\bar{p}_i - \bar{h}_i) - \gamma_{\mathrm{P}}\bar{p}_i^2]N_i^{\mathrm{P}} + m_{\mathrm{P}}(N_j^{\mathrm{P}} - N_i^{\mathrm{P}}), \quad (4)$$

where $r = r_0 - \gamma_{\mathrm{P}}V_{\mathrm{P}}$ is a rescaled baseline growth rate for the parasite, and $\bar{h}_i$ and $\bar{p}_i$ are the population mean phenotypes of host and parasite in patch i, respectively. The first term in the leftmost equation accounts for local population growth and the second for the effects of immigration and emigration. Notice that we assume there is no explicit density regulation for the parasite; its population size is limited only by the effects of selection and migration.

Evolution of the host and parasite trait means is caused by selection and gene flow. The contribution of selection is given by the product of the additive genetic variance and the selection gradient, which is calculated as the derivative of the population's intrinsic rate of increase with respect to the trait mean (Lande 1982). Thus, we have:

$$\frac{d\bar{p}_i}{dt} = G_{\mathrm{P}}\left(\frac{d}{d\bar{p}_i}\bar{r}_i^{\mathrm{P}}\right) + m_{\mathrm{P}}\frac{N_j^{\mathrm{P}}}{N_i^{\mathrm{P}}}(\bar{p}_j - \bar{p}_i)$$
$$= G_{\mathrm{P}}(\alpha_{\mathrm{P}} - 2\gamma_{\mathrm{P}}\bar{p}_i) + m_{\mathrm{P}}\frac{N_j^{\mathrm{P}}}{N_i^{\mathrm{P}}}(\bar{p}_j - \bar{p}_i) \quad \text{and} \quad (5a)$$

$$\frac{d\bar{h}_i}{dt} = G_{\mathrm{H}}\left(\frac{d}{d\bar{h}_i}\bar{r}_i^{\mathrm{H}}\right) + m_{\mathrm{H}}(\bar{h}_j - \bar{h}_i)$$
$$= G_{\mathrm{H}}[\alpha_{\mathrm{H}}N_i^{\mathrm{P}} - 2\gamma_{\mathrm{H}}(\bar{h}_i - \theta_i)] + m_{\mathrm{H}}(\bar{h}_j - \bar{h}_i), \quad (5b)$$

where $\bar{r}_i^{\mathrm{P}} = \int r_i^{\mathrm{P}}\phi_i^{\mathrm{P}}\,dp$ and $\bar{r}_i^{\mathrm{H}} = \int r_i^{\mathrm{H}}\phi_i^{\mathrm{H}}\,dh$. The rate of evolution of the parasite trait is independent of the value of the host trait mean. That is a consequence of the coevolutionary escalation scenario described by equations (3), which generates a constant force of directional selection on the parasite (seen in the $G_{\mathrm{P}}\alpha_{\mathrm{P}}$ term in 5a). Likewise, the host trait's evolution does not depend explicitly on the parasite trait mean. The parasite trait does have an indirect effect through the parasite's density, however, and we will see this has interesting consequences for their interaction.

The six equations given by (4, 5) with $i = 1, 2$ completely describe the dynamics of our model. We will now analyze its consequences, first assuming no movement of either species, then allowing for movement of either the parasite or host, and finally assuming both species move.

No Movement of Parasites or Hosts

Analysis of equations (4, 5) shows that in the absence of movement there are two possible equilibria for patch i. The first occurs when the parasite is extinct and the mean host phenotype is at its abiotic optimum, θ_i. This equilibrium is unstable, and the parasite can invade, whenever

$$N_i^* \equiv \frac{2\gamma_{\mathrm{H}}}{\alpha_{\mathrm{H}}}\left(-\theta_i + \frac{r}{\alpha_{\mathrm{P}}} + \frac{\alpha_{\mathrm{P}}}{4\gamma_{\mathrm{P}}}\right) \quad (6)$$

is positive. In that case, N_i^* is the parasite's equilibrium density. If N_i^* is negative, then patch i is a demographic sink for the parasite, and it will not persist there without migration. An important conclusion from equation (6) is that the optimum favored by stabilizing selection on hosts, represented by θ_i, influences whether the parasite invades. Specifically, the larger the host optimum θ_i, the less likely it is that the parasite will be able to invade. That is because the host will be preadapted to resist the parasite if larger values of h are favored by abiotic selection. We will refer to habitats where N_i^* is negative as ''parasite sinks'' and those where N_i^* is positive as ''parasite sources'' throughout.

When the parasite is able to invade, equations (4, 5) show it reaches an equilibrium density even though the model includes no explicit density dependence. That is because, as its density increases, the parasite exerts stronger directional selection on its host. The host then responds evolutionarily, making the biotic environment harsher for the parasite. Ultimately, this coevolutionary interaction limits the parasite's density. The host and parasite trait means evolve to a stable equilibrium at

$$p_i^* = \frac{\alpha_{\mathrm{P}}}{2\gamma_{\mathrm{P}}} \quad \text{and} \quad (7a)$$

$$h_i^* = \frac{r}{\alpha_{\mathrm{P}}} + \frac{\alpha_{\mathrm{P}}}{4\gamma_{\mathrm{P}}} = \frac{r}{\alpha_{\mathrm{P}}} + \frac{p_i^*}{2}. \quad (7b)$$

This result has a remarkable feature. At equilibrium, the parasite and host trait means are independent of many aspects of the host's biology, in particular the pattern of abiotic selection (that is, θ_i and γ_{H}) and the fitness effect of the parasite on the host (α_{H}). As a consequence, parasite density and adaptation to the host may become uncoupled. This is the first of several examples we will see of what we call ''demographic compensation.'' By that we mean there is a feedback between parasite density and biotic selection that causes the host and parasite traits to evolve to the same equilibrium, regardless of the pattern of abiotic selection acting on the host. Figure 1 shows an example that gives an intuitive explanation. If the stabilizing selection exerted by the abiotic environment favors weak resistance to the parasite, the parasite population density becomes large. This, in turn, generates strong selection on the host for greater resistance, causing the host trait to equilibrate far from its abiotic optimum (Fig. 1A). Now consider the case in which stabilizing selection exerted by the abiotic environment favors a strong resistance phenotype in the host. The parasite's density is then suppressed, generating only weak directional selection for increased host resistance. The combination of abiotic selection that favors a high level of resistance and weaker directional selection for resistance from the parasite causes the host trait to evolve to the same equilibrium as in the first case (Fig. 1B). Because the host evolves to the same equilibrium in both cases, the pattern of selection experienced by the parasite is the same in both. Consequently, the parasite trait also evolves to the same point in the two cases. In sum, demographic changes in the parasite compensate for changes in abiotic selection on the host, leading to the same evolutionary outcome.

Hosts Move, Parasites Do Not

In this section we extend our consideration to two habitats connected by host gene flow. We initially restrict our atten-

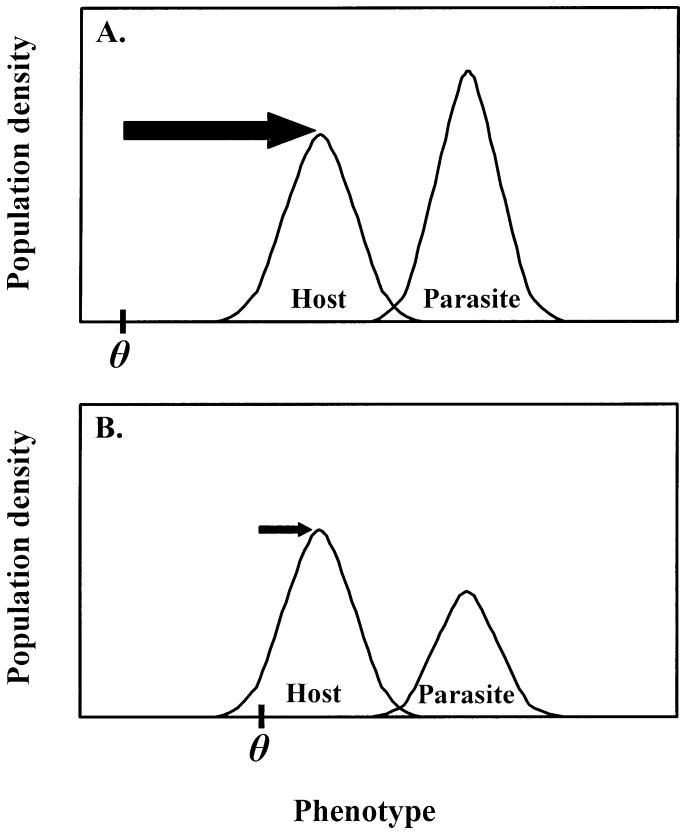

FIG. 1. A schematic diagram of demographic compensation. The phenotypic distributions for both host and parasite are shown in absolute numbers such that the height of the curve increases with increasing population size. (A) Stabilizing selection favors a low value (θ) of the host trait, strongly constraining the evolution of host resistance. As a consequence, the parasite can reach a relatively large population density that exerts strong selection for host resistance (depicted by the large bold arrow). (B) Stabilizing selection favors a larger value (θ) of the host trait, causing the host to be better adapted to the parasite. As a result, the parasite reaches a substantially lower density than in (A), leading to weaker selection for host resistance. The ultimate outcome is that the host and parasite traits evolve to the same means in (A) and (B) but parasite density is much greater in (A).

tion to host movement in isolation for two reasons. First, in the absence of parasite movement a much more thorough mathematical analysis is possible. Second, these results are directly applicable to a wide range of parasite taxa with very low rates of movement between habitat patches (Edmunds and Alstad 1978; Kaltz et al. 1999; Oppliger et al. 1999). In a later section, we will relax this assumption and consider movement of both host and parasite.

Analysis of equations (4, 5) shows that three kinds of equilibria are possible. The first occurs when the parasite is extinct in both patches. In that case, the host trait means evolve to a simple migration-selection equilibrium. The parasite can only invade this equilibrium if

$$0 < N_i^* + \frac{m_H}{G_H\gamma_H}\bar{N}^* \tag{8}$$

in at least one of the two patches. The quantity $\bar{N}^* = (N_1^* + N_2^*)/2$ is important and will appear several times in what follows. If $\bar{N}^*$ is positive, then the two patches are, on average, source populations for the parasite; if it is negative the patches are, on average, a sink.

Condition (8) shows that host gene flow can either facilitate or impede the invasion of the parasite, depending on whether $\bar{N}^*$ is positive or negative, respectively. When invasion is facilitated, gene flow in the host prevents it from coevolving effectively in response to the local parasite population. But when the environment is, on average, a sink for the parasite ($\bar{N}^*$ is negative), then gene flow from patch 2 actually enhances the host's ability to resist the parasite in patch 1. In this situation, hosts in patch 2 are well defended against the parasite and so the arrival of their genes into patch 1 improves that population's resistance. Indeed, the model shows that host gene flow can cause the parasite to become extinct globally (when condition 8 is no longer met in either patch).

A second kind of equilibrium occurs when the parasite is able to invade one but not both patches. This occurs when condition (8) holds in at least one patch, and one of the patches is a parasite source (say, patch 1) and other is a parasite sink (say, patch 2). At this second kind of equilibrium, $\hat{p}_1 = p^*$, $\hat{h}_1 = h^*$,

$$\hat{N}_1 = N_1^* + \frac{m_H}{m_H + 2G_H\gamma_H}N_2^*, \quad \text{and} \tag{9a}$$

$$\hat{h}_2 = \left(\frac{m_H}{m_H + 2G_H\gamma_H}\right)h^* + \left(\frac{2G_H\gamma_H}{m_H + 2G_H\gamma_H}\right)\theta_2. \tag{9b}$$

Again demographic compensation is at work: the parasite and host trait means in patch 1 evolve to the same values they reach in an isolated patch and are unaffected by host gene flow. Thus, parasite adaptation to the host is uncoupled from host gene flow. Parasite density is, however, always decreased by host gene flow (because N_2^* is negative).

The third kind of equilibrium is reached when $N_i^* > 0$ in both patches. The host and parasite trait means and the parasite densities then equilibrate at the single-patch values given by equations (6, 7). In this case, host gene flow has no effect on any of the trait means or parasite densities. A consequence is that substantial spatial heterogeneity in parasite population density can be maintained even when parasite adaptation to the host is homogenous across space. Demographic compensation again explains why the local selection pressures and gene flow acting on the host populations do not affect the outcome.

Parasites Move, Hosts Do Not

We next consider what happens when parasites move between patches but hosts do not. When the patches act, on average, as sources for the parasite (that is, $\bar{N}^* > 0$), a local stability analysis of equations (4, 5) shows that increasing parasite movement always favors parasite invasion. When the average habitat is a sink ($\bar{N}^* < 0$), however, movement makes invasion more difficult. In fact, it is possible to find examples in which parasite movement causes the global extinction of the parasite (Fig. 2B).

Numerical integration of equations (4, 5) shows that changes in the rate of parasite movement affect the equilibrium for the host's trait mean. When one patch acts as a source and

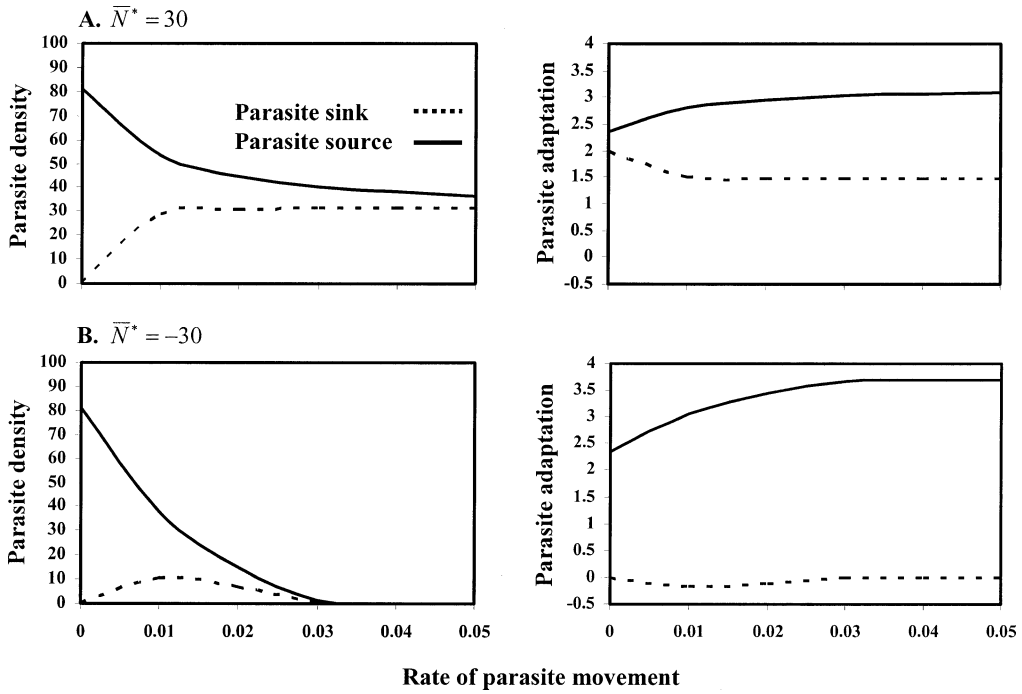

FIG. 2. Parasite densities (left) and adaptation to the host (right) when only the parasite moves. Parasite adaptation to the host was defined as $\bar{p}_i - \bar{h}_i$ such that larger values indicate increasing adaptation. In (A) $N^* = 30$ and the overall habitat acts as a parasite source. In (B) $N^* = -30$ and the overall habitat acts as a parasite sink. All panels were generated by numerical integration of equations (4, 5) with $\alpha_H = 0.0001$, $\alpha_P = 0.01$, $\gamma_P = 0.002$, $\gamma_H = 0.003$, $G_H = 4.85$, $G_P = 5$, $r = -0.011$, $\theta_1 = -1.2$, and (A) $\theta_2 = 0.5$, (B) $\theta_2 = 2.5$.

the other as a sink ($N_1^* < 0$ and $N_2^* > 0$, or $N_1^* > 0$ and $N_2^* < 0$), movement causes the difference between the host and parasite means to change in opposite directions in the two patches. In the source population, increasing movement enhances parasite adaptation to the host, whereas in the sink population parasite adaptation is generally reduced (Fig. 2). This shift is a natural consequence of parasite movement redistributing parasite density across the two habitats. As parasite density increases within the sink population, selection on host resistance becomes more intense, causing the host trait mean to increase. Within source populations, parasite density decreases, with the opposite impact on the host. These results suggest that, unlike host gene flow, parasite movement shapes patterns of reciprocal adaptation in an intuitive fashion.

Both Hosts and Parasites Move

When both species move, the demographic impact of host gene flow can be greatly magnified by parasite movement. Specifically, with parasite movement, host gene flow can cause the extinction of the parasite throughout its geographic range (Fig. 3B). Numerical analysis of equations (4, 5) suggests that this effect is most pronounced when one patch is a parasite source and the other a sink and the average habitat acts a sink ($N_i^* > 0$, $N_j^* < 0$, and $\bar{N}^* < 0$). Increasing host gene flow then leads to an overall decrease in parasite density and ultimately global extinction (Fig. 3B). Decreasing the rate of host gene flow, however, allows parasite density to increase. In extreme cases, decreasing the rate of host gene flow allows a parasite that could not invade either patch to occupy both. When the overall habitat behaves as a source ($\bar{N}^* > 0$), the impact of host gene flow is less dramatic. In this case, increasing host gene flow will never cause global parasite extinction, but will act to decrease overall parasite density nonetheless.

Numerical simulations further demonstrate that changes in host movement rates affect patterns of parasite adaptation. In particular, greater rates of host gene flow enhance parasite adaptation to the host in the sink population, but reduce adaptation in the source (Fig. 3B). This result suggests that demographic compensation, ubiquitous when only the host moves, is reduced in the presence of parasite movement (cf. Fig. 3A, B). To further explore this result, we calculated an index of relative parasite adaptation for various rates of host and parasite gene flow. This index divides the observed value of parasite adaptation for any particular level of host gene flow by the value that would occur in the absence of host gene flow. These numerical results demonstrate that parasite adaptation becomes increasingly coupled to the rate of host gene flow as parasite movement increases (Fig. 4). This suggests that increasing rates of parasite movement generally reduce the importance of demographic compensation.

Relaxing the Genetic Assumptions

We have assumed to this point that the coevolving traits of the parasite and host have Gaussian-distributed breeding values with variances that do not change in time or space. To see if any of the qualitative results hinge on this assumption, we developed a simulation model based on explicit multilocus genetics. We used the hypergeometric model (Barton 1992; Doebeli 1996; Shpak and Kondrashov 1999), which assumes each trait is controlled by haploid loci with equal

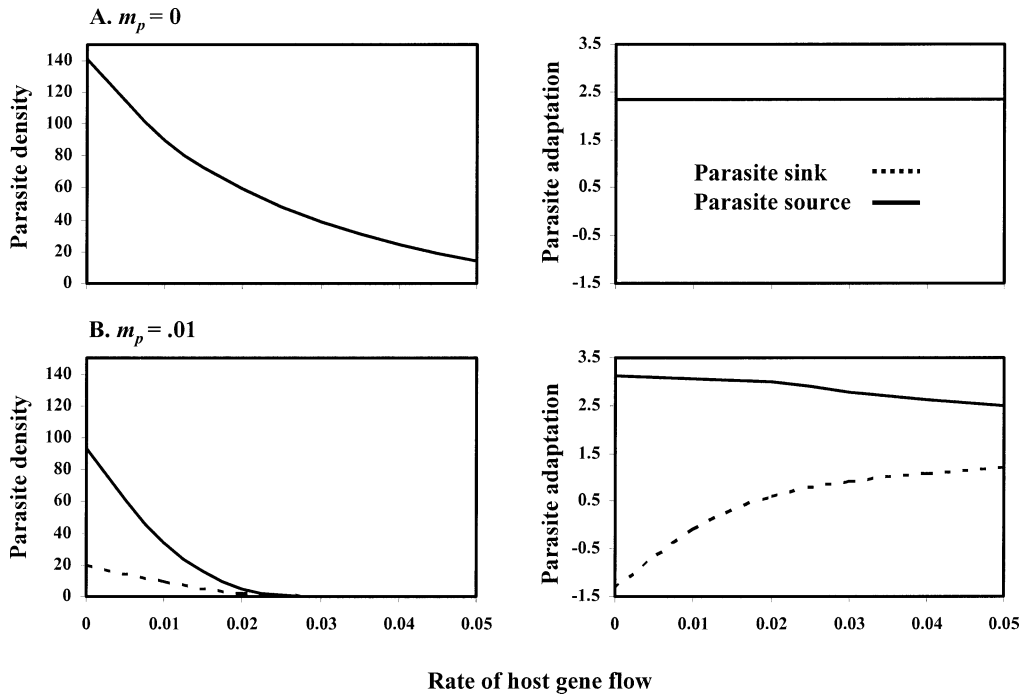

FIG. 3. Parasite densities (left) and adaptation to the host (right) when both host and parasite move. Parasite adaptation to the host was defined as $\bar{p}_i - \bar{h}_i$ such that larger values indicate increasing adaptation. In all panels the overall habitat acts as a parasite sink ($N^* = -30$). (A) Host gene flow in isolation ($m_P = 0$). (B) Host gene flow in the presence of parasite movement ($m_P = 0.01$). All panels were generated through numerical integration of equations (4, 5) with $\alpha_H = 0.0001$, $\alpha_P = 0.01$, $\gamma_P = 0.002$, $\gamma_H = 0.003$, $G_H = 4.85$, $G_P = 5$, $r = -0.011$, $\theta_1 = -2.2$, and $\theta_2 = 3.5$.

and additive effects. There are n_H loci controlling the host trait and n_P loci for the parasite trait. For simplicity, we assume both traits are completely heritable.

In contrast to the analytical model, these simulations assume discrete and nonoverlapping generations, making it necessary to assume a particular life cycle for both species. We assume the order of events in each generation is: population growth, selection caused by the other species, abiotic selection, migration, and random mating. The effects of selection follow equations (1–3). For comparisons with analytical results, the additive genetic variances, G_P and G_H, that appear in equations (4, 5) were calculated from the simulations as the average value across both habitats.

The results from these simulations suggest that the major qualitative conclusions are robust. For example, host gene flow can cause parasite extinction in the simulations, just as in our analytical treatment. The same is true for parasite movement. Similarly, qualitative predictions for population mean phenotypes frequently hold up even when the number of loci is small (e.g., five). Quantitative predictions also proved to be quite accurate for large numbers of loci but less so as the number of loci decreased or as the rate of movement increased (Fig. 5).

One striking exception occurs when the predicted mean phenotype of one of the species lies near the boundary of possible phenotypes defined by the number of loci. Under these conditions, parasite population densities may deviate wildly from their predicted values as additive genetic variance within one of the species is exhausted. For instance, if host additive genetic variance is depleted before the equilibrium phenotypic value is reached, it is possible for parasite population densities to grow without limit. This occurs simply because the host is no longer able to respond evolutionarily to the parasite despite the existence of infinitely strong selection.

An important caveat to these generally favorable results is that in all cases we assumed that mating and recombination occurred after movement but before selection. This life cycle generally leads to better agreement than would be expected if selection occurred after movement but before mating (Ronce and Kirkpatrick 2001). We would, however, expect that the qualitative results would hold across a broad range of possible life cycles. Together these results suggest that, in general, the results of the analytical model are qualitatively and quantitatively correct when the number of loci is large and rates of movement are low.

DISCUSSION

Our results demonstrate that host gene flow can be an important determinant of parasite geographic range. For the model we have considered, increasing rates of host gene flow cause reductions in parasite population densities. In some cases, this may lead to the extinction of the parasite. Alternatively, a previously absent parasite can sweep through the geographic range of the host in response to reductions in the rate of host gene flow. When both parasite and host species move between habitats, these demographic effects are amplified.

Our analyses have also revealed that demographic com-

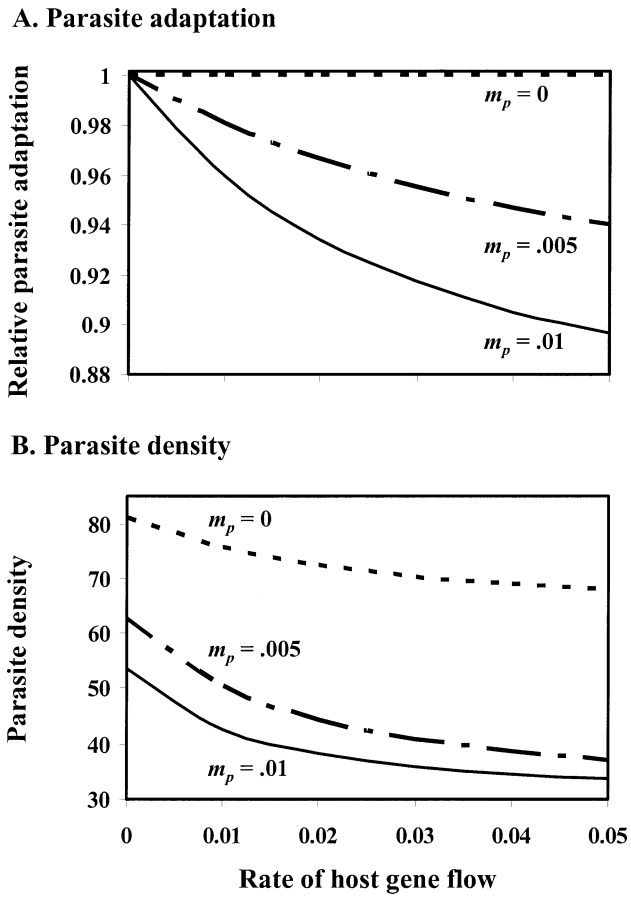

FIG. 4. Demographic compensation for different levels of host and parasite movement. (A) The index of relative parasite adaptation described in the text plotted for patch 1 (the parasite source). In the absence of parasite movement (dashed line: $m_P = 0$), this value remains fixed at one, indicating perfect demographic compensation. As the rate of parasite movement is increased (dot-dashed line: $m_P = 0.005$; solid line: $m_P = 0.01$) demographic compensation weakens and host adaptation to the parasite becomes increasingly coupled to the rate of host gene flow. (B) Corresponding parasite population densities in patch 1 (the parasite source). All lines were generated by numerical integration of equations (4, 5) with $\alpha_H = 0.0001$, $\alpha_P = 0.01$, $\gamma_P = 0.002$, $\gamma_H = 0.003$, $G_H = 4.85$, $G_P = 5$, $r = -0.011$, $\theta_1 = -1.2$, and $\theta_2 = 0.5$.

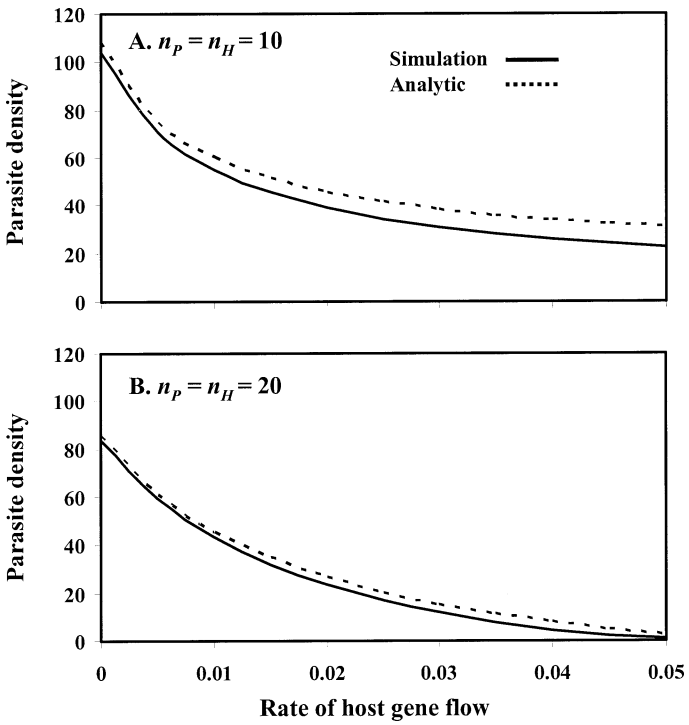

FIG. 5. A comparison of the analytical model (dashed line) and multilocus simulations (solid line). In (A) the number of loci is 10 for both species; in (B) this number is 20. Parameter values for both panels were $\alpha_H = 0.0001$, $\alpha_P = 0.005$, $\gamma_P = 0.001$, $\gamma_H = 0.002$, $r = -0.001$, $\theta_1 = -2$, and $\theta_2 = 2.5$. The additive genetic variances for each species were determined from the multilocus simulation results and varied between the two figures.

pensation can decouple parasite adaptation and population density (Fig. 1). This decoupling of parasite density and adaptation results from the feedback between demography and evolution. An important consequence is that parasite adaptation can become independent of host gene flow (Fig. 4). Thus, contrary to results from population genetics models lacking demography (e.g., Lively 1999; Nuismer et al. 2000; Gandon 2002) and verbal theory (Thompson 1994), host gene flow need not result in parasite adaptation. Although this effect is quite striking in the absence of parasite movement, it becomes less important as the rate of parasite movement is increased. Relaxing other model assumptions, such as the absence of explicit parasite density regulation or fixed host population densities, may also reduce the impact of demographic compensation. In light of this, our expectation is that demographic compensation in its absolute form, where parasite adaptation and population density are completely uncoupled, will be rare in natural populations. We anticipate, however, that a general form of demographic compensation, where this linkage is relaxed, will emerge as a general property of coevolving systems.

Our central result, that host gene flow can play a role in shaping a parasite's geographic range, has not been reported for previous spatial models of host-parasite coevolution. There are several reasons for this discrepancy. First, our model explicitly assumes that there is spatial variation in the optimum favored by abiotic selection, in contrast to previous models (Gandon et al. 1996; Hochberg and van Baalen 1998; Thrall and Burdon 2002). This explanation seems particularly likely given the demonstrated importance of such variation in previous models of species range evolution (Kirkpatrick and Barton 1997; Case and Taper 2000). Second, our model assumes that coevolution is mediated by quantitative traits rather than by the gene-for-gene or matching alleles systems assumed in previous spatial models. There is no a priori reason, however, why quantitative traits should facilitate species range evolution. Finally, it may simply be that patterns of parasite range evolution were not observed because most previous models have considered much more complex stochastic dynamics that have prohibited mathematical analysis. As a consequence, regions of parameter space resulting in parasite range evolution may not have been explored.

But the results of our model have much in common with previous models of species range evolution. Of particular importance is the necessity of spatial variation in the optimum

favored by stabilizing selection. The dependence of range evolution on such variation has been demonstrated both for single species (Kirkpatrick and Barton 1997; Ronce and Kirkpatrick 2001) and coevolving competitors (Case and Taper 2000). Our results demonstrate that this is likely to be true for host-parasite or predator-prey coevolution as well. In the absence of spatial variation in the optimum favored by stabilizing selection, host gene flow does not shape parasite range. Additionally, our results demonstrate that changes in rates of movement can lead to rapid shifts in geographic range. This outcome has been previously described for both the single species and competitive models. The novel twist in the current model is that these effects can be driven entirely by environmental gradients and gene flow in an interacting species.

In a broader sense, our results have implications for the management of infectious disease. One of our most important results in this regard is the demonstration that parasite range can be limited by host gene flow. Increasing the rate of host gene flow leads to reductions in parasite density and a potential contraction of parasite range. Decreasing the rate of host gene flow has the opposite effect. These results may be particularly important for vector-borne parasites such as malaria, which have the potential to rapidly coevolve with both their insect vectors and human hosts (Hill et al. 1997; Ferguson and Read 2002). For these coevolving associations, reductions in the rate of vector gene flow, due to habitat fragmentation or vector control programs, may have the unwelcome side effect of leading to increases in parasite density or geographic range.

To evaluate the biological relevance of these results, we need to know something about the distribution of parameter values found in natural host-parasite interactions. It appears that there are no systems where all of the required parameters have been estimated. Despite this lack of parameter estimates, it is still possible to evaluate the generality of our primary result in light of available data. The crucial question is whether the host optimum favored by stabilizing selection is sufficiently variable to make some areas parasite sources, but others parasite sinks. Two lines of evidence suggest that this may often be the case. First, there is abundant evidence that host resistance phenotypes vary over space (Ruwende et al. 1995; Berenbaum and Zangerl 1998; Brodie and Brodie 1999; Kraaijeveld and Godfray 1999). This is often attributable to changing costs of resistance or variation in the optimum host phenotype. Second, the fact that many parasite taxa do not occupy the entire geographic range of their host (e.g., Kiple 1993; Storfer and Sih 1998; Ayala and Rich 2000), suggests that some host populations are, for whatever reason, parasite sinks, whereas others are parasite sources.

A more crucial question may be the extent to which our results can be extended to other genetic mechanisms of coevolution. We have assumed that coevolution proceeds via an arms race governed by additive polygenic traits. This is clearly the case for several well-studied interactions (Berenbaum and Zangerl 1998; Brodie and Brodie 1999; Kraaijeveld et al. 2001). Other interactions, however, may be better characterized by alternative polygenic models. For instance, host resistance may depend upon not matching the phenotype of the parasite, rather than simply exceeding it (Dieckmann et al. 1995; Doebeli 1997; Gavrilets 1997; Abrams 2000). Alternatively, coevolution may be governed by very different genetic systems. Many plant-pathogen interactions, for instance, are governed by gene-for-gene interactions (Thompson and Burdon 1992; Burdon and Thrall 1999; Bergelson et al. 2001). Extending the current modeling framework to these alternative forms of coevolution will be an important focus of further work.

We have considered a simple model of spatially structured coevolution that follows joint changes in population sizes and population mean phenotypes. Despite its simplicity, this model has demonstrated that host gene flow, in conjunction with coevolution, can actively limit a parasite's geographic range. We hope this demonstration stimulates interest in linking the dynamics of geographically structured coevolution to the evolution of a species' range.

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