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Effects of Environmental Heterogeneity in a Host-Parasite Coevolutionary Chase

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To the Graduate Council:

I am submitting herewith a thesis written by Barry D. DeRennaux entitled "Effects of Environmental Heterogeneity in a Host-Parasite Coevolutionary Chase." I have examined the final electronic copy of this thesis for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Master of Science, with a major in Ecology and Evolutionary Biology.

Sergey Gavrilets, Major Professor

We have read this thesis and recommend its acceptance:

James Fordyce, Michael Gilchrist

Accepted for the Council:
Carolyn R. Hodges

Vice Provost and Dean of the Graduate School

(Original signatures are on file with official student records.)

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EFFECTS OF ENVIRONMENTAL HETEROGENEITY ON HOST-PARASITE COEVOLUTIONARY CHASE

A Dissertation
Presented for the
Master of Science
Degree
The University of Tennessee, Knoxville

Barry DeRennaux
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ABSTRACT

Species-species interactions are ubiquitous and it is thought that selection is very strong in many of these interactions, resulting in reciprocal evolution by natural selection. In antagonistic coevolution, one species benefits at the cost of another, resulting in a system where selection favors the strengthening of the interaction in one species, and acts to reduce the interaction in the other species. Previous theoretical work in homogeneous systems has identified a wide range of possible behaviors (including limit cycles, heteroclinic cycles, and equilibria) as well as explored how parameters effect local adaptation in species. Here we explore how heterogeneous systems and spatial structure affect the dynamics behavior and local adaptation.

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INTRODUCTION

Research Purpose

The primary purpose of this research is to study the behavior and properties of a very simple host-parasite model that incorporates spatial structure and spatial heterogeneity. The combination of ecology and genetics is prone to producing complex and analytically intractable equations. The goal of this research is to incorporate analytic results where possible, expanded upon by numerical results.

Research Problem

The major areas of interest in this model include: (1) what conditions maintain genetic variation in the long-term and at what levels, (2) what are the dynamics of the system (equilibria, cycles, etc.), and (3) what conditions promote local adaptation within a patch and throughout the system.

Significance of Study

Species-species interactions are ubiquitous and it is thought that selection is very strong in many of these interactions, subsequently resulting in reciprocal evolution by natural selection (so-called hot spots) (Thompson 1994, Thompson 2005, Wade 2007). Antagonistic coevolution is when one species benefits at the cost of another, resulting in a system where selection favors the strengthening of the interaction in one species, and acts to reduce the interaction in the other species. These interactions can be very strong and may play major roles in the evolution of the involved species. Examples include the wild parsnip and the parsnip webworm or *Arabidopsis thaliana* and *Pseudomonas*.

Parsnip webworms can reduce seed output by as much as 45% in wild parsnip. This is however dependent on the ability of the webworm to metabolize plant toxins. Metabolism and toxins both show variation in populations and are heritable (Berenbaum et al 1986, Berenbaum and Zangerl 1998).

Rpm1 in *A. thaliana* is important in recognition of *Pseudomonas* pathogens. Long-term persistence of resistance polymorphisms in some populations while absent in others suggests a trade-off between resistance and costs to maintain resistance. Furthermore, this long-term maintenance requires temporal or geographical variation in selection (Stahl et al. 1999).

Indirect evidence of the importance of parasites in the evolution of hosts exists in studies of local adaptation experiments with reciprocal transplant experiments or common garden experiments, which usually show parasites perform better on sympatric hosts. Studies of nonsynonymous substitutions in host immune systems also suggest pathogens can influence host evolution. Artificial environments (labs and agriculture) have had some success in showing host-parasite interactions to be an evolutionary force, but natural studies have been largely inconclusive. This may be the result of the observation window being too short, constraints, or lack of understanding of the metapopulation (Little 2002).

The last point ties into the geographic mosaic theory of coevolution (Thompson 1994, Gomulkiewicz et al. 2000, Thompson 2005) which holds that genotype-by-genotype-by-environment interactions drive coevolutionary change as species interact with one another across heterogeneous landscapes. One of the aims of the geographic mosaic theory is to understand why some of interactions can persist over long periods of time.

Many recent models predict cycling to be common in antagonistic systems (e.g. Gavrilets 1997 (a polygenic trait model), Gavrilets and Hastings 1998 (a single locus, 2 allele model), Kopp and Gavrilets 2006 (a multi-locus model)). Gavrilets and Hastings (1998) have shown that a lack of cycling within some models is a result of allowing only one species to evolve. This simplification allows analytic results to be carried further, but can force behavior that is not representative of the system (notably a lack of *coevolution*). Additionally many models have been more focused on local adaptation (how fit organisms are at their location compared to if they were transplanted elsewhere in the system) and the factors influencing local adaptation (Gandon et al. 1996, Gandon et al. 2002, Gandon and Michakalis 2002, Nuismer 2006).

The effects of heterogeneous environments on single-species systems have been well studied (both analytically and empirically) and heterogeneity generally encourages the maintenance of genetic variation (Ludwig 1950, Da Cunha and Dobzhansky 1954, Powell 1971).

The current model is an adaptation of Levene's 1953 model, which is heavily cited (554 citations in Web of Science as of 4/2008) and gives conditions for the maintenance of two alleles in a heterogeneous environment with gene flow. The current model follows the Levene model by having each species in a deme subject to different selection pressures, which then are sent to a migrant pool and redistributed evenly across all islands.

Thus the current model incorporates a truly coevolutionary system where the species interact and evolve with one another, with the strengths of these interactions (possibly asymmetric with respect to parasite and host) being mediated by local conditions. Given the difficulty of studying populations over long periods of times at several locations sufficient to observe possible cycling, theoretical work will likely play a major role in the understanding of these types of systems.

BACKGROUND

Empirical Background

Empirical studies in this area have taken two major approaches. One is the identification of hot spots (areas where strong reciprocal selection is occurring) and cold spots and the maintenance of polymorphisms over long periods of time (e.g. Thompson 1994, Gomulkiewicz et al. 2000, Thompson 2005). Others have focused on factors influencing local adaptation, ideally, how well species perform where sampled versus transplants to other locations (see Kawecki and Ebert 2004 for a review). Notably, these approaches are indirect as direct observation of

coevolution in a metapopulation would require intense sampling over time and space.

In the *Arabidopsis thaliana* and *Pseudomonas* system, populations where resistance polymorphisms are present and absent are identified, but large variation in samples from different continents was observed. Also, homologues to *Rpm1* exist in related species suggesting the polymorphism has been maintained at least partially through the diversification of Brassicaceae and coalescent models suggest at least 9.8 million years (Stahl et al. 1999).

In a study of anther-smut fungus and its host plant *Silene latifolia*, three locations showed resident fungal strains to be locally adapted and 5 locations were neither significantly adapted nor maladapted. Overall, however, the fungus was locally maladapted despite the general trend of locally adapted pathogens (Kaltz et al. 1999).

Results from empirical work indicate factors such as generation time, dispersal rates, and relative strengths of selection are important to local adaptation (Kawecki and Ebert 2004 for a review). Models have largely corroborated these findings (e.g. Gandon 2002, Gandon and Michalakis 2002, Morgan et al. 2005, Nuismer 2006).

Much of the literature shows a strong trend for local adaptation (parasites perform better with sympatric hosts than allopatric hosts) in parasites at most or all sampling sites (e.g. Kaltz et al. 1999, Manning et al. 1995) given that they usually have faster generations, higher dispersal, stronger selection, etc.

Summed across all sampling sites, the systems as a whole tend to show a strong signature for parasite local adaptedness (across the system parasites tend to be locally adapted) with sites of maladaptation usually being few and small in magnitude. In these types of studies, transplant experiments, where a species is physically relocated to other sites for observation, are considered ideal (though not always possible, Kawecki and Ebert 2004). Local adaptation within this model emulates transplant experiments (the difference between the average fitness where found and the average fitness elsewhere, Gandon and Zandt 1998, Lively 1996).

Theoretical Background

Gavrilets 1997, Gavrilets and Hastings 1998, and Kopp and Gavrilets 2006 explore single deme coevolutionary dynamics under a variety of genetic assumptions. These papers together suggest the cycling of allele frequencies are possible under a wide range of parameter values and underlying genetics. Other papers have focused on exploring factors affecting local adaptation which have largely corroborated empirical findings (Gandon 2002, Gandon and Michakalis 2002, Nuismer 2006).

Gavrilets 1997 modeled an antagonistic coevolutionary system with stabilizing selection and continuously varying traits in a single deme. Dynamics were found to include polymorphic equilibria (stable and unstable) as well as cycles (stable or unstable).

Gavrilets and Hastings 1998 modeled a 1 locus, 2-allele trait in 2 coevolving species in a single deme. In the results, monomorphic equilibria were

identified (stable and unstable) as well as unstable polymorphic equilibrium and stable heteroclinic cycles. Also shown was that mutation added to a heteroclinic cycle results in a limit cycle. Together these two models suggest that both cycling and equilibria are relatively easy to achieve and may be common in nature.

A multilocus model (Kopp and Gavrilets 2006) encompasses similar dynamics to the above models, but additionally shows the existence of multiple simultaneously stable states. Additionally, results showed that at equilibrium hosts showed large genetic variance, while exploiters were polymorphic at only 1 locus and that, in general, increasing the number of loci destabilizes the system. This loss of genetic variation is also observed in Van Doorn and Dieckmann 2006, which modeled a frequency-dependent disruptive selection in a single species. Similar to the exploiter results, all but 1 locus becomes monomorphic.

Gandon 2002 is a haploid 1-locus, 2 allele species model very similar to the one here. The results focused on how migration, specificity, and virulence affected local adaptation. Differential equations were again used and simulations suggested that intermediate migration values were necessary for local adaptation to exist (with the species possessing the higher rate being adapted). Virulence and specificity's effects on local adaptation were dependent on migration rates (in general higher virulence and lower specificity increased local adaptation in agreement with much of the empirical literature).

Gandon and Michikalis 2002 simulations explored the importance of mutation rate and migration and generation time in local adaptation. In general these were found to promote parasite local adaptation. Generation time, however, if too short compared to selection strength resulted in loss of genetic variance and an inability to adapt to new hosts.

Nuismer 2006 looked at a 2 island diploid model with emphasis on local adaptation under a variety of different interaction models (matching alleles, inverse matching alleles, and gene-for-gene). Findings showed that matching alleles produces the lowest occurrence of local adaptation with gene-for-gene being the highest. However, for local adaptation to persist in the system required spatial heterogeneity.

MODEL DESCRIPTION

Model Design

With the desire to carry analytic investigations as far as possible, the model's genetics are highly simplified. This is a frequency-based, haploid, island dispersal model with a host species possessing 1 locus with 2 alleles, and a parasite species possessing 1 locus with 2 alleles. Hosts with allele 1 are susceptible to parasites with allele 1 while being resistant to parasites with allele 2 (and vice-versa). The current model is completely deterministic (no mutation or drift) and in discrete time. The discrete nature of the model allows for strong selection; models done with differential equations assume "small" changes over small increments of time, which often involves the direct or indirect assumption that selection is much less than 1.

Fitnesses of hosts 1 & 2 and parasites 1 & 2 on a particular island

$w_{h1} = 1 - \alpha \cdot p$

$w_{h2} = 1 - \alpha \cdot (1 - p)$

$w_{p1} = 1 - \beta \cdot (1 - h)$

$w_{p2} = 1 - \beta \cdot h$

where w_{h1} is the fitness of hosts with allele 1,

α & β control the strength of the interaction for hosts and parasites repectively,

and $0 < \alpha < 1, 0 < \beta < 1$ and h & p are the frequencies of hosts and parasites with allele 1.

Host fitness is linearly dependent on the frequencies of hosts and parasites (or more generally a victim and an exploiter) in a deme; the intensity of the interaction is modified by a spatial parameter specific to that island which affects only host fitness (α). Similarly, parasite fitness is also linearly dependent on frequencies and spatial parameter (β) affecting only parasite fitness. Lastly, symmetry is assumed in the effects of parasites and hosts, i.e. there is only one α & β per island mediating both morphs of the parasites and both morphs of the hosts. This is actually a reparameterization of the Gandon 2002 model (figure 1; all figures can be found in the index).

From these fitness equations, after-selection frequencies can be calculated for each island. All islands then contribute a proportion of hosts, m_h, to the migrant pool, and likewise parasites at m_p. These pools are then evenly divided back to all islands (all islands contribute equally to migrant pools and receive equally from them, thus there are no sources or sinks). These are recorded as the final frequencies for the generation. (Full equations can be found in Appendix I.)

Unfortunately, the number of parameters scales linearly with the number of islands and quickly becomes unwieldy. In a system of i islands, there are a total of $2i$ independent variables (host and parasite frequencies in each deme) and $2+2i$ parameters (α and β for each deme and migration rates). Given that the number of parameters becomes unwieldy with large numbers of islands, investigations have focused on randomly generating α's & β's from a uniform distribution range; this reduces the number of parameters to 6 (host and parasite migration rates, and the upper and lower bounds of the distribution). Analytical results are being produced with *Maple* while numerical simulations are being written and performed in *MatLab*.

RESULTS

Equilibria

Analytical results (results for analytical claims are in Appendix III) for the single deme case and a special case of the 2 and 4 deme systems show that 5 biologically reasonable equilibria exist for allele frequencies of host and parasite. Four correspond to monomorphic equilibria where 1 of the alleles has fixed (and

the other gone extinct) in both species. The other corresponds to a polymorphic equilibrium where all allele frequencies are equal to ½. Numerical simulations with greater than 2 demes have indicated no other stable equilibria exist.

Heteroclinic cycles

Heteroclinic cycles can emerge when all equilibria are unstable. This results in increasingly large fluctuations in allele frequencies that oscillate nearer and nearer to 0 and 1 as time progresses (lack of stochastic processes in the model prevents fixation). Time spent near 0 and 1 also increases over time (Gavrilets and Hastings 1998).

Analytical results show that a single deme has no stable equilibria and that the polymorphic equilibrium is an unstable focus. Simulations suggest that the resulting heteroclinic cycle is always stable (figure 2A). Systems of 2 identical demes (all α's equal and all β's equal), which correspond to homogeneous environments, also have unstable equilibria with the polymorphic equilibrium as an unstable focus. Simulations suggest that the resulting behavior is either a heteroclinic cycle (figure 2B, figure 3) or a limit cycle (figure 3). Limit cycles require sufficiently low migration rates that 1 or more demes is trapped out of synchrony with the other demes and are dependent on initial frequencies. With sufficiently high migration rates, the heteroclinic cycle is stable.

Finally, multiple demes with no migration among or between them are identical to single deme systems. Even though systems ultimately lose genetic variation, this can take several thousands of generations as oscillations in frequencies can be either slow or grow slowly.

Analytical results for the special case of $m_h=m_p=1$ indicate the heteroclinic cycle in a heterogeneous environment is always unstable. This corresponds to $\rho<1$ and simulations suggest that ρ has some use in predicting how close and how quickly a system will approach the axes; values near 1 should result in oscillations close to the axes and oscillations that approach more quickly. Smaller values of ρ correspond to increasing selection or increasing heterogeneity (figure 5).

For a given collection of parameters (figure 6), runs were ended at either 200,000 generations or when an allele came within 10^{-10} from an axis, this value was chosen because of limitations in machine precision much beyond this. If allele frequencies never dropped this low, the full 20,000 generations were run, otherwise the run ended early. Figure 6 shows that runs with ρ values near 1 were more likely to terminate early, while figure 7 shows that of those that terminated early, those with values close to 1 tended to terminate sooner. However, ρ values do not appear to be good predictors of the cycles just 1% from the axes; this is likely the result of stable limit cycles emerging within this range for the set of parameters used.

Simulations suggest small amounts of migration and variation in selection coefficients can be sufficient to convincingly destabilize the heteroclinic cycle. This can result in a stable polymorphic equilibrium or limit cycles (figure 8).

Stability of the Equilibria

A lower bound for migration ($m=m_h=m_p$) for the stability of the polymorphic equilibrium in the 2-deme case has been solved and the lower bound increases with increased strength in selection. It can also be shown that letting $m \rightarrow 1$ results in an unstable polymorphic equilibrium, thus, only intermediate migration rates can be a stable polymorphic equilibrium. With the additional assumption of weak selection, a condition on the upper bound of m can be solved and increased heterogeneity widens the conditions for stability.

The Jacobians of both the 2 and 4 deme system have been found and have been useful in numerically calculating the stability of the polymorphic equilibria (a magnitude greater than 1 of the largest eigenvalues in discrete time indicates instability of the polymorphic equilibrium).

In the 2-deme system, numerical simulations suggest that if one deme's α & β are both larger than the second deme's, the polymorphic equilibrium will be stable over a large range of migration values, however, should $\alpha < \beta$ in each deme (or $\alpha > \beta$ in each deme) numerical simulations suggest no stable polymorphic equilibrium can be present under any migration rates. Thus, an island with species under "strong" selection exchanging migrants with species under "weak" selection is likely to maintain genetic variation. Furthermore, the space of stable polymorphic equilibrium in the m_h, m_p phase plane appears to always be continuous (figure 9).

In the 4-deme case conditions for the existence of a stable polymorphic equilibrium do not appear to be so simple. Additionally in the parasite-host migration space, the area corresponding to stable equilibria can be discontinuous (figure 10). This might suggest that even more complex systems may have complicated patterns of equilibria and cycling throughout the migration plane.

In all cases stability, or lack there of, appears to be symmetric with respect to parasite and host migration rates. Host and migration rates can be swapped and the long-term behavior is unchanged. This is despite the fact that selection intensities on hosts and parasites can be very different. Additionally, this is in contrast to empirical data which suggests migration rates to be important in local adaptation as well as some models (Gandon 1996, Gandon 2002, Gandon and Michakalis 2002). This is likely a result of island model dispersal or simplifying assumptions in the construction of the model.

The interplay of selection and heterogeneity on the stability of the polymorphic equilibrium can be seen in figure 11. There is a general trend that increasing selection reduces the probability of a stable polymorphic equilibrium while increasing heterogeneity encourages the stability of the polymorphic equilibrium.

Amplitude of Frequency Oscillations

Amplitude behavior is complex. Strong selection coefficients in general increase the amplitude of allele frequency oscillations but relative values of selection coefficients to one another are also important. Conditions that are prone to producing stability are also prone to reducing the amplitude of allele frequency oscillations.

Low migration rates produce large amplitudes as they are behaving largely as isolated demes. Extremely high values of migration also tend to produce large amplitudes. In general "intermediate" values of migration tend to produce the smallest amplitudes and sometimes stable polymorphic equilibria (figures 12 & 13). This can be interpreted as the systems with low migration rates behaving similarly to isolated demes (which have unstable equilibria), and similarly the systems with high migration rates behaving similarly to a single deme (which also has unstable equilibria).

Periodicity of Frequency Oscillations

When investigating periodicity, there is an observed trend that higher selection coefficients decrease the period (the faster the system oscillates) and that heterogeneity has little effect (figure 14). Linearization of a discrete time system results in a system where the largest magnitude eigenvalue (λ_1, which is complex) predicts the period near the bifurcation point (Mardsen and McCracken 1976). Period near the bifurcation point is estimated by

$$period = \frac{2\pi}{\arctan(A/B)}, where$$

$$\lambda_1 = A + Bi$$

Simulations consistently show A to be near 1 and B near 0, so the period can be further simplified to $2\pi/B$. Given that this is a linearization, this estimate is only accurate in the neighborhood on the bifurcation point.

Local Adaptation

Unlike much of the empirical work on local adaptation (e.g. Kaltz et al. 1999, Manning et al. 1995) simulations in the current model do not show significant tendencies for systems to be locally adapted (generally below .1%), this is similar to the results of Ridenhour and Nuismer 2007. Contrary to Gandon 2002 and Ridenhour and Nuismer 2007 (cross infection results), host local adaptation is not equal in magnitude and opposite in sign to parasite local adaptation.

Within a stable polymorphic equilibrium, hosts and parasites in demes with weaker selection are more locally adapted since the only change in fitness from transplants is based on the selection coefficients. Values for local adaptation within deme i for hosts and parasites are

$$LA_{hi} = \frac{n \cdot (\bar{\alpha} - \alpha_i)}{2(n-1)}$$

$$LA_{pi} = \frac{n \cdot (\bar{\beta} - \beta_i)}{2(n-1)}$$

When summed across all demes local adaptation of the system is 0.

During oscillations, spikes of adaptedness or maladaptedness occur as the frequencies in demes reach maxima or minima out of phase with one another. Simulations show that these spikes sum to zero and local adaptedness over time is very near equal to the local adaptation at the polymorphic equilibrium.

The observation that overall local adaptedness is very near 0 can be explained by F_{st} values (Wright 1965). Throughout the explored parameter space F_{st} values tend to be very low (figure 15); this indicates that allele frequencies between demes are largely synchronized and there isn't much opportunity to be locally adapted, however, systems with more heterogeneity did exhibit larger F_{st} values.

Sensitivity to Initial Frequencies

Assuming the initial frequency does not lie on an unstable equilibrium and migration rates are sufficiently high, systems that tend to limit cycles or equilibria appear to have only 1 stable equilibrium or limit cycle despite initial allele frequencies. This implies that even within a system with occasionally acting stochastic processes we can expect the same long-term behavior to always return. In systems with more than 2 demes with sufficiently low migration rates, asynchrony in allele frequencies can persist.

In systems with sufficiently low migration rates, behavior (limit cycles or heteroclinic cycles) is dependent on initial allele frequencies. As the number of demes increases, so does the upper limit on migration rates that allows for dependence on initial conditions (Gavrilets, personal communication).

Symmetry of stability and spatial structures

The open-boundary stepping stone model appears to be the only model that has the polymorphic equilibrium asymmetric with respect to migration rates. This is likely due to a normalizing step where h and p are divided by $1-m_h/2$ and $1-m_p/2$ to correct for individuals that "fell out" of the model. It appears that the equilibrium is most sensitive to the migration rates of the species under stronger selection (figure 16, lower right).

Spatial structure and stability of polymorphic equilibria

Exploration of spatial structure reveals that stepping-stone systems appear to have stable polymorphic equilibria over a larger range of migration values than the island model (figure 17). This is likely the result of the indirect nature that the demes affect each other. In the island model, individuals from any deme migrate to all other demes and therefore the system is very connected and allele frequencies more synchronized. The stepping stone models, however, send migrants to only 2 (at most) demes and therefore allele frequencies are much more likely to be asynchronous.

The addition of more demes also increases the range of migration combinations that can result in stable equilibrium (compare figures 17 and 18, figure 19). Additionally, the addition of more islands to the homogeneous island model increases the migration rate necessary remove dependence on initial allele frequencies

DISCUSSION

Presented here is a simple antagonistic coevolution model, which incorporates spatial variation in multi-deme, 1-locus, 2-allele haploid system. Unlike 1-deme models, equilibria and limit cycles can be stable without the incorporation of stabilizing selection. Additionally, the effects of heterogeneity and average strength of selection on amplitude, wavelength, local adaptation, and F_{st} (primarily in a 2-deme island system) were investigated. The stability of the equilibrium was investigated over a much larger range of parameters and spatial structures.

Homogeneous systems were found capable of exhibiting ever-growing oscillations (heteroclinic cycles), similar to 1-deme systems. Under sufficiently low migration rates, this heteroclinic cycle is only locally stable and depending on initial frequencies a limit cycle can emerge. Results suggest that any amount of environmental heterogeneity is sufficient to destabilize the heteroclinic cycle.

The coefficient ρ for the island model case where migration rates are maximal appears to have some predictive power in how close a cycle will approach the axes and how quickly. In the homogeneous case, $\rho=1$ and a heteroclinic cycle results. As heterogeneity is introduced, ρ is reduced and simulations show the system is less likely to approach close to the axes and does so at a slower rate.

The equilibrium frequencies of $h=½$, $p=½$ can be stable or unstable in the heterogeneous system. Again, this stability of the equilibrium is without stabilizing selection. Upper and lower migration bounds in the 2-deme case with equal migration rates can be solved analytically and along with the support of simulations (which relaxes the 2-deme and equal migration assumptions), it appears that intermediate migration rates are the most likely to result in a stable polymorphic equilibrium. If migration rates are too low, the demes behave similarly to 1-deme systems, exhibiting limit cycles with large amplitudes close to the axes, these however are not heteroclinic cycles. When migration rates are too high, allele frequencies among demes become largely synchronized and again, cycles with large amplitudes result.

Environment can also encourage stability of the polymorphic equilibrium. Environments with more heterogeneity have a stable equilibrium over a larger range of migration rates, the heterogeneity promotes asynchrony in the frequencies among demes, which results in limit cycles or can collapse into equilibrium. The addition of more demes similarly encourages more asynchrony among allele frequencies. Lastly, spatial structures also are capable of significantly increasing stability of the equilibrium. Linear stepping stone models, and to a lesser extend the ring system reduce connectivity among demes which again results in a more stable equilibrium across ranges of migration rates.

For the 2-deme system, amplitude and wavelength were investigated along with local adaptation values and F_{st}. Increasing the average strength of selection (α's and β's) tended to produce systems with smaller wavelengths whereas increasing heterogeneity tended to produce systems with smaller amplitudes. Also, a particular species in a particular deme will have larger oscillations if it is

under stronger selection than in other demes (demes with relatively large α's and/or β's tend to have large amplitudes in the corresponding species). Lastly, average local adaptation in the 2-deme system was always very near 0. However, particular species in particular demes could be strongly locally adapted or maladapted or even oscillate between the two through time. Species in demes under strong selection respond more quickly and intensely to shifts in allele frequencies allowing them to be locally adapted while the species in demes under weaker selection were maladapted. F_{st} values in general were low, indicating a large degree of synchrony between demes, but was highest when heterogeneity was high.

It remains to be seen how the properties of limit cycles are affected in island systems with more demes or in stepping stone models. The time required for frequency oscillations in particular would be of interest to empirical researchers as it has the potential to be a confounding factor, as well as local adapataion and F_{st} values which are the primary measurements being taken in the field.

Empirical implications, which have focused largely on local adaptation, are discouraging. First, local adaptation can vary through time and even change sign both on average across the entire system and within particular demes. Secondly, sampling only a subset of the demes in a metapopulation can result in strongly adapted or maladapted signatures despite the fact that average values were near 0 in this model. Lastly, the time required for the frequencies to oscillate once are likely prohibitive for most empirical systems- 50 to 400 generations. These findings combined suggest intense, long-term sampling would be required to be confident of a particular system. These findings in general cast doubt on the meaningfulness of 1-time or short-term measurements of local adaptation while also suggesting that long-term studies may have wildly varying local adaptation values over time.

With all the difficulty thus far in observing coevolution in the field, it might be that antagonistic coevolution is best demonstrated in laboratories where there has been some success already. Within lab settings, the number of demes and species can be controlled as well as the migration rates. Using short-lived organisms and strong-selection, it might be possible to do the intense sampling required for meaningful results with a feasible amount of effort in a realistic timeframe.

This research expands upon previous theoretical work illustrating the possibility of long-term stability in the interaction of antagonistic species. The addition of a heterogeneous spatial structure allows for a wide range of parameter values that maintain genetic variation both in the form of limit cycles away from the axes and stable equilibrium. A variety of stepping-stone models and the addition of more demes widened this range even further. In general, this model suggests that more realistic spatial structures encourage the maintenance of genetic variation in antagonistic coevolutionary systems. This model could also be useful in identifying empirical systems in which coevolution might be observed, and also lends support to some explanations of why coevolution may be so difficult to observe in the field.

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APPENDICES

APPENDIX I: FIGURES

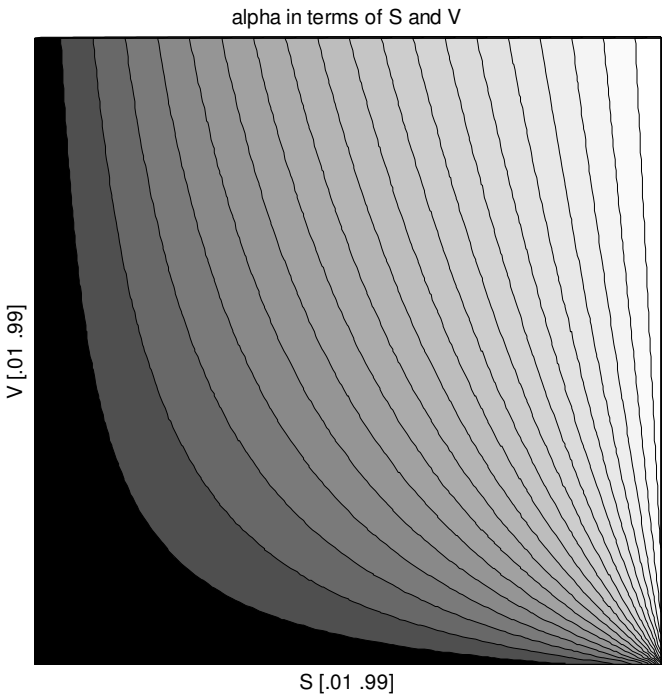
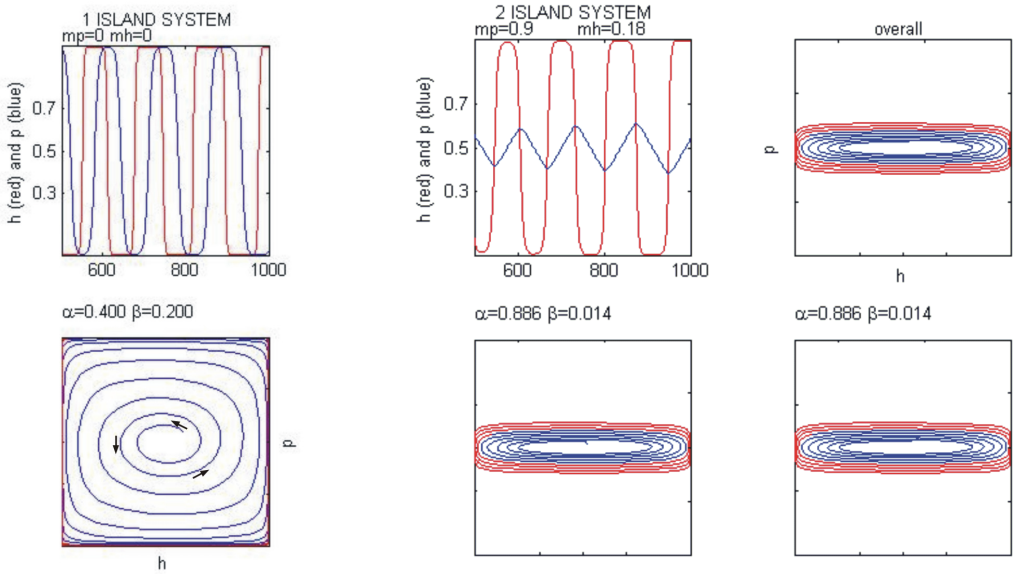


Figure 1. Reparameterization of Gandon 2002. α in terms of S (specificity) and V (virulence), β=S. Values from 0 (black) to 1 (white).



A. B.

Figure 2. Heteroclinic cycles. A: a single deme evolving to a stable heteroclinic cycle. Top: Allele frequencies over time. Bottom: phase plot of frequency of host allele 1 and parasite allele 1. α=.4, β=.2. Arrows indicate the trajectory in the phase plane. B: a 2-deme system evolving towards a heteroclinic cycle. Bottom: phase plots of the two islands (last 500 generations in red). Top right: phase plot of overall allele frequencies. m_p=.9, m_h=.18, a_1=a_2=.886, b_1=b_2=.014

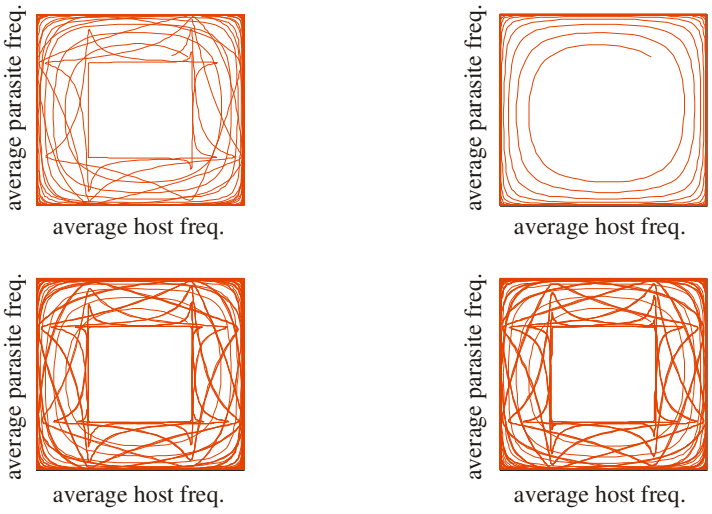


Figure 3. Sensitivity to initial conditions in low migration systems. X and y-axes: average host and parasite frequency across all demes, 4 runs. 4-demes, m=.0001, α=β=.2. In the upper right plot, allele frequencies synchronize and a heteroclinic cycle emerges. In the other plots allele frequencies fail to synchronize. Upper right plot has an F_{st} value of .008, the other plots have values greater than .3.

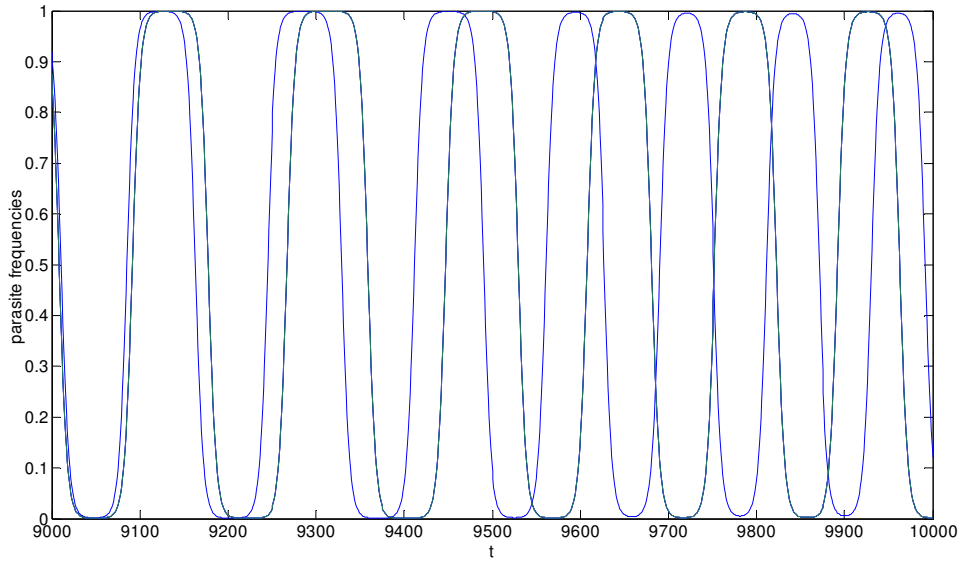


Figure 4. Asynchrony in parasite frequencies among demes in a homogeneous system. 3 of 4 demes synchronize (green) and 1 does not (blue). Parameters the same as figure 3.

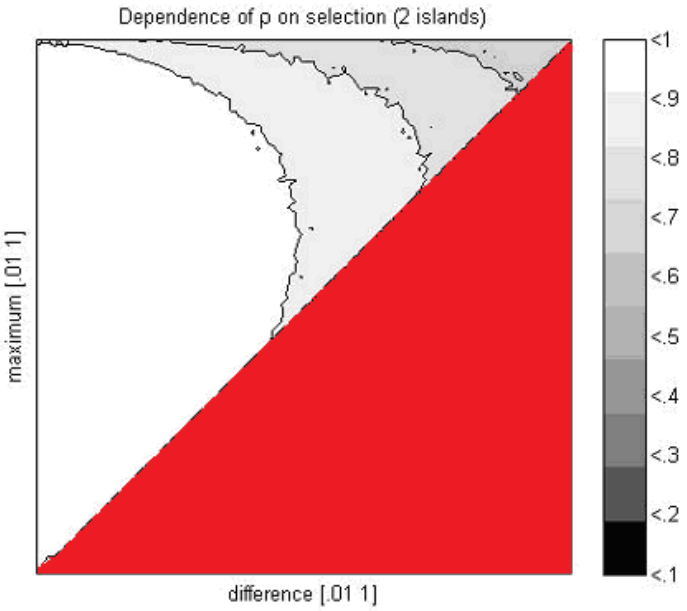


Figure 5. Dependence of ρ on selection and heterogeneity, average value of 500 randomly generated sets of α's and β's. The x-axis is the difference between the upper and lower bounds of the uniform distribution from which the α's and β's are chosen; the y-axis is the upper bound.

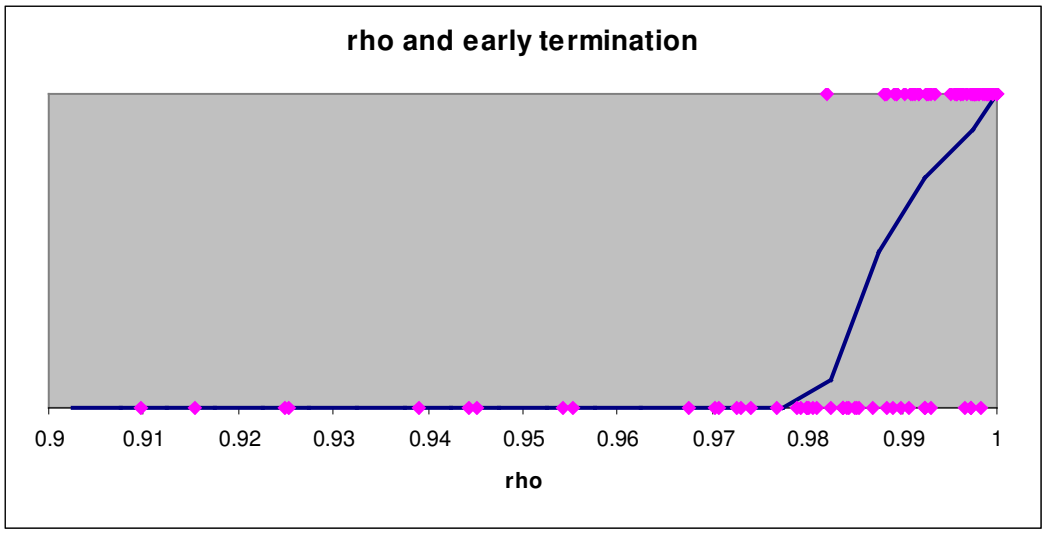


Figure 6. ρ versus early termination (an allele frequency near an axis) in 94 runs (parameters as in figure 7). If average allele frequency came within 10^{-10} from fixation the run terminated. Runs which terminated early at the top of the plot, ones which did not are at the bottom. The estimated probability distribution function in blue.

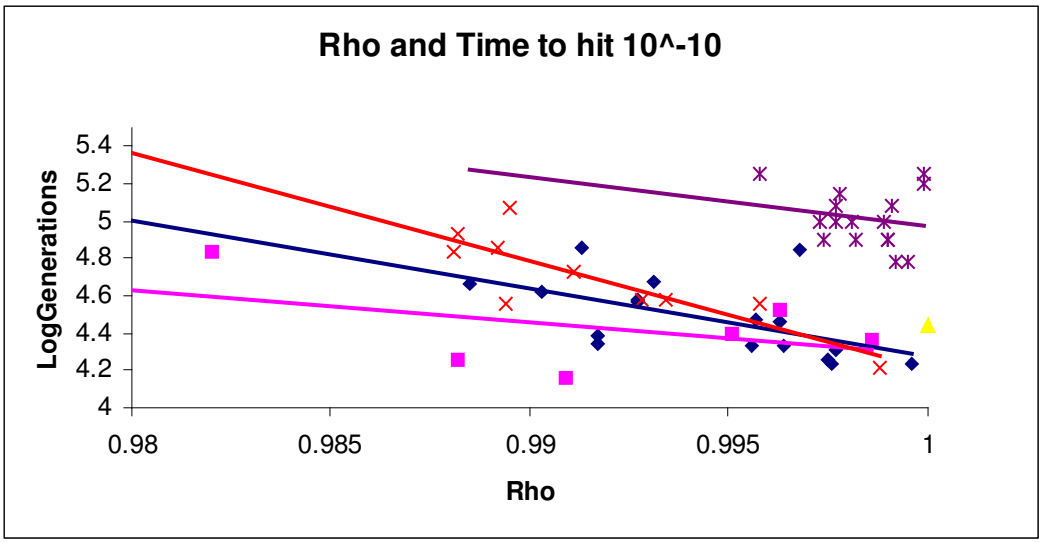


Figure 7. ρ versus time to early termination (in runs that terminated early). Migration rate=1, 2 demes except where noted. Trend lines added to emphasize the trend; higher ρ tends to a faster approach to the axes. α's and β's randomly generated from the following intervals: blue- [.05 .15], pink- [0 .2], purple- [.025 .075], red (4 demes)- [.05 .15], and yellow is a heteroclinic cycle with α=β=.1.

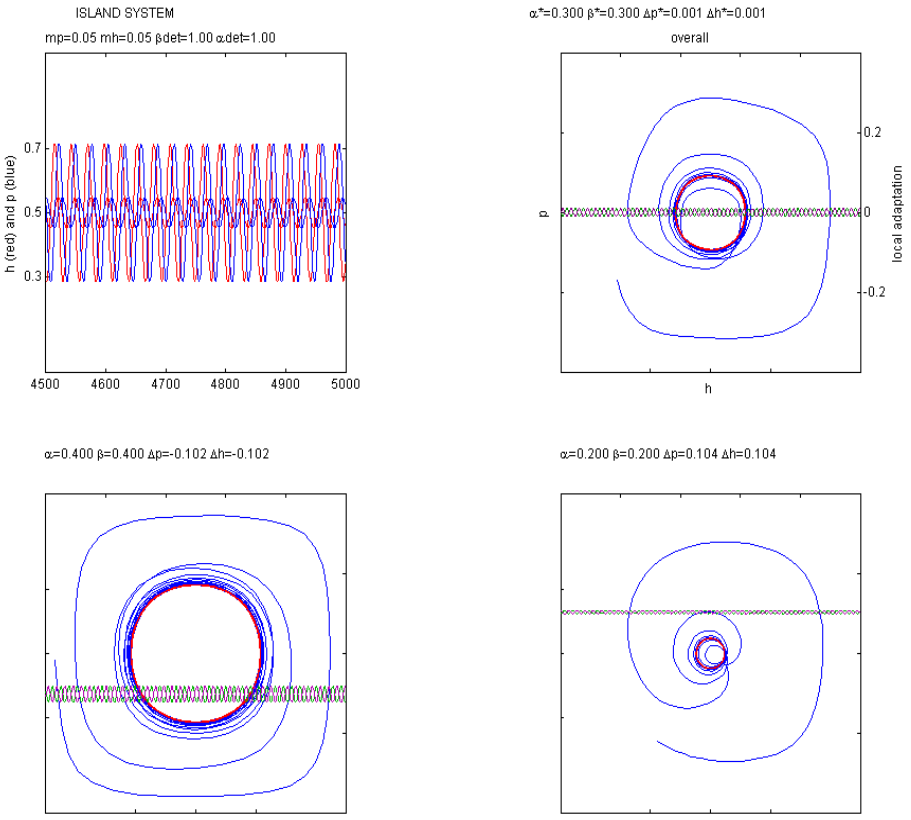


Figure 8. A pair of demes evolving towards a stable limit cycle, α_1=.4, β_1=.4, α_2=.2, β_2=.2 and m_h=m_p=.05. Note the local adaptation values similar results predicted by the analytical results for a polymorphic equilibrium.

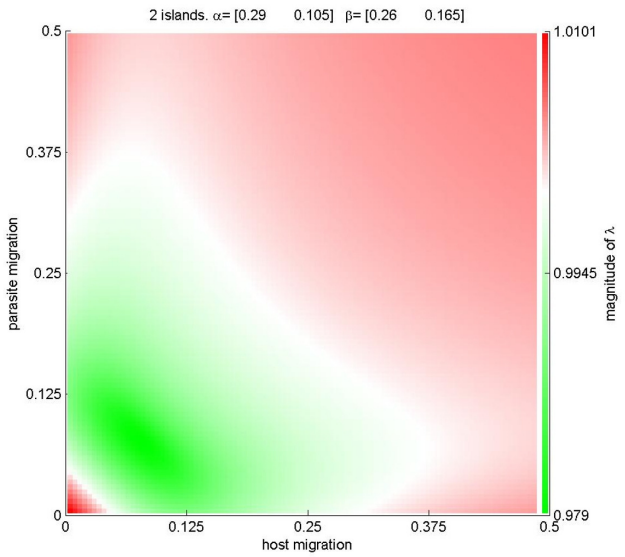


Figure 9. Stability of the polymorphic equilibrium. A pair of demes and the magnitude of the largest eigenvalue across a range of parasite and host migration rates. α_1=.29, β_1=.26, α_2=.105, β_2=.165. Parasite migration varied on the y-axis from 0 to .5, host migration on the x-axis. Color key on right with values greater than 1 indicating an unstable polymorphic equilibrium (green is stable, white is neutrally stable in the linearization, red is unstable). Note the space corresponding to a stable equilibrium is continuous.

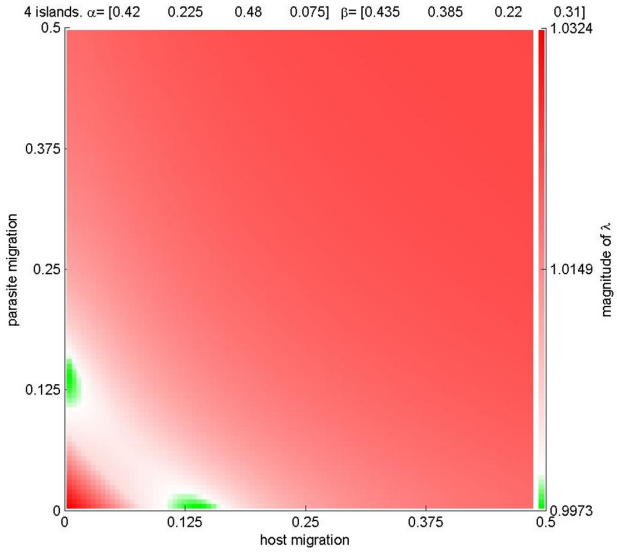


Figure 10. A system of 4 demes with a discontinuous range of stable polymorphic equilibrium. α_1=.42, β_1=.435, α_2=.225, β_2=.385, α_3=.48, β_3=.22, α_4=.075, β_4=.31. Parasite migration varied on the y-axis from 0 to .5, host migration varied on x-axis. Color key on right with values greater than 1 indicating an unstable polymorphic equilibrium (green is stable, white is neutrally stable in the linearization, red is unstable). Note the space corresponding to a stable equilibrium is discontinuous.

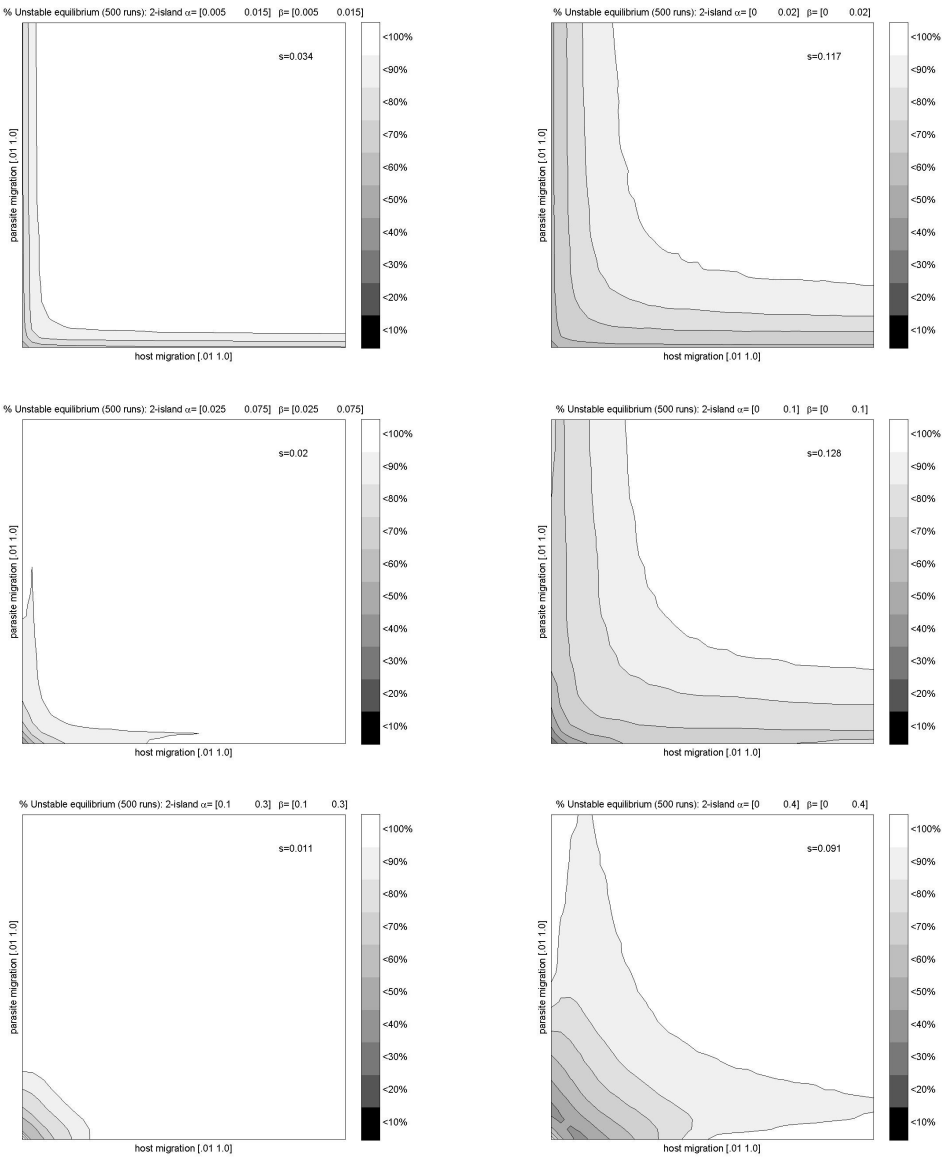


Figure 11. Effects of selection and heterogeneity on stability of the polymorphic equilibrium. Host and parasite migration rates are on the axes (from 1% to 100%). For each plot 500 sets of α's and β's are randomly generated and stability analyzed at the various combinations of migration rates. The 3 rows have increasing average α's and β's (1%, 5%, 10%) while the left column represent "low" heterogeneity (±50% from the average as boundaries) and the right as "high" heterogeneity (±100% from the average as boundaries). *s* is the probability of randomly selecting a run and a combination of migration rates and being at a stable polymorphic equilibrium.

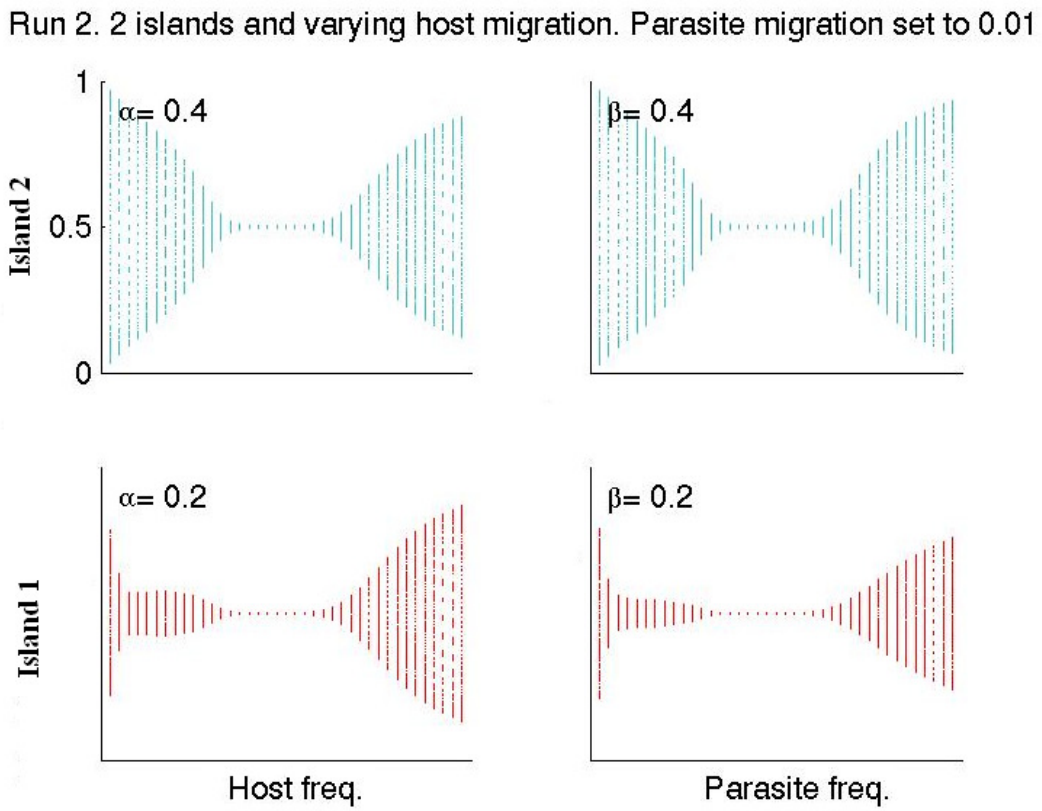


Figure 12. Bifurcation of the polymorphic equilibrium. A bifurcation diagram showing a stable equilibrium at intermediate ranges and cycles at high and low migration rates. m_p=.01, m_h varying from .01 to .4, α_1=.4, β_1=.4, α_2=.2, β_2=.2. Top left: host allele frequencies in deme 2. Lower left: host allele frequencies in deme 1, right plots are for parasite frequencies.

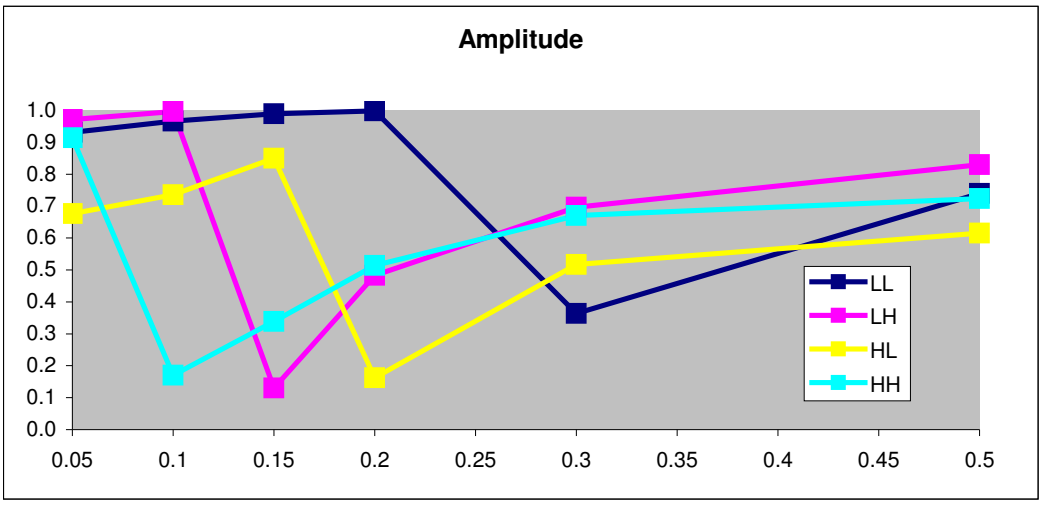


Figure 13. Effects of selection and heterogeneity on amplitude of allele frequency oscillations. Average amplitude of 50 runs under 4 uniform distributions of selection coefficients (H is "high" and L is "low, with the first letter indicating heterogeneity and the second selection. LL, LH, HL, HH are the ranges [.025 .075], [.05 .15], [.00 .10] and [.00 .20] respectively). Y-axis: amplitude, x-axis: migration rate. Increasing heterogeneity decreases the average amplitude.

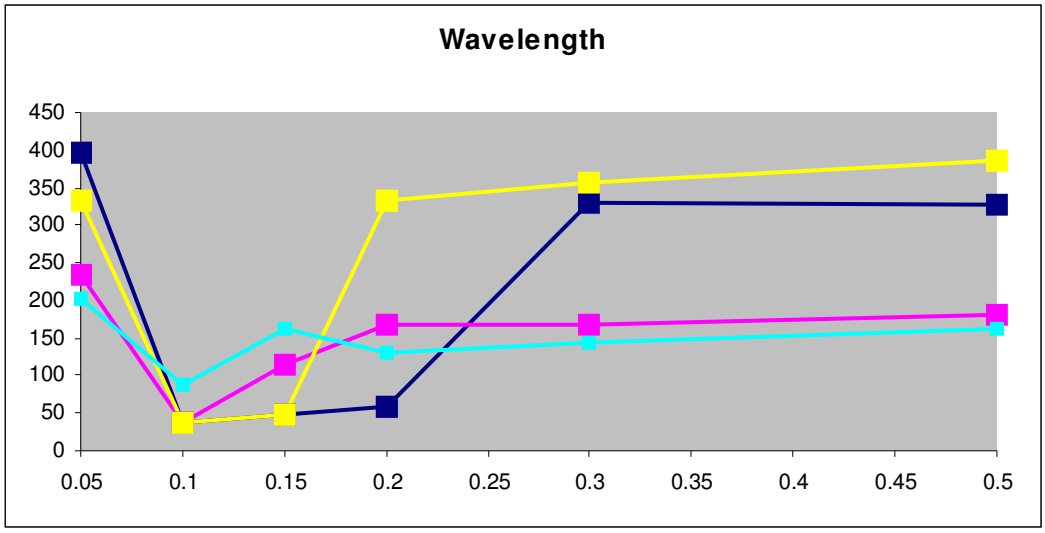


Figure 14. Effects of selection and heterogeneity on wavelength of allele frequency oscillations. Parameters the same as figure 13. Increasing selection makes the system cycle faster (smaller wavelength) whereas heterogeneity has little effect.

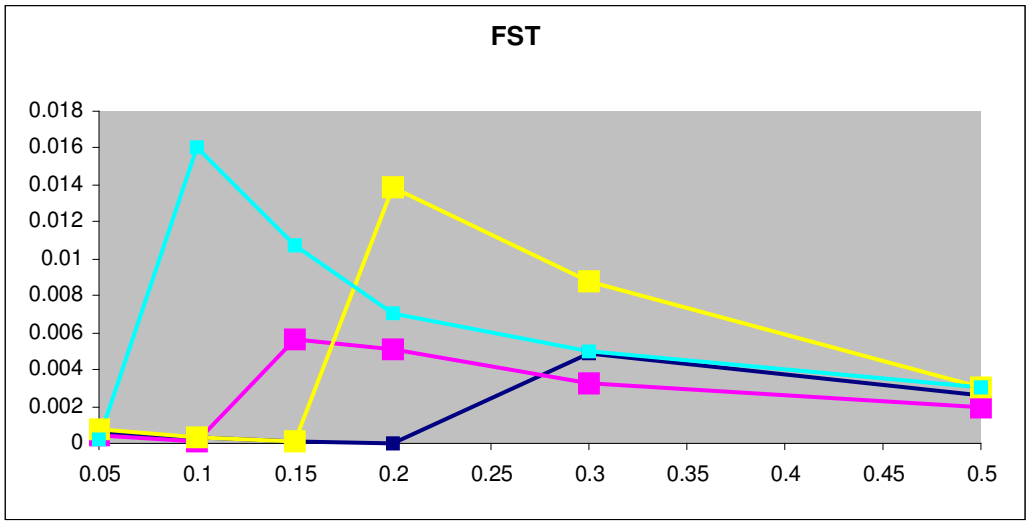


Figure 15. Effects of heterogeneity and selection on F_{st}. Parameters the same as figure 13. Y-axis: F_{st}, x-axis: migration rate.Comparing with figure 13, we can see that F_{st} is highest when amplitudes tend to be small.

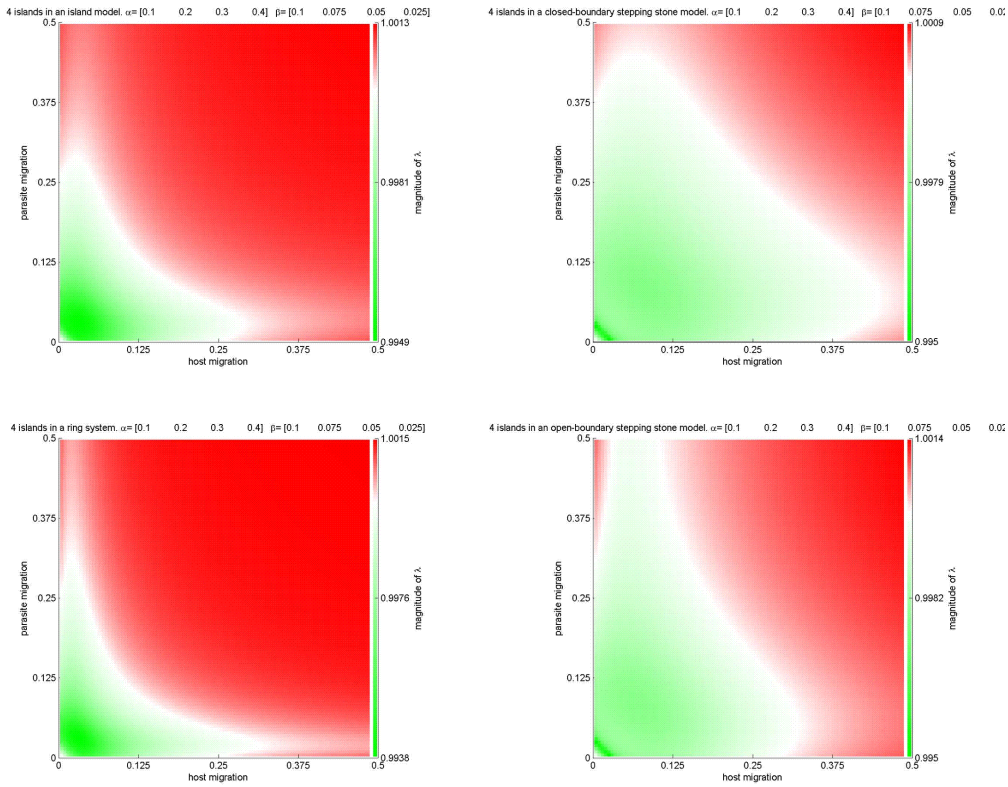


Figure 16. Stability of the polymorphic equilibrium in different spatial structures. The magnitude of the largest eigenvalue at polymorphic equilibrium in 4 demes across a range of parasite and host migration rates (α_1=. 1, α_2=.2, α_3=.3, α_4=.4, β_1=.1, β_2=.075, β_3=.05, β_4=.025) and various spatial structures (upper left-island model, upper right-closed boundary stepping-stone model, lower left-ring system, lower right- open boundary stepping-stone model)

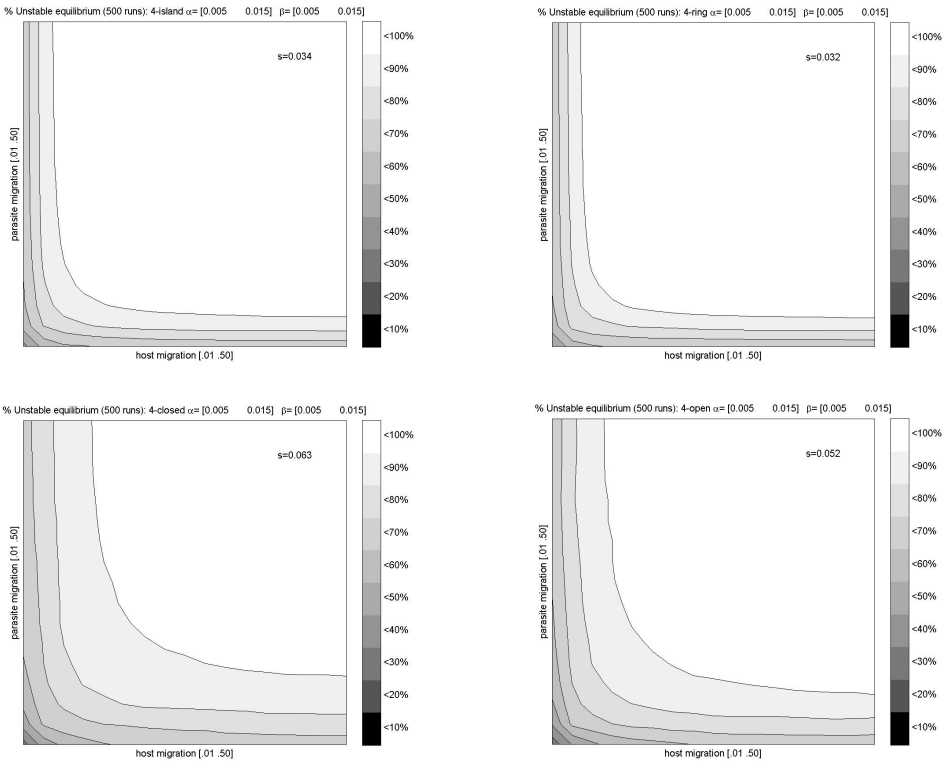


Figure 17. Effect of spatial structure on stability of the polymorphic equilibrium (4 demes). Upper left: island, upper right: ring system, lower left: closed-boundary stepping-stone, lower right open-boundary stepping-stone. Shading indicates probability of a run having a stable polymorphic equilibrium. Host and parasite migration rates varied on the x- and y-axes. As a general trend, stepping-stone models (bottom row) are more likely to have a stable polymorphic equilibrium. We can see that *s* (the probability of a run and a particular set of migration rates having a stable polymorphic equilibrium) is almost double in the stepping-stone models (*s* is calculated for migration rates up to 100%).

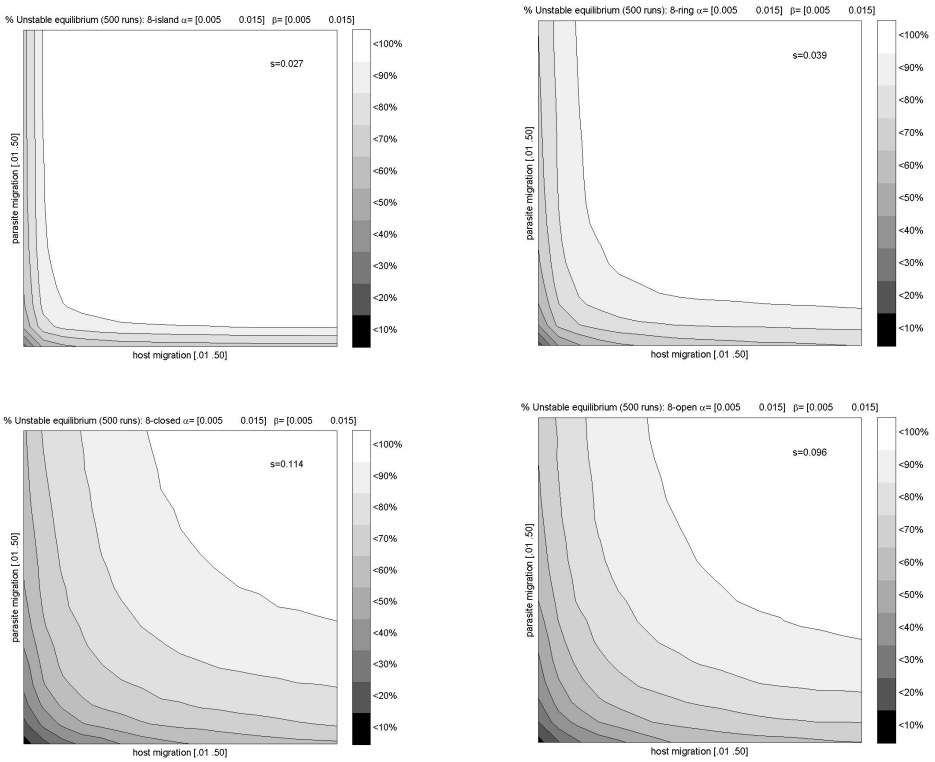


Figure 18. Effect of spatial structure on stability of the polymorphic equilibrium (8 demes), otherwise the same as in figure 16. Again, stepping-stone systems are more likely to have stable polymorphic equilibrium and adding demes makes them more stable (compared with s values in figure 16).

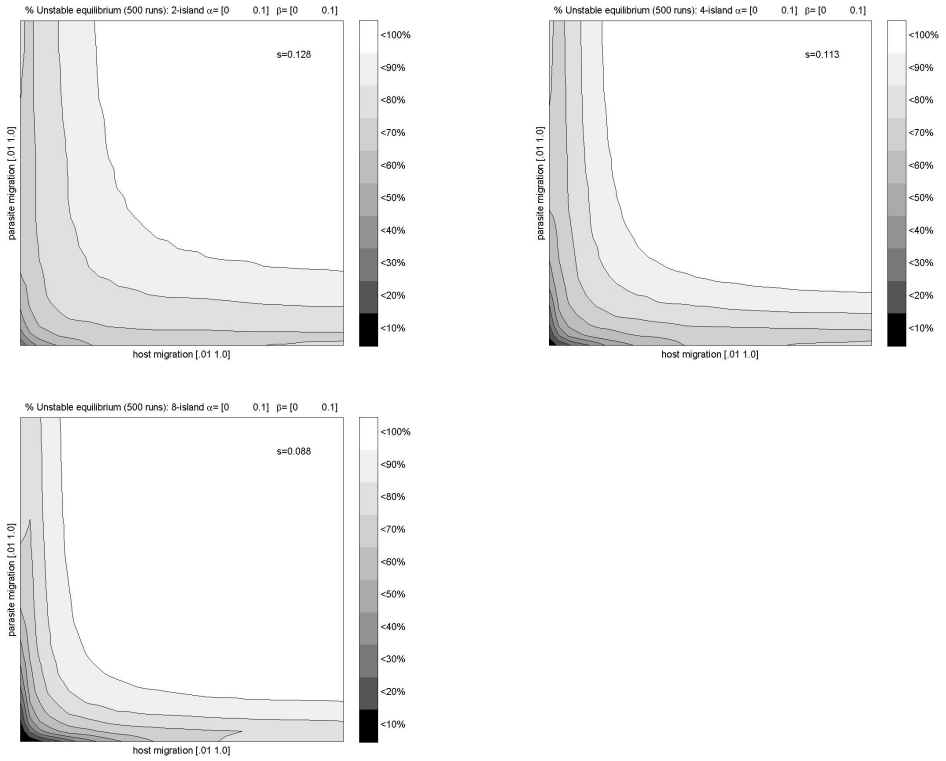


Figure 19. Effect of increasing island number on the stability of the polymorphic equilibrium (2, 4, and 8 islands). Percent stable of 500 runs with α's and β's from [0 .1], host migration varied on the x-axis and parasite migration on the y-axis.. We observe that adding more islands to the system decreases the probability of being at a stable polymorphic equilibrium from s=.128 in the 2 island case to s=.088 in the 8 island case.

APPENDIX II: MODEL EQUATIONS

1) Island Model

Species selection is symmetric frequency-dependent with fitnesses being given by linear functions of the genotypes in the other species.

$$w_{A,\,i} = 1 - \alpha_i \cdot p_i$$
$$w_{a,\,i} = 1 - \alpha_i \cdot (1 - p_i)$$
$$w_{B,\,i} = 1 - \beta_i \cdot (1 - h_i)$$
$$w_{b,\,i} = 1 - \beta_i \cdot h_i$$

Where *A, a* and *B, b* are species genotypes and $0 < \alpha_i, \beta_i < 1$ are coefficients controlling the strength of selection in patch *i*.
p_i and h_i are the frequencies of *A* and *B* in patch *i*.

Average fitness in patch *I* are

$$\bar{w}_{h,\,i} = w_{A,\,i} \cdot h_i + w_{a,\,i} \cdot (1 - h_i)$$
$$\bar{w}_{p',\,i} = w_{B,\,i} \cdot p_i + w_{b,\,i} \cdot (1 - p_i)$$

Allele frequencies after selection

$$h_i' = \frac{w_{A,\,i}}{\bar{w}_{h,\,i}} \cdot h_i$$
$$p_i' = \frac{w_{B,\,i}}{\bar{w}_{p',\,i}} \cdot p_i$$

Assume migration is uniform across all *n* patches, the migrant pools are then

$$\bar{h} = \frac{\sum h_i'}{n}$$
$$\bar{p} = \frac{\sum p_i'}{n}$$

Assume patches contribute to the migrant pools at rates m_h for hosts and m_p for parasites, after migration the allele frequencies are then

$$h_i'' = (1-m_h)\cdot h_i' + m_h \cdot \bar{h}$$
$$p_i'' = (1-m_p)\cdot p_i' + m_p \cdot \bar{p}$$

Fully expanded

$$h_i'' = \frac{(1-m_h)\cdot(1-\alpha_i \cdot p_i)\cdot h_i}{(1-\alpha_i \cdot p_i)\cdot h_i + (1-\alpha_i \cdot (1-p_i))\cdot(1-h_i)} + m_h \cdot \sum_{j=1}^{n} \frac{(1-\alpha_j \cdot p_j)\cdot h_j}{n\cdot((1-\alpha_j \cdot p_j)\cdot h_j + (1-\alpha_j \cdot (1-p_j))\cdot(1-h_j)}$$

$$p_i'' = \frac{(1-m_p)\cdot(1-\beta_i \cdot h_i)\cdot p_i}{(1-\beta_i \cdot h_i)\cdot p_i + (1-\beta_i \cdot (1-h_i))\cdot(1-p_i)} + m_p \cdot \sum_{j=1}^{n} \frac{(1-\beta_j \cdot h_j)\cdot p_j}{n\cdot((1-\beta_j \cdot h_j)\cdot p_j + (1-\beta_j \cdot (1-h_j))\cdot(1-p_j)}$$

2) Equations after migration for other spatial systems (for *n* demes)

for i≠1, n in all following models

$$h_i'' = \frac{m_h}{2} h_{i-1}' + \frac{m_h}{2} h_{i-1}' + (1-m_h) h_i'$$

i) Ring System (periodic boundary)

for i=1

$$h_1'' = \frac{m_h}{2} h_2' + \frac{m_h}{2} h_n' + (1-m_h) h_1'$$

for i=n

$$h_n'' = \frac{m_h}{2} h_1' + \frac{m_h}{2} h_{n-1}' + (1-m_h) h_n'$$

ii) Linear Stepping Stone Model (closed-boundary)

for i=1

$$h_1'' = \frac{m_h}{2} h_2' + (1-\frac{m_h}{2}) h_1'$$

for i=n

$$h_n'' = \frac{m_h}{2} h_{n-1}' + (1 - \frac{m_h}{2}) h_n'$$

iii) Linear Stepping Stone Model (open-boundary)

for i=1

$$h_1'' = \frac{\frac{m_h}{2} h_2' + (1 - m_h) h_1'}{1 - \frac{m_h}{2}}$$

for i=n

$$h_n'' = \frac{\frac{m_h}{2} h_{n-1}' + (1 - m_h) h_n'}{1 - \frac{m_h}{2}}$$

APPENDIX III: DERIVATIONS BY DR. GAVRILETS

1) Single Deme- Stability of the equilibrium

Solving the single deme system for equilibria yields four monomorphic equilibria and a single polymorphic equilibrium.

The monomorphic equilibrium $h_1=p_1=1$ and $h_1=p_1=0$ are saddle points with eigenvalues

$$\lambda_1 = \frac{1}{1-\alpha} > 1$$
$$\lambda_2 = 1-\beta < 1$$

.

Similarly the equilibrium $h_1=p_2=1$ and $h_1=p_2=0$ are saddle points with eigenvalues

$$\lambda_1 = 1-\alpha < 1$$
$$\lambda_2 = \frac{1}{1-\beta} > 1$$

.

The polymorphic equilibrium $h_1=p_1=½$ has the characteristic equation

$$\lambda^2 - 2\lambda + 1 + \frac{\alpha}{2-\alpha}\cdot\frac{\beta}{2-\beta}.$$

Since $0 < \alpha < 1$ and $0 < \beta < 1$, the last term is positive.

This has complex roots $\lambda_{1,2} = 1 \mp \sqrt{-\frac{\alpha}{2-\alpha}\cdot\frac{\beta}{2-\beta}}$ with

$\left|\lambda_{1,2}\right| = \sqrt{1+\frac{\alpha}{2-\alpha}\cdot\frac{\beta}{2-\beta}} > 1$. Thus the equilibrium is an unstable focus.

2) Maximum migration ($m_h=m_p=1$) in *n* number of demes

After a single generation the allele frequencies become equal across all demes (as in the Levene model) and the system can be characterized by two variables h_m, p_m. Where

$$h_m = \frac{1}{n}\sum_i \frac{1-\alpha_i p}{h(1-\alpha_i p)+(1-h)[1-\alpha_i(1-p)]}h,$$
$$p_m = \frac{1}{n}\sum_i \frac{1-\beta_i(1-h)}{p[1-\beta_i(1-h)]+(1-p)(1-\beta_i h)}p,$$

.

Similar in form to the single deme system, the monomorphic equilibrium $h_1=p_1=1$ and $h_1=p_1=0$ are saddle points and have eigenvalues

$$\lambda_1 = \frac{1}{n}\sum \frac{1}{1-\alpha_i} > 1$$
$$\mu_1 = \frac{1}{n}\sum (1-\beta_i) < 1$$

.

Likewise, equilibrium $h_1=p_2=1$ and $h_1=p_2=0$ are saddle points and have eigenvalues

$$\lambda_2 = \frac{1}{n}\sum \frac{1}{1-\beta_i} > 1$$
$$\mu_2 = \frac{1}{n}\sum (1-\alpha_i) < 1$$

.

The polymorphic equilibrium $h_1=p_1=½$ has eigenvalues

$$\lambda_{1,2} = 1 \mp \sqrt{-\frac{1}{n}\sum \frac{\alpha_i}{2-\alpha_i} \cdot \frac{1}{n}\sum \frac{\beta_i}{2-\beta_i}}$$

and is always an unstable focus.

3) Stability of heteroclinic cycle at maximum migration ($m_h=m_p=1$) in *n* number of demes (assuming spatial heterogeneity in selection).

Following derivations in Hofbauer and Sugmund (1998) for difference equations, the stability of a simple heteroclinic cycle is controlled by the coefficient

$$\rho = \prod_i \left(\frac{\ln \mu_i^{-1}}{\ln \lambda_i} \right),$$

where $\mu_i < 1$ and $\lambda_i > 1$ are the eigenvalues corresponding to "incoming" and "outcoming directions" for the *i*th saddle point. In this model, $\rho < 1$ because

$$\frac{1}{1-E\{x\}} < E\left\{\frac{1}{1-x}\right\},$$

where $E\{x\}$ is the expectation of a random variable x. $\rho < 1$ implies the cycle is unstable with smaller values having more "repelling" cycles.

4) Spatially homogeneous selection in two demes ($\alpha_1= \alpha_2= \alpha$, $\beta_1= \beta_2= \beta$)

For the monomorphic equilibria $h_1=p_1= h_2=p_2=1$and $h_1=p_1= h_2=p_2=0$ are unstable with eigenvalues

$$1-\beta,\ (1-m_p)(1-\beta)<1,\ \frac{1}{1-\alpha}>1,\ \frac{1-m_h}{1-\alpha}$$

For the monomorphic equilibria $h_1= h_2= 1$ & $p_1=p_2=0$ and $h_1= h_2= 0$ & $p_1=p_2=1$ are unstable with eigenvalues

$$1-\alpha,\ (1-m_h)(1-\alpha)<1,\ \frac{1}{1-\beta}>1,\ \frac{1-m_p}{1-\beta}$$

The polymorphic equilibrium $h_1=p_1= h_2=p_2=½$ with a characteristic equation identical to the polymorphic equilibrium is S2.1 and is an unstable focus.

5) Stability of the polymorphic equilibrium in 2 demes

The stability matrix has the form

$$S=\frac{1}{2}\begin{bmatrix} 1-\frac{m_h}{2} & -A_1\left(1-\frac{m_h}{2}\right) & \frac{m_h}{2} & A_2\frac{m_h}{2} \\ B_1\left(1-\frac{m_p}{2}\right) & 1-\frac{m_p}{2} & B_2\frac{m_p}{2} & \frac{m_p}{2} \\ \frac{m_h}{2} & -A_1\frac{m_h}{2} & 1-\frac{m_h}{2} & -A_2\left(1-\frac{m_h}{2}\right) \\ B_1\frac{m_p}{2} & \frac{m_p}{2} & B_2\left(1-\frac{m_p}{2}\right) & 1-\frac{m_p}{2} \end{bmatrix}$$

where $A_i=\alpha_i/(2-\alpha_i)$, $B_i=\beta_i/(2-\beta_i)$.

The eigenvalues of S are given by the roots of a fourth order polynomial:

$R=c_4\lambda^4+ c_3\lambda^3+ c_2\lambda^2+ c_1\lambda+ c_0$, where

$$c_4 = 1$$
$$c_3 = -(2 + \tilde{m}_h + \tilde{m}_p)$$
$$c_2 = \left[1 + \frac{(A_1 + A_2)(B_1 + B_2)}{4}\right](1 + \tilde{m}_h\tilde{m}_p) + \left[2 + \frac{(A_1 - A_2)(B_1 - B_2)}{4}\right](\tilde{m}_h + \tilde{m}_p)$$
$$c_1 = -\left(1 + \frac{(A_1B_1 + A_2B_2)}{2}\right)(\tilde{m}_h + \tilde{m}_p + 2\tilde{m}_h\tilde{m}_p),$$
$$c_0 = (1 + A_1B_1)(1 + A_2B_2)\tilde{m}_h\tilde{m}_p.$$

with $\tilde{m}_h = 1 - m_h, \tilde{m}_p = 1 - m_p$. Let $\lambda = (1+\mu)/(1-\mu)$. Then μ satisfies to the polynomial

$$T = C_4\mu^4 + C_3\mu^3 + C_2\mu^2 + C_1\mu + C_0$$

where

$$C_4 = c_0 - c_1 + c_2 - c_3 + c_4,$$
$$C_3 = -4c_0 + 2c_1 - 2c_3 + 4c_4,$$
$$C_2 = 6c_0 - 2c_2 + 6c_4,$$
$$C_1 = -4c_0 - 2c_1 + 2c_3 + 4c_4,$$
$$C_0 = c_0 - c_1 + c_2 - c_3 + c_4.$$

According to the Liénard-Chipart version of the Routh-Hurwitz criterion, the roots of the polynomial T have negative real parts if and only if

$C_0, C_1, C_3, C_4 > 0, \Delta_3 \equiv C_1C_2C_3 - C_0C_3^2 - C_1^2C_4 > 0.$

If all μ's have negative real parts, then all λ's lie within the unit circle of the origin in the complex plain. Thus the above give conditions for stability of the polymorphic equilibrium.

6) Bounds on migration that produce a stable polymorphic equilibrium.

Let $s_1 = A_1B_1, s_2 = A_2B_2, \overline{A} = (A_1 + A_2)/2$, and $\overline{B} = (B_1 + B_2)/2$. Let migration rates be equal, i.e. $m_p = m_h = m$ and $\tilde{m} = 1 - m$. Then

$$C_0 = \tilde{m}^2 s_1 s_2 + (1-\tilde{m})^2\overline{A}\overline{B} + 4(1+\tilde{m})^2 + 2\tilde{m}(1+\tilde{m})(s_1 + s_2) > 0$$
$$C_1 = 2\tilde{m}(1-\tilde{m})(s_1 + s_2) - 4\tilde{m}^2 s_1 s_2$$

which is positive if

$$m > \frac{2s_1s_2}{s_1 + s_2 + 2s_1s_2}$$

$$m > m_l \equiv 1\text{-}\frac{1}{2}\frac{\sqrt{(s_1+s_2)^2+16(4+3s_1+3s_2+2s_1s_2)}-(s_1+s_2)}{4+3s_1+3s_2+2s_1s_2}$$

which also satisfies the condition on C_1.

$$\Delta_3 \equiv 64\tilde{m}[1-\tilde{m}(1+s_1)][1-\tilde{m}(1+s_2)][3(1+s_1)(1+s_2)(s_1+s_2+s_1s_2)\tilde{m}^3$$
$$-(s_1+s_2-2s_1s_2)\tilde{m}^2-(s_1+s_2-3s_1s_2)\tilde{m}+s_1+s_2]$$
$$-64(1-\tilde{m})^2[1-\tilde{m}^2(1+s_1)(1+s_2)]^2\overline{AB}$$

Note that as $m \to 1, \Delta_3 \to -64\overline{AB} < 0$. Therefore the polymorphic equilibrium can only be stable for intermediate migration rates.

Assume selection is weak so that $A_i = \sqrt{\varepsilon}a_i$, $B_i = \sqrt{\varepsilon}b_i$, where $\varepsilon << 1$. Then

$$\Delta_3 = 64(1+\tilde{m})(1-\tilde{m})^4[\tilde{m}(\overline{AB}+\delta)-\overline{AB}]+o(\varepsilon),$$

where $\overline{AB} = (A_1B_1 + A_2B_2)/2$ and $\delta = (A_1 - A_2)(B_1 - B_2)/4$.

Note that $\delta = \overline{AB} - \overline{AB}$ and thus is a covariance. Assume $\overline{AB} + \delta > 0$. Then $\Delta_3 > 0$ if $m < m_u \equiv \frac{2\delta}{\overline{AB}+\delta}$ and $\delta > 0$.

Note that increasing spatial heterogeneity (characterized by δ) widens the conditions for stability of the polymorphic equilibrium.

Thus under the assumptions of equal migration rates a lower bound on migration rates can be found on the stability of the polymorphic equilibrium and adding the assumption of weak selection, and upper bound on migration rates can be solved.

VITA

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