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Coevolving parasites improve host evolutionary search on structured fitness landscapes

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Abstract

Evidence suggests that host-parasite coevolution can often result in host diversification. However, the host traits that coevolve often have primary functions affecting growth, creating the potential for conflicting selection pressures. For example, bacteriophage often infect bacteria by binding to nutrient uptake receptors, thus diversification of bacteria due to coevolution with phage may have an impact on resource competition. This paper uses a model of bacteria and phage in a chemostat to study the impact of coevolution with phage on the evolution of host growth rates, when infection and growth are affected by the same trait. Comparing (co)evolutionary outcomes on different growth rate fitness landscapes, with and without phage, shows that coevolutionary diversification allows hosts to cross fitness valleys and improve search efficiency on rugged landscapes, although it also prevents the whole community from reaching global optima. In effect, coevolution with parasites increases *exploration* but decreases *exploitation* in host evolutionary search.

Introduction

All biological evolution is coevolution, in the sense that any evolving population has a selective environment formed of, and created by, other organisms. The biotic environment of an organism determines its direct ecological interactions and also ultimately shapes the character of its abiotic environment through niche construction effects (Odling-Smee et al., 2003; Williams and Lenton, 2008). In general, coevolution is a diffuse process, with most species having a negligible impact on the evolution of any focal species. However, when species interact closely and have a strong direct impact on each other's fitness, coevolution can be a signficant determinant of evolutionary outcomes (Thompson, 2005). In host-parasite systems, for example, the parasite depends on the host for survival and reproduction. Such close interaction between hosts and parasites often leads to significant antagonistic coevolution, in which the host evolves to lessen the impact of the parasite, while the parasite evolves to maintain its infective and reproductive ability on the host (Buckling and Rainey, 2002; Woolhouse et al., 2002; Thompson, 2005).

A well-studied class of host-parasite interactions is the infection of bacteria by bacteriophage (viruses that infect bacteria). Phage are obligate intracellular parasites that infect bacteria by binding to a cell surface receptor before injecting their DNA. Phage are commonly classified as having either lysogenic or lytic lifestyles. Lysogeny involves the integration of phage DNA into the genome of the host cell, so that the phage is propagated by host reproduction for many generations until some trigger causes lysis (cell burst) and the release of new phage particles. In the lytic lifestyle, phage infect the host cell and subvert its metabolism to produce new phage, which are then released by lysis. Lytic infection suppresses host replication and always results in cell death, hence the interaction between bacteria and lytic phage is literally a matter of life and death; the phage must infect if they are to reproduce, while the cell must avoid infection if it is to survive. The selection pressure each partner exerts on the other is thus intense and antagonistic coevolution can produce rapid genetic change. For this reason, bacteria and lytic bacteriophage are often used for experimental studies of coevolution (Bohannan and Lenski, 2000; Buckling and Rainey, 2002; Brockhurst et al., 2007).

Coevolution has been hypothesised to have a significant impact on the diversity of hosts and viruses. Two models for the genetics of host-parasite coevolution are commonly discussed, the 'gene-for-gene' and 'matching-alleles' models (Agrawal and Lively, 2002). Each model makes a different prediction for diversity. The gene-for-gene model is adapted from plant-pathogen interactions and assumes that hosts have either resistant (res) or susceptible (sus) alleles at each infection locus, while at each paired locus the parasite has either virulent (vir) or avirulent (avi) alleles. At a single locus, infection occurs for cases: $\{res - vir, sus - vir, sus - avi\}$ but not for case $\{res - avi\}$. The gene-for-gene model predicts that coevolutionary arms races can occur, in which the host gains res alleles and the parasite gains vir alleles, but also predicts low-diversity outcomes in which the host and parasite populations are dominated by the most resistant and most infectious genotypes respectively. The matching alleles model is derived from self/non-

self recognition mechanisms in invertebrates and assumes that some form of genetic match between host and parasite is needed at relevant loci for infection to occur. Thus with matching-alleles genetics, a single host mutation can make infection impossible, but can be countered by a single parasite mutation. The matching-alleles model predicts diversification of hosts due to negative density-dependent selection from parasites; hosts diversify in order to escape infection, while parasites diversify as they counter-adapt. Various studies have demonstrated that stable polymorphisms are a common outcome from matching-alleles coevolution (Agrawal and Lively, 2002). Empirical data to support either matching-alleles or gene-for-gene as a general model for coevolution of bacteria with bacteriophage is equivocal. Other genetic systems have been hypothesised (Fenton et al., 2009; Hall et al., 2011) and it also seems likely that multiple mechanisms may operate concurrently (Agrawal and Lively, 2003; Fenton et al., 2012), so no simple generalisation can be made.

In natural microbial communities, coevolution with phage has been hypothesised as a possible explanation for widespread observations of high marine prokaryote diversity. Theoretical models of planktonic food-web ecology predict that selective viral predation can maintain host diversity by preventing dominance of host types that would otherwise monopolise available resources (the 'kill-the-winner' model (Thingstad and Lignell, 1997; Thingstad, 2000)). However, the action of coevolution on marine microbial communities is difficult to measure directly. Metagenomic data for marine prokaryotes so far suggests that phage are responsible for a high proportion of prokaryote diversity. The 'constant diversity' hypothesis (Rodriguez-Valera et al., 2009) states that bacteriophage maintain high diversity in prokaryote communities via negative density-dependent selection, based on evidence that high-diversity genomic islands in prokaryote genomes often code for traits associated with phage infection, e.g. surface proteins, CRISPR arrays, etc. The relationship between phage predation and host diversity was directly tested for *Prochlorococcus* and cyanophage by experiments that showed resistance mutations mostly occurred in hyper-variable regions of the genome and that any single phage strain could only infect a subset of the bacterial population (Avrani et al., 2011). Experiments with *Synechococcus* and cyanophage also showed rapid coevolutionary diversification of both host and phage (Marston et al., 2012).

Experimental coevolution with bacteria and bacteriophage in chemostats has shown that resistant mutant strains can enter the host population via selective sweeps, displacing susceptible strains; limited diversity can be sustained when trade-offs between growth rate and resistance allow stable coexistence of a growth-specialist and a resistance-specialist (Bohannan and Lenski, 2000). Meanwhile, experimental coevolution with bacteria and phage in batch culture has repeatedly shown that hosts can rapidly acquire resistance to new phage while maintaining resistance to ancestral phage (Buckling and Rainey, 2002; Brockhurst et al., 2007). These 'arms race' dynamics are consistent with the gene-for-gene model and might be expected to lead to low diversity.

While it is hard to generalise the relationship between host-virus coevolution and diversity, there appears to be strong evidence that in many cases coevolution with viruses leads to host diversification (Rodriguez-Valera et al., 2009; Avrani et al., 2011; Marston et al., 2012). How does this virus-driven diversity affect the evolution of non-virus-associated traits? When coevolving traits do not affect other functions, coevolution and evolution may be orthogonal and proceed independently. However, coevolving traits often have a large impact on growth and/or reproduction (Lennon et al., 2007). Pleiotropic interactions may then lead to conflicts and trade-offs that shape adaptive trajectories. For example, phage often bind to nutrient uptake receptors on the bacterial cell surface, thus the evolution of these receptors is subject to (potentially conflicting) selection pressures for uptake efficiency and phage resistance (Rodriguez-Valera et al., 2009). Receptor mutations will thus affect both infection rate and resource competition, and may have opposing effects on each component of overall fitness.

The general scientific question addressed by this paper is whether diversification caused by coevolution with parasites has an impact on host adaptation to environmental selection pressures. Diversity is a pre-requisite for any form of evolution, since phenotypic differences form the basis of selectable variation in fitness. Hence a reasonable hypothesis is that increased diversity caused by coevolution with parasites (under a matching-alleles-like model) might lead to improved evolutionary search and faster adaptation of hosts. In particular, this study focuses on the evolution of a host trait that affects both growth rate and parasite infection, inspired by (amongst others) the natural example of bacterial resource uptake receptors that are also the attachment site for bacteriophage. A simple model of bacterial hosts coevolving with phage in a chemostat is used to show that (i) phage predation causes host diversification, and (ii) the diversity that is thus created improves the ability of the host population to optimise growth rates on structured adaptive landscapes. The next section defines the model and methods used. This is followed by results showing the adaptation of the host population on a variety of adaptive landscapes, with and without coevolving phage. The paper concludes with some discussion of the relevance of these findings for artificial and biological evolution.

Model & Methods

Multi-species chemostat model. The model represents the growth and interaction of a diverse community of bacteria and bacteriophage growing in a single-resource chemo-

stat. The model scheme is a variant of a reasonably well-studied type originally formulated for single-species studies of bacteria and bacteriophage growing on a single resource (e.g. (Levin et al., 1977; Bohannan and Lenski, 2000)). Here a multi-species version of the model is used in which mutations can introduce new variants of bacteria and phage, while species are removed (go extinct) when their density falls below a threshold level (Weitz et al., 2005). This creates a simple model in which bacteria and phage phenotypes can evolve by natural selection.

State dynamics for resource concentration R and the density of each host N and phage V population in the chemostat are governed by the following equations:

$$\frac{dR}{dt} = -\omega(R - R_0) - \sum_i \varepsilon\gamma \frac{RN_i\delta_i}{R+K} \quad (1)$$

$$\frac{dN_i}{dt} = -\omega N_i + \gamma \frac{RN_i\delta_i}{R+K} - \sum_j \theta_{ij} N_i V_j \quad (2)$$

$$\frac{dV_j}{dt} = -\omega V_j + \sum_i \beta\theta_{ij} N_i V_j \quad (3)$$

Resource concentration is determined by supply concentration R_0 , flow rate ω, and by the total uptake of resource by all bacterial populations (determined by their growth rate scaled by a resource conversion rate ε). The density N_i of the i^{th} bacterial population is controlled by washout, growth, and mortality from phage. Growth is determined as a function of resource concentration, maximum uptake rate γ, half-saturation constant K, and a strain-specific scaling factor δ_i). The density V_j of the j^{th} phage population is determined by washout and production. Phage production is determined as the sum of production on all available hosts, assuming fixed burst size β and adsorption rate θ_{ij} for phage j on host i. All symbol definitions and parameter values are given in Table 1.

Evolutionary process. Every distinct bacterial genotype h_i and phage genotype v_j is instantiated as a population within the community. Bacterial genotypes are mapped to phenotypic traits for resistance and growth rate. Phage genotypes map to an infection trait. The model assumes that bacteria and phage each evolve within a one-dimensional genetic space, i.e., each distinct genotype can be represented by a point on a line and adaptation occurs by movement along the line. Following mutation, a new population that instantiates the novel phenotype is added to the system. If the density of any population falls below 1 (possible due to the continuous nature of the mathematical abstraction), that population is removed from the system.

The model assumes that mutations are small and occur with low probability for each new cell or virion produced. For bacterial genotype h_i, the instantaneous rate of production of new cells is $\gamma\frac{RN_i\delta_i}{R+K}$ and the probability of mutation

Symbol	Description	Value	Unit
R	Resource concentration	Variable	$\mu g\, ml^{-1}$
N_i	Density of host strain i	Variable	$cells\, ml^{-1}$
V_i	Density of virus strain i	Variable	$virions\, ml^{-1}$
N_{init}	Initial host density	4.6×10^4	$cells\, ml^{-1}$
V_{init}	Initial virus density	8.1×10^5	$virions\, ml^{-1}$
ω	Chemostat dilution rate	0.0033	min^{-1}
R_0	Resource supply concentration	2.2	$\mu g\, ml^{-1}$
ε	Resource conversion rate	2.6×10^{-6}	$\mu g\, cell^{-1}$
γ	Maximum resource uptake rate	0.0123	$\mu g\, min^{-1}$
K	Half-saturation constant	4	$\mu g\, ml^{-1}$
δ_i	Growth scaling for host h_i	Variable	$scalar$
δ_{min}	Min. growth scaling factor	0.8	$scalar$
δ_{max}	Max. growth scaling factor	1.2	$scalar$
ϕ	Maximum adsorption rate	0.104×10^{-8}	$ml(min\, cell)^{-1}$
θ_{ij}	Ads. scaling for v_j on h_i	Variable (range $[0, \phi]$)	$scalar$
β	Burst size	71	$virions$
h_i	Genotype of host i	Variable (range $[0, 1]$)	$scalar$
v_j	Genotype of phage j	Variable (range $[0, 1]$)	$scalar$
s	Specificity of phage	Manipulated	$scalar$
M_B	Host mutation rate	0.0001	$cell^{-1}$
M_V	Virus mutation rate	0.0001	$virion^{-1}$
σ_B	Std. dev. of host mut. range	0.005	$scalar$
σ_V	Std. dev. of virus mut. range	0.005	$scalar$
Δt	Integration timestep	10	min
T	Simulation duration	10^7	min
L	Chemostat volume	1	ml

Table 1: Model parameters and variable definitions.

of each new cell is M_B, so the number of mutants in each integration timestep for a chemostat of fixed volume L can be calculated. Similarly, the number of mutants of each viral genotype v_j can be calculated using the rate of virion production $\sum_i \beta\phi\theta_{ij}N_iV_j$ and the probability M_V of mutation of each new virion. For each mutation event, the mutant genotype is found by adding a normal deviate to the parental genotype, that is, $h_{mut} = h_i + \mu_h$ (or $v_{mut} = v_i + \mu_v$) where μ_h (μ_v) is a value drawn from a normal distribution with mean 0 and standard deviation σ_B (σ_V).

Infection model. The model uses a similarity-based infection scheme where the likelihood of infection of a host by a phage depends on their genetic 'similarity'. This scheme captures the basic properties of the matching alleles genetic model and is used to instantiate a density-dependent coevolutionary process. The adsorption coefficient θ_{ij} sets the rate of adsorption to host i by phage j, calculated from the host (h_i) and phage (v_j) genotypes according to:

$$\theta_{ij} = \phi e^{-s(h_i - v_j)^2} \quad (4)$$

where ϕ is the maximum adsorption rate and s is a sensitivity parameter that controls host specificity of phage. This function gives a sigmoidal form with slope determined by s, i.e. tuning the value of s alters the rate of decline in adsorption rate as dissimilarity increases. Every successful adsorption event is assumed to result in infection and instantaneous cell lysis, releasing a burst of β new phage particles.

Host growth rate landscape. To explore the ability of phage-driven diversification to improve host evolutionary search, a bestiary of growth rate functions is used to instantiate different kinds of constraint on the evolutionary

process. In all cases, growth rates perform some mapping of host genotype $h_i \in [0,1]$ to growth rate scaling factor $\delta_i \in [\delta_{max}, \delta_{min}]$. The landscapes used are:

1. *Flat*. All bacteria have the same growth rate ($\delta_i = 1$).

2. *Single-peak*. A single smooth peak given by:

$$\delta_i = \delta_{min} + (\delta_{max} - \delta_{min}) f_1(h_i)$$

where $f_1(h) = e^{-20(h-0.5)^2}$. See Figures 2(a) & 3(a).

3. *Multi-peak*. Multiple smooth peaks given by:

$$\delta_i = \delta_{min} + (\delta_{max} - \delta_{min}) f_2(h_i)$$

where:

$$f_2(h) = e^{-100(h-0.2)^2} + 2e^{-50(h-0.5)^2} + 3e^{-50(h-0.8)^2}$$

f_2 is normalised so that the maximum value is 1. See Figures 2(b) & 3(b).

4. *Stepped*. A piecewise linear function of multiple flat plateaus, given by:

$$\delta_i = 0.5 \quad if 0 \leq h_i < 0.5$$

$$\delta_i = 0.75 \quad if 0.5 \leq h_i < 0.75$$

$$\delta_i = 1 \quad if 0.75 \leq h_i \leq 1$$

See Figures 2(c) & 3(c).

5. *Rugged slope*. A linearly increasing function with uniform noise added to introduce ruggedness, given by:

$$\delta_i = \delta_{min} + \frac{1 + 2(h_i + \alpha)}{4}(\delta_{max} - \delta_{min})$$

where α is a uniform random variable drawn from the range $[-d, d]$. See Figures 2(d) & 3(d).

Method. The model is initialised with a single bacterial population and infectious phage, then integrated forward for T minutes using a 4th order Runge-Kutta method with timestep Δt. Data are presented by binning host and phage diversity according to genotype similarity at a resolution of 0.01. Model code, integration and visualisation are performed in MATLAB; code is available on request.

Results

To illustrate the negative density-dependent selection pressure imposed by viral predation, the model was configured so that all host types had the same growth rate (the *flat* landscape), so that the only selectable variation was in host resistance and virus infection traits (Figure 1). The striking feature of this scenario is that there is rapid and sustained diversification of hosts, with correlated diversification of phage. As more host strains enter the system, resource concentrations are drawn down and total bacteria

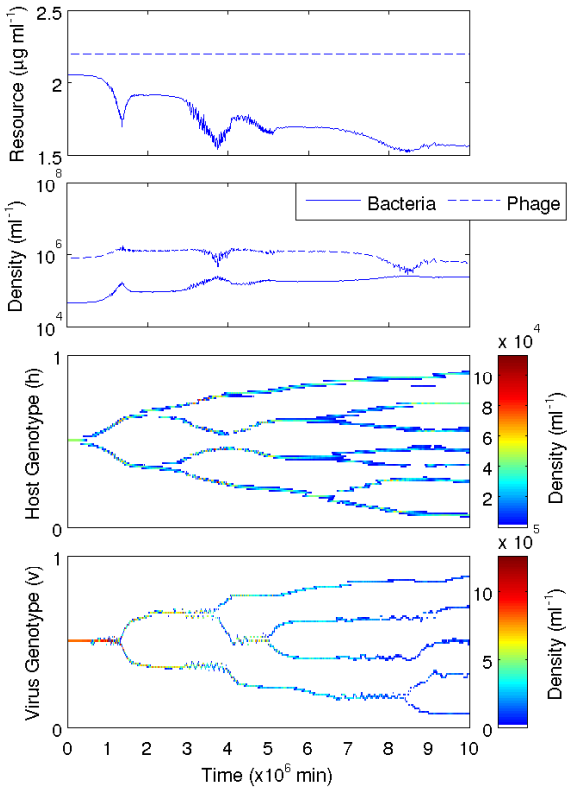

Figure 1: Phage predation causes host diversification. Time-series from a case study using the flat growth landscape ($s = 200$). Plots show: resource concentration (*top*, shown with supply concentration (dashed)), total bacterial and phage density (*middle*), and density of bacteria and phage in genetic space (*bottom*).

density rises. As resource concentrations fall, host growth rates are reduced. Since phage production is proportional to host growth rate (since lysis rate must balance growth rate at steady state), this means that total phage density falls slightly, despite increased host density. The dominant host clusters are relatively evenly distributed across the potential genetic space, reflecting the selective advantage gained from being far enough apart so that each host type is only significantly affected by a single phage strain; moving closer together would expose the host strain to predation by multiple phages and is thus maladaptive. The distance between host clusters, and hence the total genetic variance produced by phage predation, is thus determined by the level of host specificity, i.e. the parameter s setting the decline in adsorption rate with increasing genetic dissimilarity.

The next experiment was to run simulations of (co)evolutionary dynamics on structured growth landscapes,

comparing evolutionary outcomes when hosts evolve without viruses (Figure 2) and with viruses (Figure 3). On the *single-peak* landscape, hosts evolving with and without viruses were able to easily reach the optimum growth rate. However, the diversifying effect of viruses meant that the coevolving hosts were pushed off the peak growth rate (Figure 3(a)), while hosts evolving alone were able to maintain their population close to the peak (Figure 2(a)). The mean growth rate across the evolving host community was close to the maximum achievable value, while mean growth rate for the coevolving hosts was significantly lower.

On the *multi-peak* landscape, hosts evolving alone were able to find the closest local peak to their origin, but became trapped at this local optimum (Figure 2(b)). However, hosts coevolving with viruses were able to reach the global optimum (Figure 3(b)). The coevolving host community was able to escape the local optima, since viral predation caused host diversification into multiple strains that were sufficiently separated in genetic space to cross the fitness valleys between the growth rate optima. Only part of the host community reached the global optimum and several strains remained on the intermediate peak. Therefore the mean growth rate of the host community did not reach the maximum value. Nonetheless the community as a whole had significantly higher growth rates than the host population evolving alone.

On each plateau of the *stepped* landscape, there is no selectable variation in growth rate, so any genetic change with hosts evolving alone is due to drift. However, since populations are large (e.g. $2.74 \times 10^5 cells\, ml^{-1}$ in the example shown), drift does not cause any significant change in genotype frequencies. Thus with hosts alone (Figure 2(c)), no adaptation is observed and the host community remains undiversified at its original position in gene space. When bacteria coevolve with phage (Figure 3(c)), diversification causes the host community to diffuse across the plateau until it reaches the boundary with the next plateau. At that point, selection can allow the community to 'step up' to the next plateau. In this example, although resource competition does not remove all strains on the lower plateau, these strains grow too slowly to support phage.

The *rugged slope* landscape is a linearly increasing slope of growth rate with the addition of uniform noise to create ruggedness. The amplitude d of the noise distribution determines the amount of ruggedness and hence the difficulty of the evolutionary search task; populations must be able to cross small fitness valleys in order to climb the slope towards optimal growth rates. With hosts evolving alone (Figure 2(d), populations quickly get stuck at a local optimum and are unable to climb the slope. When hosts coevolve with phage (Figure 3(d)), diversification enables the host community to climb the slope effectively so that growth rates are steadily increased.

Discussion

Here a simple model of coevolution between bacteria and bacteriophage was used to explore the impact of coevolution on adaptation of non-phage-related bacterial traits. Coevolution using a similarity-based model of infection (that approximates the operation of the matching-alleles genetic model) showed that phage predation creates negative density-dependent selection that causes diversification of hosts on infection-related traits. When these traits are linked to growth rate, this diversification introduces new variety that can be selected for increased growth rate; that is, it enables evolutionary search. Tests with a variety of growth landscapes show that enhanced evolutionary search promoted by coevolution with phage enables hosts to effectively evolve higher growth rates on structured landscapes.

Coevolutionary diversification of hosts allows more effective search of the genetic space for 'good' growth rate solutions. In effect, it increases *exploration* of the space. However, this comes at a cost of reduced *exploitation* of good solutions once they are discovered. Diversity implies that only one sub-population can occupy the current best location in the search space; all other sub-populations are forced away from the optimum by negative density-dependent selection that prevents convergence. This effect is shown clearly in Figure 3(a). However, on landscapes with multiple local optima and fitness valleys (Figures 3(b) & 3(d)), diversification means that the population as a whole does not get trapped on local optima and can move more effectively towards global optima.

The mechanism identified here might have utility in evolutionary computation, where it might suggest an effective algorithm for search on rugged or multi-peak fitness landscapes. The key component of such an algorithm, here provided by selective phage predation, is negative density-dependent selection; it is this feature of the coevolutionary process that creates diversity and affords enhanced search. This feature could be implemented quite simply in a genetic algorithm, perhaps by imposing a fitness penalty on candidate solutions proportionate to their current representation in the population.

The ability of coevolution with parasites to introduce selectable variation in host traits unrelated to infection depends on the genetic linkage between infection-related traits and other functional traits. There are many cases in nature where parasites attack host traits that have an alternative primary function, e.g. bacteriophage adsorbing to nutrient uptake receptors, or pathogenic fungi inserting hyphae through host plant stomata. Indeed, this should be expected, since any host trait with the sole function of enabling parasitism would be entirely maladaptive and quickly lost by natural selection. Thus it should be expected that mutations with an impact on fitness in the dimension of parasite infection will also impact fitness in the dimension of the trait's original function.

Space constraints in this paper preclude a full analysis of

the sensitivity of these results to model structure and parameters. The model used here is deliberately simple and the number of evolvable parameters has been minimised to reduce the degrees of freedom in the evolutionary process. Alternative formulations might have allowed other traits to evolve, such as half-saturation constant K, burst size β, or maximum adsorption rate ϕ. However, allowing such variation in the current experiment would have obscured the primary result without altering the underlying logic of the argument. The formulation used (evolvable host range of phage, pleiotropy linking evolvable host growth rate and resistance) is sufficient for the current purpose. Two key parameters of the model are mutation range σ_B, σ_V and host specificity of phage s. The results presented are robust to variation in these parameters, so long as mutation range is small and phage have a narrow host range, in relation to the size of structural features in the fitness landscape (e.g. the width of fitness valleys).

The model presented here shows that diversification due to phage predation aids evolutionary search on structured landscapes. On landscapes with multiple peaks, coevolutionary diversification allows hosts to reach global optima; on landscapes incorporating neutral plateaus, coevolutionary diversifiation causes the population to diffuse and rapidly traverse the plateau; on rugged landscapes, coevolutionary diversification prevents populations becoming trapped by local fitness gradients, so that they can evolve steadily towards optimum growth rates. Biological evolution is far more complex than the simple model presented here, yet biological fitness landscapes are known to often display multiple local optima, neutrality, and ruggedness. Thus it is interesting to hypothesise that diversification due to coevolution with parasites might improve host evolvability in natural systems.

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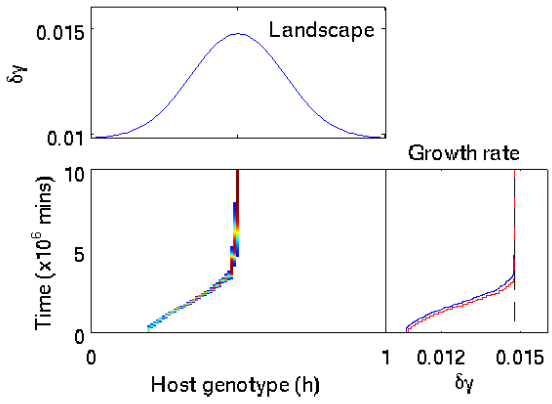
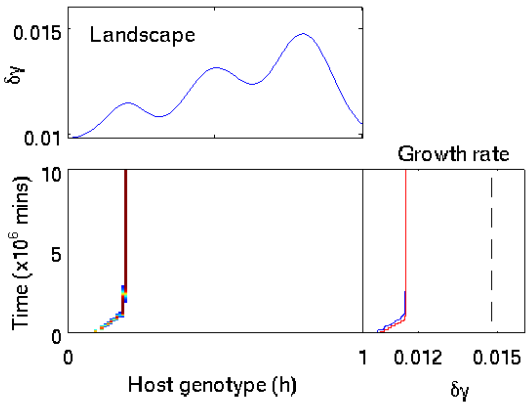
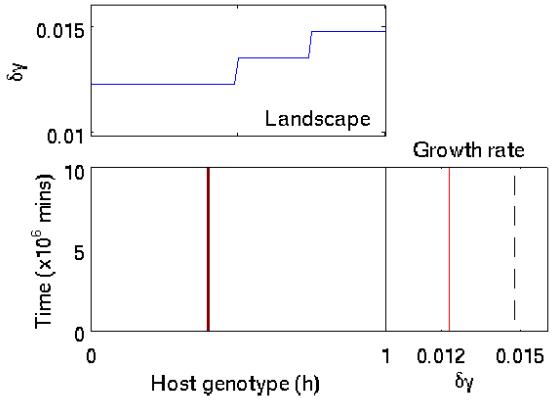


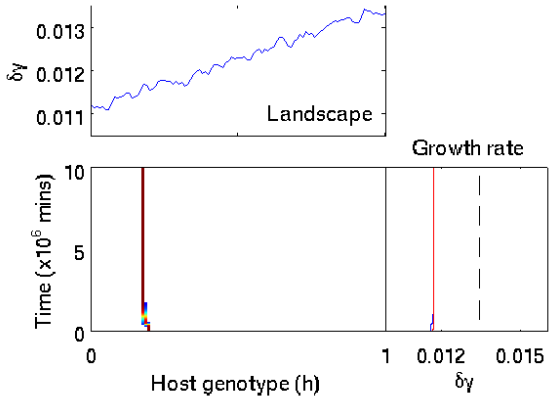
(a) Single-peak landscape (no viruses).



(b) Multi-peak landscape (no viruses).

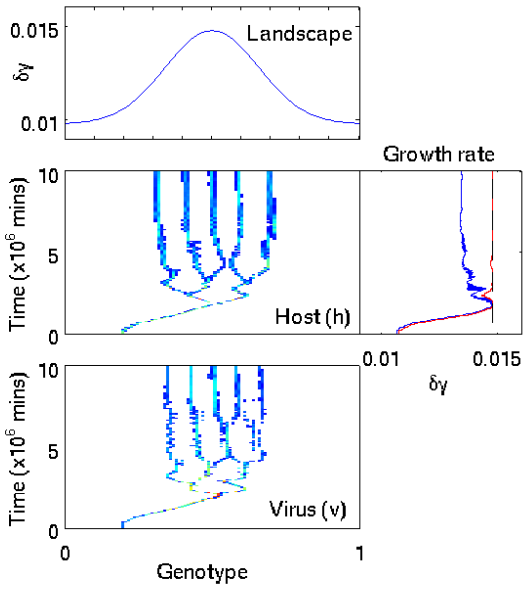


(c) Stepped landscape (no viruses).

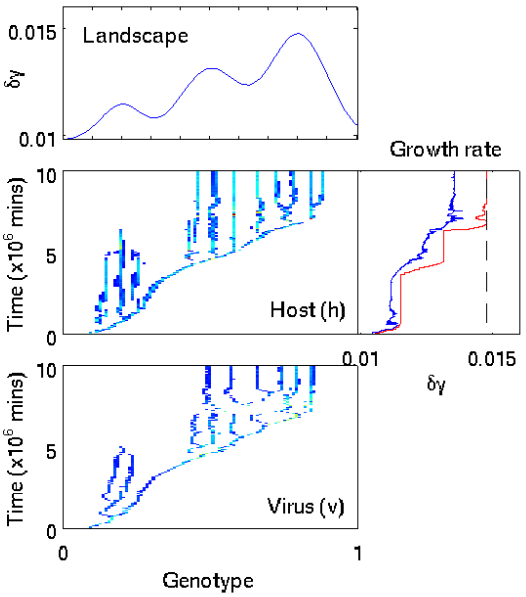


(d) Rugged slope landscape ($d = 0.1$, no viruses).

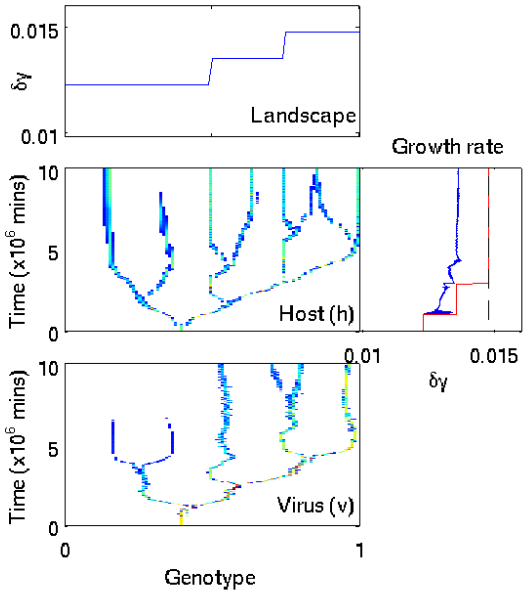
Figure 2: Case study simulations showing host evolutionary dynamics on various growth landscapes in the absence of viruses. Plots show the growth landscape (*top*, given as the value of $\delta_i\gamma$ for all possible host genotypes h_i), the distribution over time of hosts in genetic space (*middle*), and the observed growth rates over time of the host community (*right*, shows mean (blue), actual maximum (red), potential maximum (dashed)).



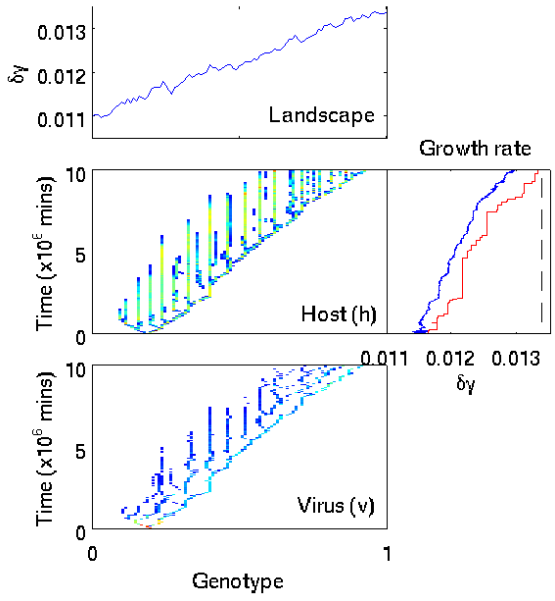
(a) Single-peak landscape ($s = 200$).



(b) Multi-peak landscape ($s = 500$).



(c) Stepped landscape ($s = 100$).



(d) Rugged slope landscape ($d = 0.1$, $s = 1000$).

Figure 3: Case study simulations showing coevolutionary dynamics and host growth rate adaptation on various growth landscapes. Plots show the growth landscape (*top*, given as the value of $\delta_i\gamma$ for all possible host genotypes h_i), the distribution over time of hosts and viruses in genetic space (*middle* and *bottom*), and the observed growth rates over time of the host community (*right*, shows mean (blue), actual maximum (red), potential maximum (dashed)).