Network Models of Phage-Bacteria Coevolution

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Bacteria and their bacteriophages are the most abundant, widespread and diverse groups of biological entities on the planet. In an attempt to understand how the interactions between bacteria, virulent phages and temperate phages might affect the diversity of these groups, we developed a novel stochastic network model for examining the co-evolution of these ecologies. In our approach, nodes represent whole species or strains of bacteria or phages, rather than individuals, with “speciation” and extinction modelled by duplication and removal of nodes. Phage-bacteria links represent host-parasite relationships and temperate-virulent phage links denote prophage-encoded resistance. The effect of horizontal transfer of genetic information between strains was also included in the dynamical rules. The observed networks evolved in a highly dynamic fashion but the ecosystems were prone to collapse (one or more entire groups going extinct). Diversity could be stably maintained in the model only if the probability of speciation was independent of the diversity. Such an effect could be achieved in real ecosystems if the speciation rate is primarily set by the availability of ecological niches.

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Introduction

Bacteria and the bacteriophages that infect them are present in huge numbers in a wide range of natural environments, e.g. \( \sim 10^6 \) bacteria and \( 10^7 \) phages per ml of seawater [1]. Phages are significant factors in determining bacterial mortality [2], and thereby have a major influence on global recycling of nutrients and carbon in the biosphere [3]. The diversity of these populations is also staggering, with estimates of \( \sim 10^6 \) different bacterial species and \( \sim 10^3 \) phage genotypes per few litres of seawater [4] and at least \( 10^4 \) phage genotypes per kg of marine sediment [5]. Further, because most phages only infect very few host strains, the composition of phage strains is likely to be an important determinant of the composition of bacterial communities. Moreover, bacteria and phage populations are dynamic: they have been observed to fluctuate wildly on timescales ranging from weeks to months [6].

Natural phage populations comprise both virulent and temperate phages. Replication of a virulent phage kills the host bacterium (lytic life cycle), whereas a temperate phage can replicate either lytically or by temporarily combining its genome with that of the bacterium to form a lysogen (lysogenic life cycle). The phage genome in a lysogen (prophage) provides its bacterial host with immunity to lytic infection by the same strain of phage. Deterministic predator-prey modeling [7,8] of phage-bacterial ecosystems with virulent and temperate phages have shown that these may be stable (all three classes coexisting) or unstable (one or more classes collapsing), depending on predation and reproduction parameters.

In this paper we build several more coarse-grained models, consisting of a network of nodes, representing bacterial and phage strains, and links, representing interaction between strains, which evolves stochastically in discrete time steps according to a set of rules. The nodes of the network are bacterial and phage strains, i.e., subpopulations, however we do not explicitly model the populations as dynamical variables. Instead, the rules for adding or removing nodes and links use only the structural properties of the network at that time. For instance, we take the extinction rate of a bacterial strain to be a simple function of the number (and type) of phage strains that can infect it, i.e., the number of links pointing to it from phage strains. In contrast, in a model where populations were modeled explicitly, the rule would be that an extinction occurs whenever the population of a strain falls to zero. The population, in turn, would typically be derived from a differential equation that would depend on the number of links pointing from phages to the given bacterial strain. In our modelling approach, we short-circuit this step, replacing populations and their differential equations by a simple rule based on properties like the number of links.

Our model rules incorporate various biological facts concerning phage and bacteria interactions. For instance, we take into account the ability of temperate phages to carry genes that make the lysogenic host resistant to infection by virulent phages [8], providing bacteria with weapons in the co-evolutionary arms race with virulent phages. We also incorporate horizontal transfer of genes between phages sharing the same host in the rules that determine the evolution of new phage strains. Since our models coarse-grain the system at the level of strains of bacteria and phage, they are particularly suited to examine questions about the diversity of bacterial and phage populations, rather than their sizes.
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ated with environmental loads common to all strains,
The second rule implements random extinction associ-
ation). We let the speciation rate define our time step.
Thus at every time, \( t \), two types of events occur to change
the system:
- **Speciation**: We select a random strain and duplic-
cate it, \( N_B(t) = N_B(t-1) + 1 \).
- **Extinction**: We remove each strain, \( i = 1, 2, ..., N_B(t) \), with a probability \( N_B/N_0 \).

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ated with environmental loads common to all strains, like eukaryotic predators, scarce resources and crowding.
The parameter \( N_0 \) represents the carrying capacity of the ecosystem. In this simple non-interacting system
\( N_B \) fluctuates around \( N_0 \), as illustrated in Fig. 2. Note
that removing each strain with probability \( 1/N_0 \) would
produce the same behaviour. Instead we choose \( N_B/N_0 \)
to take into account the reduced extinction rate when
there are fewer strains and therefore more biomass per
strain. We denote this scenario of non-interacting bac-
terial strains, with no phages, “model A”.

On top of this basic system of independent bacteria
we add a self adjusting number, \( N_V \), of virulent phage
strains. This extended model B now also contains links
between phage and bacterial strains as illustrated in Fig.
(1). Such a link represents the ability of a phage to infect
and lyse the bacteria it points to. As before, the bacterial
speciation rate defines the basic time step. At each time,
\( t \), the following events occur:
- **Bacterial speciation**: We select a random bacterial
  strain and duplicate it, along with its original links,
  and then remove a random link, if possible.
- **Phage speciation**: We select randomly a number
  of phage strains, the number being drawn from a
  Poisson distribution with mean \( \mu \). For each selected
  phage we create a duplicate, copying all original
  links, and then adding a link to a single bacterial
  strain. This bacterial strain is selected randomly
  or locally (explained below) with equal weight.
- **Extinction**: We remove each bacterial strain, \( i \),
  with a probability \( n/N_0^2 \) (where \( n \) is an effective
  total number of strains, explained below) and, in
  addition, with a probability \( \beta/N_0 \) for each link from
  a virulent phage to that bacterial strain. Similarly,
  we remove each phage strain \( j \) with a probability
  \( \sigma/N_0 \) for each link from that phage to a bacterial
  strain. We also remove all phages that are left with-
  out any host, i.e., with zero links.

In case the number of bacterial or phage strains falls
to zero, we reintroduce a single strain with a random link
to/from the other group.

The bacterial speciation rule is a simple modification
from model A, the removal of one link representing the
possibility of new strains improving their fitness by de-
veloping resistance to existing phages. The parameter \( \mu \)
spacifices the rate of phage evolution, relative to the bac-
terial evolution, being the average number of new phage
strains that arise per bacterial duplication.

The addition of a link represents the possibility of a new
phage strain evolving the ability to infect a different
host. A “local” choice of the new host bacterial strain
models horizontal transfer, between phages, of genes for
infecting bacteria. For instance, if two phages infect the
same bacterium then one could gain genes from the sec-
ond phage which could allow it to infect one of the lat-
ter phage’s hosts. We implement this by first making a
list of all other phage strains that share a common host
with the phage strain just duplicated. Then we find all
the bacterial strains having links from this set of phage
strains, but not from the duplicated phage. Finally, we
randomly choose one out of this set of bacterial strains
and add a link to it from the duplicated phage. For exam-
ple, if the top phage (phase 1) in Fig. 1 duplicates, the
duplicate will add a link to the bacterium in the mid-
dle because it shares the top bacterium with phage 2
which has the middle bacterium as a host. Note that we
make such a local choice half the time. The other half
of the speciation events are non-local, i.e., the bacterial
strain is chosen randomly, representing evolution of new
functionality in the phage, or horizontal transfer between
bacteria, which allows the phage to infect a completely
new bacterial strain.
The extinction rules are also a simple extension of model A rules. Each link now results in a “load”, \( \beta \), on the corresponding bacterial strain, which increases its extinction probability. In addition, there is an extinction rate common to all strains given by \( n/N_0^2 \), with \( n = \sum_{i=1}^{N_B} e^{-\beta a_i} \) replacing \( N_B \) in the extinction rule of model A (\( a_i \) is the number of links from phages to the bacterial strain \( i \)). Instead of taking just \( N_B \) we reduce the weight of each bacterial strain to take into account the load from the phages that infect it. Then, the probability that a particular bacterial strain \( i \) survives is \((1 - n/N_0^2) \times (1 - \beta/N_0)^{a_i} \approx (1 - n/N_0^2) e^{-\beta a_i/N_0} \) when \( N_0 \) is large. The total probability for extinction of a bacterial strain due to phage load is therefore \( 1 - (1 - n/N_0^2) e^{-\beta a_i/N_0} \).

Similarly, each link also sets a load \( \sigma \) on the phage because it should allocate genes to deal with the strain-specific chemistry of its potential hosts. The genes may code for proteins that change the host machinery to accommodate phage replication, or for proteins used for the attachment or injection of the phage genome into the host, or for proteins fighting the countermeasures taken by the bacteria. A phage that can enter several different strains of bacteria would need more genes, which in turn would reduce its replication rate, here represented by a phage extinction probability \( \sigma/N_0 \) per link. This is implemented by making the net extinction probability of a phage strain \( 1 - e^{-\sigma v_i/N_0} \), where \( v_i \) is the number of out-links it has (this formula is similar to the bacterial extinction probability above except the extra common extinction rate \( n/N_0^2 \) which does not apply to the phage strains.

To avoid systematic errors we randomize the order in which we perform multiple duplications as well as the order in which the strains are selected in the extinction step. In general we will assume that \( \beta > \sigma \), reflecting a larger load on a bacteria than on the phage infecting it. A value of the load \( \beta \sim 1 \) corresponds to a situation where each virulent phage imposes a load on the bacterial ecology which is similar to the background extinction rate (set by \( 1/N_0 \)).

In Fig. 2b we show the dynamics of model B with \( \beta = 2, \sigma = 0.2 \) and \( \mu = 2.5 \). Comparing with Fig. 2a, the first observation is the smaller number of bacteria, reflecting the load, \( \beta \), on the bacteria imposed by the phage. Further, the number of strains in the ecosystem fluctuates relatively more than for model A. This is partly expected as adding links introduces correlations, and thus reduces the effective number of independent variables from \( \sim N_B \) to a smaller number. In addition, the process of duplication in itself includes a positive feedback from the number of links to itself, a feedback that is only limited by the bound on link density set by \( \sigma \).

Finally we introduce temperate phages, that can insert their own genome into their hosts’ genome, forming a lysogen. These phages kill a fraction of the bacteria upon infection, but also leave some of them immune to superinfection. As a consequence, they cannot drive the population of a bacterial strain to extinction. Nevertheless they present a load on a bacterial strain (i.e., affect its extinction rate), in part because they often manipulate the bacteria’s metabolism and also because they increase the length of the bacterial genome and thereby its generation time (typically one finds 0-10 prophages in bacterial genomes \( 1 \)). We represent this in the network by links connecting temperate plague strains to bacterial strains (see Fig. 4).

Another important characteristic of lysogenic phages is that they confer immunity not only to superinfection by their own strain, but can also provide resistance towards infection from other phages. We implement this in our model C by adding links between temperate and virulent phages, as illustrated in Fig. 4a. Such a link implies that infection of a bacterium by that temperate phage confers on the bacterium a resistance to infection by the virulent phage the link points to. (In our model we ignore temperate phages providing resistance to other temperate phages.) Every link from a virulent phage to a bacterial strain is either “strong”, if the bacteria have no link from a temperate phage that can provide resistance to the lytic phage, or “weak” if there does exist such a link (in the network picture, every link from a virulent
phage to a bacteria is either part of a triangle, in which case it is weak, or not, in which case it is strong). In contrast, every link from a temperate phage to a bacterial strain is a weak link. A strong link always results in a large load, $\beta$, on the bacterial strain the link points to. A weak link, results in a weak load, $\sigma$, on the bacterial strain. All links also result in a weak load, arbitrarily set to $\sigma$, on the phages from which the links originate.

The final model C incorporating bacteria, virulent phages and temperate phages is defined below. At each time step (with a timescale set by the bacterial speciation rate) the following events occur:

- **Bacterial speciation**: We select a random bacterial strain and duplicate it by copying it with all the originals links, and then remove one link if possible. In choosing which link to remove we give highest priority to strong links, then to weak links from virulent phage strains and finally to weak links from temperate phages.

- **Virulent phage speciation**: We choose a number of phages to duplicate, drawn from a Poisson distribution with mean $\mu$. For each chosen phage we make a duplicate with all the original links and then make a local or random modification (as in model B) with equal weight. The modification is either the addition of a link to a bacterial strain or the removal of a link from a temperate phage.

- **Temperate phage speciation**: We choose a number of temperate phages to duplicate, drawn from a Poisson distribution with mean $\mu$. For each chosen phage we make a duplicate with all the original links and then either add a link to a bacterial strain or to a virulent phage (chosen locally or randomly as in model B).

- **Bacterial extinction**: Each bacterium $i$ is removed with probability $1 - (1 - n/N_0^2)e^{-\beta b_i/N_0}e^{-\sigma v_i}/N_0$, where $b_i$ is the number of strong links pointing to it, $v_i$ is the number of weak links pointing to it, and $n = \sum_{i=1}^{N_B} e^{-\beta b_i - \sigma v_i}$ is an effective number of bacterial strains.

- **Phage extinction**: Each phage $j$ is removed with probability $1 - e^{-\sigma v_j}/N_0$, where $v_j$ is the number of out-links it has. In addition, every phage without a bacterial host is removed.

This model is a straightforward extension of model B. Speciation is assumed to occur by duplication of an existing strain with small modifications that are likely to increase the fitness of that strain. Thus, for bacteria the modification is always the loss of a link, while for virulent phages it is the gain of a new host or the evolution of means to overcome resistance due to some temperate phage. For a temperate phage the modification is either the gain of a new bacterial host or the gain of genes that provide resistance (for the bacteria) to some virulent phage. In either case, the temperate phage receives a new link, which points to a bacterial strain or virulent phage, that is chosen locally or randomly with equal weight. As in model B, a local choice means that the temperate phage gains such a link by copying it from another phage with which it shares a common host bacterial strain.

We represent the load of temperate phages on a bacterial strain by the same weak load parameter $\sigma$ as used before. Also we use $\sigma$ to characterize the load that the ability to infect a bacterial strain puts on the temperate phage due to increased demand on the phage gene repertoire. In short, the overall model can be described in terms of speciation and extinction events whose rates depend on the load on bacteria and phages. Here we simplify matters by allowing only two types of load, “strong” ($\beta$) and “weak” ($\sigma$). Thus, the model has 3 key parameters:

1) $\beta/\sigma$, the ratio of strong to weak load,
2) $\beta$, which sets the scale of loads for links in the system,
3) $\mu$, the relative speciation rate of phages.

In addition, we have a hidden parameter in the fifty-fifty choice of local versus random link formation in the phage speciation rules. Varying this ratio does not affect any of our conclusions (more details are below).

Fig. 2 illustrates the dynamics of model C. Comparing with Fig. 2b, we see that presence of temperate phages allows the existence of more virulent strains. This is likely due to the lowering of the average load of virulent phages on bacterial strains due to the resistance provided by temperate phages. This conclusion is bolstered by Fig. 2c where we show the dynamics that results when the model is modified so that temperate phages provide no resistance (i.e., when all links from virulent phages to bacteria are strong). This plot also shows that the resistance conferred allows a higher number of bacterial strains to exist than when there is no resistance.

Another observation that can be made from Fig. 2: is that the presence of temperate phages tends to increase fluctuations. This is likely due to the intermittent increase in links from the temperate to virulent phages, that can be seen in the inset of Fig. 2. The number of links from temperate to virulent phages fluctuates especially strongly, as a result of which the network structure also varies enormously (as evident from the network snapshots in Fig. 2). Thus, one feature of our model is that the network structure is more variable and dynamic than could be guessed from observing the total numbers of bacterial and phage strains alone. This conclusion also holds if we vary the ratio between local and random choice of link formation in the phage speciation rule. Quantitatively, increasing the proportion of random link formation moderately reduces the number of links from...
temperate to virulent phage strains, whereas increasing
the proportion of local link formation reduces the number
of bacterial strains connected to phages, leaving a larger
number of them isolated.

We have examined the model against variations of the
three basic parameters, \( \beta, \sigma \) and \( \mu \). First of all, reduc-
ing \( \beta \) and \( \sigma \) while keeping \( \beta/\sigma \) fixed produces an ecology
with a larger number of phages and a larger number of
links per phage. One can also increase the phage to bac-
teria ratio without changing link density by assigning an
especially weak load for temperate phages on bacteria.
Thus, the overall ratio of vira to bacteria is easily re-
scaled. The total size of the ecosystem, bacteria plus
phages, on the other hand, is primarily set by \( N_0 \).

Given fixed \( \sigma \) (and fixed \( \mu \)) we examine, in Fig. 4, the
behavior of the model ecology as function of the strong
to weak load ratio, \( \beta/\sigma \). Fig. 4a shows that an increase
in the ratio seems to reduce the overall numbers of both
bacteria and phages. This is not surprising, since an
increased ratio corresponds to an increased load \( \beta \). Tem-
perate phages seem to fare marginally better than viru-
 lent ones only for intermediate values of the ratio, while
bacteria do better when the ratio is smaller. Interest-
ingly, the fractional size of the largest connected cluster
in the network (shown in Fig. 4b) does not change much
though it fluctuates more for larger \( \beta/\sigma \) ratios. This is a
result of the increased interconnectedness at higher \( \beta/\sigma \)
which is revealed in the number of triangles, shown in
Fig. 4c. Note that in our model a triangle necessarily
has to be between one bacterial strain, one virulent and
one temperate phage strain, which provides resistance to
that virulent phage, i.e., the number of triangles reflects
the number of weak links between virulent phage and
bacteria. The figure suggests that resistance due to tem-
perate phages plays a larger role at higher \( \beta/\sigma \) ratios but
also that this resistance is intermittent, with large fluctu-
ations from time to time. Overall, we observe a network
structure that, while being usually one large, connected
cluster, is nevertheless highly dynamic as indicated by
the wildly fluctuating number of links and triangles.

The last important parameter of the model is \( \mu \), the
speciation rate of phages relative to that of bacterial
strains. Fig. 5 shows that the state of the system is quite
sensitive to this parameter in both model B (Fig. 5a) and
model C (Fig. 5b). Not surprisingly, when \( \mu \) is increased
sufficiently, the number of bacterial strains falls, while the number of phage strains increase. What is surprising
is the steepness of the fall: a threefold change in $\mu$ (from 1 to 3) causes more than an eightfold change in bacterial
numbers for model C.

Although the behaviour is sensitive to $\mu$, at all values the number of virulent phage strains and the number of
temperate phage strains are comparable. This is in part
due to a bias in the phage speciation rule. Because we always add a fixed number, $\mu$, of new virulent and new
temperate phage strains in each time step, the speciation
rate per strain is not a constant. It increases as the
number of strains decreases, and this negative feedback
prevents strain numbers from becoming very small. A
more unbiased way of implementing the speciation is to
make the rate per strain constant. To investigate this
scenario, we define a model D that is identical to model
C in all respects except that we modify the phage speciation rule as follows: We choose (on average $\mu$) phages to
duplicate randomly from the combined set of temperate
and virulent strains. This ensures that the probability
for selecting a phage of a given type is proportional to
the number of strains of that type. As a consequence the
duplication of phages in the larger group becomes more
likely and coexistence of the two groups becomes difficult.
This is indeed what we see from Fig. 6a: For standard
parameters the virulent phage population may be constantly
supplemented by temperate phages that lose their
immunity region, e.g. [10] (the opposite is probably
not possible, simply because loss of such a complicated
function requires less mutations than gain). We find
that the effect of this temperate-to-virulent switching
is very similar to allowing virulent phages to speciate
faster. That is, as the probability of mutating from
being temperate to virulent increases, the number of
virulent phage strains rises at the cost of the other two
groups.

Discussion

We have suggested a coarse-grained framework for un-
derstanding the essential ingredients in a world gov-
erned by a co-evolutionary, dynamical arms race between
phages and their hosts. An arms race where the elemen-
tary moves are not the fate of individual members of the

![FIG. 5: Variation in phage duplication rate $\mu$. Other parameters are kept fixed at the same values as in Fig. 2 and 3. Plots show strain numbers for (a) model B, and (b) model C.](image)

![FIG. 6: Time course of strain numbers for (a) model D, (b) a variant of model D where virulent strains speciate faster than temperate ones ($\mu_V = 2\mu_T$), and (c) same variant with $\mu_V = 3\mu_T$. (d) shows the average strain numbers as a function of the ratio $\mu_V/\mu_T$, with error bars showing one standard deviation. In all plots the total phage speciation rate is fixed ($\mu_V + \mu_T = 3$). Other parameters as in Fig. 2 and 3.](image)
community, but rather the collapse or creation of new strains by modification of old ones. The purpose in suggesting a mathematical model of this kind is to remain on a level of description that reflects our lack of knowledge of basic parameters of infection probability and replication rates in real world ecologies.

Phage-bacterial ecologies are in fact quite extensive on our planet and govern a major fraction of the known biomass: There are about $5 \times 10^{30}$ procaryotes on the planet, and viral infection is the most common way in which bacteria die, especially in the ocean. However, exceedingly little is known about this very interesting part of life on our planet. The one basic fact that a model of phage-bacterial ecologies can attempt to reproduce is the high diversity and coexistence of temperate and virulent phage strains.

In practice, ecological models, whether based on population dynamics or a more network-like approach, have great difficulty in producing viable and diverse ecosystems where many different species and strategies coexist. For instance, in population dynamics models that use Lotka-Volterra or replicator equations a handful of species can coexist for a short while but are soon destroyed by parasites. The main reason for this is the exponential growth of self-replicating populations that results when replication rates are proportional to the population size. This typically results in a “winner-take-all” situation where the population of a slightly faster growing species can completely repress the other populations. Only when limits are applied (sometimes artificially) on the exponential growth can species coexist.

One of the reasons we chose a network-like approach to modelling phage-bacterial ecologies, rather than a population dynamics approach, was to try and circumvent this problem of exponential growth and coexistence. However, our work shows that even in these kinds of models coexistence of species is not easy to achieve. We have tried several variants of the basic models, all within the same framework described above, and found that the phage speciation rule was a major determinant of the viability of coexistence of temperate and virulent phages. Model D, which makes the straightforward assumption that the speciation rate per strain is constant, does not in fact exhibit robust coexistence of virulent and temperate phages. Model D, which makes the straightforward assumption that the speciation rate per strain is constant, therefore the rate of increase of strains (ignoring extinction for the moment) is proportional to the number of strains. Thus, the number of strains would grow exponentially resulting in a similar winner-take-all situation, now at the strain level. In model C, however, by making the speciation rate independent of strain number, the growth is no longer exponential and we see coexistence of a large number of strains. Thus, one “prediction” resulting from our modelling is that there may be some mechanism at work that keeps the speciation rate independent of the number of strains. We speculate that this might happen if speciation involves the discovery of new ecological niches by randomly mutated individuals. If the number of such new ecological niches is small then it could be what limits the speciation rate, rather than the population size. In that case the speciation rate would be independent of strain numbers.

Since model C was the one case where we did find robust coexistence, we mainly focus on how different phage groups influence each other in that model. The main result of this analysis was that:

1) Temperate phage strains in fact appear to help maintain a higher diversity of virulent strains by providing a “refuge” for a few strains of bacteria to escape to, preventing them from being completely destroyed by virulent phages.

2) The ecosystem is highly dynamic, especially its network structure. In particular, the number of links between temperate and virulent phages (and hence triangles) show large intermittent fluctuations. In other words, periods where bacterial strains are largely protected from virulent phages alternate with periods where there is little resistance and most virulent attacks present huge extinction risks for the bacterial strains. Thus, the stabilization provided by temperate phages is sometimes very important, and at other times nearly without consequence.

We emphasize that these two results only hold for model C, where each phage group produces a given fixed number of new strains at each timestep of the model.

Outlook

The difficulty of finding a model where phage types coexist indicates that we nevertheless miss some important insight into how such ecosystems actually work on this very basic information-exchange level. One intriguing possibility is that mutation mechanisms and speciation rates could themselves change and adjust as the network evolves. For instance, one could imagine that if viral phage strains were allowed to evolve their specia-
tion rate, they would die out both in clusters where they had too low a rate ($\mu < 1/2$ in Fig. 5b) and in clusters where they had too high a rate by forcing their hosts, the bacterial strains, to collapse ($\mu > 3$ in Fig. 5b). The result might be the self-organization of speciation rates to values that allow coexistence of all groups.

More realistic scenarios could also consider interactions between temperate phage species. For example prophages can confer resistance not only to virulent phages but also to temperate phages. Another feature is phage-independent genetic transfer between bacteria such as mediated by bacterial conjugation. We have loosely tried to take this into account by the random allocation of new links from time to time. However, this could be implemented more carefully in a non-random manner.

Overall, we have presented a flexible framework for modelling phage-bacterial interactions. By working at strain level, ignoring detailed population dynamics, these models are particularly suited for producing questions related to the diversity of different groups in the ecosystem.

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[1] M. Breitbart and F. Rohwer, Trends Microbiol. 13, 278 (2005).
[2] M. G. Weinbauer and F. Rassoulzadegan, Environ. Microbiol. 6, 1 (2004).
[3] C. A. Suttle, Nature 437, 356 (2005).
[4] M. Breitbart, B. Felts, S. Kelley, J. M. Mahaffy, J. Nulton, P. Salomon, and F. Rohwer, Proc. R. Soc. Lond. B 271, 565 (2004).
[5] S. Chibani-Chennoufi, A. Bruttin, M.-L. Dillmann, and H. Brussow, J. Bacteriol. 186, 3677 (2004).
[6] B. R. Levin, F. M. Stewart, and L. Chao, Am. Nat. 111, 3 (1977).
[7] F. M. Stewart and B. R. Levin, Theor. Popul. Biol. 26, 93 (1984).
[8] R. W. Hendrix, J. G. Lawrence, G. F. Hatfull, and S. Casjens, Trends Microbiol. 8, 504 (2000).
[9] S. Casjens, Mol. Microbiol. 49, 277 (2003).
[10] S. Lucchini, F. Desiere, and H. Brussow, Virology 260, 232 (1999).
[11] J. M. Smith, Nature 280, 445 (1979).
[12] U. Niesert, D. Harnasch, and C. Bresch, J. Mol. Evol. 17, 348 (1981).
[13] R. Happel and P. F. Stadler, J. Theor. Biol. 195, 329 (1998).
[14] S. Jain and S. Krishna, Proc. Natl. Acad. Sci. (USA) 99, 2055 (2002).