Evolution, 2026, **80**(6), 1365–1373
https://doi.org/10.1093/evolut/qpag061
Advance access publication 11 April 2026
Brief Communication

Responsive lysogeny under nonproductive phage binding

Bryan Wu and Călin C. Guet

Institute of Science and Technology Austria, Am Campus 1, 3400 Klosterneuburg, Austria
Corresponding author: Institute of Science and Technology Austria, Am Campus 1, 3400 Klosterneuburg, Austria. Email: calin@ist.ac.at

Abstract

Upon infecting a bacterial cell, temperate phages make a decision between lysis and lysogeny. While research has previously explored how phages sense environmental information to make this choice, most studies have focused on modelling known mechanisms that impact the decision. These mechanisms tell us what environmental information the phage does respond to, but not what it should respond to, as the signals sensed by the phage may serve as proxies for other sources of information. Here, using a mechanism-agnostic population dynamics model, we find that irreversible phage binding to lysogens protects sensitive host cells from infection. This results in lysogens being an additional environmental factor that the phage should sense while making its decision to undergo lysis or lysogeny. Using this model, we derive a responsive lysogeny probability for phages that respond to both cell and lysogen densities optimized towards invading phage-occupied systems, and show that it is more capable of invading and resisting invasion than phage with fixed lysogeny probabilities across different environmental conditions.

Keywords: lysis-lysogeny decision, phage-bacteria interactions, lysogeny responsiveness, cell fate, herd immunity, invasion analysis

Introduction

Bacteriophages are viruses of bacteria that generally kill their hosts in order to produce more of themselves through the process of lysis. However, temperate phages have an additional strategy to replicate their genome alongside that of their host as a prophage, thus tying their reproductive fitness to that of their host. These prophage-carrying bacteria, known as lysogens, can reactivate at a later point in time, ultimately releasing phage particles through the lysis and death of the lysogen (Ptashne, 2004).

The existence of these two different modes of replication suggests that conditions exist where each mode of replication is advantageous over the other. It has been suggested that the lytic mode is favored at high susceptible host densities and low resources, whereas the lysogenic mode is favored at low host densities and high resources (Steward & Levin, 1984; Wahl et al, 2019; Li et al, 2020). Mathematical models of phage-bacteria populations have sought to examine these conditions, as well as conditions that favor intermediate strategies, where phages choose lysogeny or lysis with some probability (Stewart & Levin, 1984; Maslov & Sneppen, 2015; Sinha et al, 2017; Wahl et al, 2019).

Temperate phages, however, do not necessarily use a fixed probability of lysogeny. Among the different phage species, the process of undergoing lysis or lysogeny is a responsive choice, decided upon during the infection of the host, that is capable of integrating various sources of information, the most salient of which is the number of co-infecting phages (Zeng et al., 2010). However, various phages use a variety of other mechanisms to gather information from environmental factors, such as those tied to the state of the cell (St-Pierre & Endy, 2008) and the concentration of phage quorum-sensing molecules (Erez et al., 2017; Bruce et al, 2021). Responsive mechanisms to different sources of information demonstrate that the lysis-lysogeny decision can be a dynamic process, changing with environmental conditions.

Phages also have a variety of mechanisms to confer superinfection inhibition, where upon infecting a cell, the phage prevents its host from being infected by identical or similar phages. Superinfection inhibition can be broadly grouped into two categories: superinfection exclusion, where superinfection is interrupted prior to the injection of the superinfecting phage DNA, and superinfection immunity, which inhibits the replication of the post-translocated DNA (Biggs et al., 2021). Although the host is protected from superinfection by either superinfection exclusion or immunity, the superinfecting phage experiences drastically different outcomes, as phage adsorption leads to irreversible binding, which is generally tied to the injection of phage DNA into the host (Silva et al., 2016). With superinfection exclusion, the invading phage is either unable to inject the DNA or unable to bind at all, and thereby generally has the opportunity to unbind from the protected host and search for another target; however, with superinfection immunity, the phage has already irreversibly injected its DNA into the immune host and has no opportunity to back out; it is already dead. This process is known as sorptive scavenging, originally termed to describe the binding of phages to sediment particles and removal from seawater (Hewson & Fuhrman, 2003), but has later been expanded to describe the sequestration of phages by resistant cells (Simmons et al., 2020). Sorptive scavenging increases the decay rate of phages in environments with lysogens that can irreversibly bind to the phage, and has implications on the lysis-lysogeny decision and the dynamics of a phage-bacteria system (Berryhill & Levin, 2025).

A previous model examining the conditions for lysis and lysogeny made the assumption that lysogen resistance was conferred by downregulating the binding receptor, and as such the phage cannot bind to lysogens (Wahl et al., 2019).

Received December 5, 2024; revisions received March 5, 2026; accepted March 31, 2026
Associate Editor: Ben Ashby; Handling Editor: Jason Wolf

However, this model did not examine how the choice of immunity mechanism affects the behavior of the lysis-lysogeny decision. Other models do include the nonproductive binding of phages to lysogens, but do not focus on the impact that sorptive scavenging has, instead often extending the model to focus on additional mechanisms that impact the lysis-lysogeny decision (Bruce et al., 2021). As superinfection immunity would create an environment where phages continue to bind and inject their DNA into immune lysogens, this would likely alter the optimal decision choice.

We begin by examining the impact of nonproductive binding of phages to lysogens on the lysis-lysogeny decision in order to determine a responsive function that can be used as a responsive lysogeny function. We then calculate responsive rates of lysogeny optimizing for invasion when rare in environments with and without binding to lysogens, and show that phages that do not respond to lysogens perform poorly in environments with binding to lysogens. Finally, we show that the responsive lysogeny rate is capable of invading systems under more conditions than a fixed lysogeny probability, suggesting the number of lysogens in the environment is an important source of information in determining the outcome of the lysis-lysogeny decision in environments with sorptive scavenging by lysogens.

Methods

Epidemiological model

Our model is a simple no-delay mass-action kinetic model with implicit resources in a chemostat-like setup (Figure 1). We track uninfected sensitive host cells S, lysogenic cells L and free phage particles V. All cells grow at the same rate ψ, which is dependent on the total number of living cells and the carrying capacity K of the system, with a maximum rate of τ (Figure 1A). All species flow out of the system at the same rate ω, and there is a constant inflow of sensitive cells at rate c, as in a two-stage chemostat. Phage particles bind to both sensitive cells and lysogens at rate b and are removed from the system. If a phage particle binds to a sensitive cell, the cell either transforms into lysogen with a probability p, or immediately undergoes lysis, producing β new phage particles with a probability of $1\text{-}p$ (Figure 1B). Additionally, lysogens induce at a rate i, dying and producing β new phage particles (Figure 1C). We assume lysogens cannot be reinfected, and are perfectly immune to all modelled phages (Figure 1D). This model can be extended for up to N phages, but in this study are limited to 1 or 2 phages.

This model was chosen to emphasize intermediate lysis-lysogeny rates, as it has been shown that pure lysogeny is preferred in any non-fluctuating system without an inflow of sensitive cells (Wahl et al., 2019). The inflow of sensitive cells may occur in different environments such as rivers, sewage systems, or any such environment with a unidirectional flow, in addition to environments with a resistant population of bacteria that loses resistance at high rates, such as under phase variation (Shkoporov et al., 2021).

This results in the following model:

$$\frac{dS}{dt} = \psi S - \omega S - bS\sum_{x=1}^{N} V_x + c \tag{1}$$

$$\frac{dL_x}{dt} = \psi L_x - \omega L_x + p_x bSV_x - iL_x \tag{2}$$

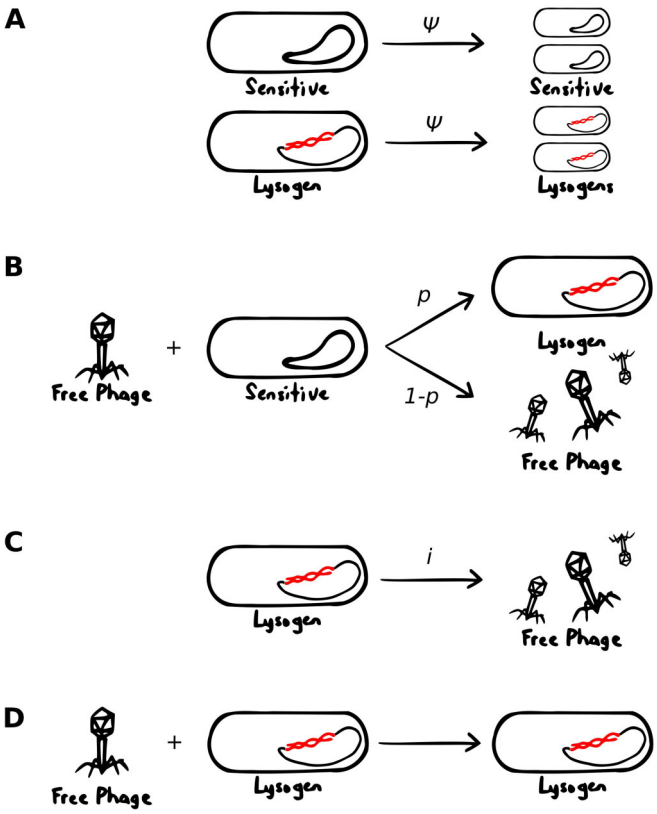

Figure 1. Major transitions in the mathematical model. (A) In the model, both sensitive and lysogenic cells self-replicate with rate ψ, which is dependent on the total number of cells and the carrying capacity of the system. (B) When a phage binds with a sensitive cell (with a rate of b), the phage is consumed and the cell turns into a lysogen with a probability p, otherwise the cell lyses and becomes β phages. (C) Lysogens have a probability i of inducing, lysing and producing β phages. (D) Phages also bind with lysogens at rate b, which destroys the phage. Not pictured: all species flow out of the system at rate ω, and new sensitive cells are added with a rate c.

$$\frac{dV_x}{dt} = (1-p_x)\,\beta bSV_x - \omega V_x - b\left(S + \sum_{x=1}^{N} L_x\right)V_x + \beta iL_x \tag{3}$$

where the growth rate ψ is equal to:

$$\psi = \tau\left(1 - \left(S + \sum_{n=1}^{N} L_n\right)K^{-1}\right) \tag{4}$$

For ease of modeling, we assume a no-delay model, where lysis and lysogeny are both instantaneous upon binding to a sensitive cell, though we include models with an intermediate state in Supplementary Material section 5. Adsorption is modelled as a function combining an adsorption rate constant and the concentration of phages and bacteria in the system, and follows standard mass-action kinetics. These assumptions are in line with similar models (Wahl et al., 2019, Bruce et al., 2021).

For our calculations and simulations, the parameters and default values are provided in Table 1, unless otherwise stated.

During invasion analysis, 0.001 of invading phage and lysogens were added to the system to begin the invasion.

Table 1. List of parameters in the model.

Symbol	Description	Default value
τ	Maximum growth rate	1
K	Maximum carrying capacity, at flow rate 0	10000
ω	System flow rate	0.2
β	Phage burst size	100
b	Phage binding rate	0.01
i	Phage induction rate	0.01
c	Sensitive cell inflow rate	150

We refrain from using units, as all parameter choices are arbitrary.

Analytical calculations and simulations were done in Mathematica 11.1 (Wolfram Research, Inc., 2017).

Results

Nonproductive binding protects sensitive cells

In previous studies, it has been experimentally shown that bacteria which are immune to phage but can still bind have a protective effect on the sensitive cells in the community, with results akin to herd immunity (Payne et al., 2018; Brown et al., 2022), but those studies limited their models to epidemic infections. We therefore examined whether sorptive scavenging produces similar protective effects in a simulated chemostatic model, and found similar results. We find that nonproductive phage binding to lysogens greatly increases the number of sensitive cells at equilibrium which is driven by a marked reduction in free phage concentrations, whereas the number of lysogens remains relatively unaffected (Figure 2). This suggests that the lysogens serving as sinks for phage particles lowers the free phage levels and protect sensitive cells in the environment, even under continuous flow conditions.

Numerical simulations of fixed responses for invasion when rare

As nonproductive binding of phages to lysogens has an effect on the equilibrium of the system (Figure 2), we examined how this affects how well phages can invade equilibria of systems already occupied by a phage, identical to the invading phage other than a different fixed lysogeny probability. To this end we simulated pairwise combinations of phages with fixed lysogeny probabilities over extended periods of time, where a small amount of the invading phage and corresponding lysogen is added to a system at equilibrium already occupied by a resident phage (Figure 3A), thus invading the system when the invader is rare. The results are similar to a pairwise invasibility plot (Brännström et al., 2013), but additionally plots the degree of coexistence.

We find that an optimal intermediate lysogeny probability exists, which is capable of both resisting invasion and invading any non-optimal lysogeny probability (Figure 3A, intersection of the cross, white square). A resident phage with a lysogeny probability less than the optimum can be invaded by any phage with a greater lysogeny probability, even $p = 1$ (Figure 3A, red regions on the left), whereas resident phages with a lysogeny probability greater than the optimal value can be invaded by any phage with a lower lysogeny probability, even $p = 0$ (Figure 3A, red regions on the right). Additionally, two coexistence regions exist, where both phage strains are mutually invasible and coexist to varying degrees.

Our results are qualitatively similar to the pairwise invasibility plot described in Wahl et al. (2019), which modeled epidemic infections with an inflow of sensitive cells but did not include sorptive scavenging by lysogens. This suggests that nonproductive binding to lysogens does not greatly impact the dynamics of phage invasion when rare, as both resident and invading phage are equally impacted by binding to lysogens. A closer comparison between environments with and without nonproductive binding to lysogens shows that the optimal fixed lysogeny probability is slightly greater in environments without binding to lysogens (Figure 3B). This may be due to the number of sensitive cells at equilibrium; in environments where phages bind to lysogens, the number of sensitive cells at equilibrium increases (Figure 2), which may be more easily invaded by a phage that tends more towards lysis.

We also note the difference in behavior slightly above and slightly below the optimal fixed lysogeny probability. A phage with a lysogeny probability slightly below optimal can take over all systems below the optimal fixed lysogeny probability and coexists with phages with a higher fixed lysogeny probability (Figure 3C, left). A phage with a lysogeny probability slightly above optimal has the opposite behavior: it can take over all systems above the optimal fixed lysogeny probability and coexists with phages with a lower fixed lysogeny probability (Figure 3C, right).

Although our simulations borrow the "invasion when rare" assumption from adaptive dynamics (Brännström et al., 2013) and yield similar results to the pairwise invasibility plot from Wahl et al. (2019), our interest does not solely lie with long-term evolutionary outcomes. We are also interested in the space of all possible equilibria, and the subset of which it is possible to invade.

Invasibility of equilibrium states by lytic phages and lysogens

As all single-phage occupied equilibria have some number of phages, lysogens and sensitive cells, we wished to determine the set of these equilibria susceptible to invasion by. Since the resident phages do not directly interact with the invading phages or lysogens at the moment of invasion (as the initial growth of invading phages and lysogens only indirectly depend on resident phages, see Supplementary Material section 2.2–2.3), invasion is dependent solely on the number of sensitive cells and resident lysogens at equilibrium. We then analytically calculated the regions in which lytic phages and lysogens are capable of invading when rare (Supplementary Material section 2), for systems both with and without nonproductive phage binding to lysogens (Figure 4).

Without nonproductive binding of phage particles to lysogens the ability for a lytic phage to invade is solely dependent on the number of sensitive hosts at equilibrium and fixed environmental parameters (Supplementary Material section 2.1.2), where the lytic phage can invade under the following circumstances:

$$S > \frac{\omega}{b\,(\beta - 1)} \tag{5}$$

This directly follows from the assumption that invading phages do not directly interact with resident phages, but only indirectly through the sensitive cells. The number of sensitive cells required for invasion by lytic phage increases

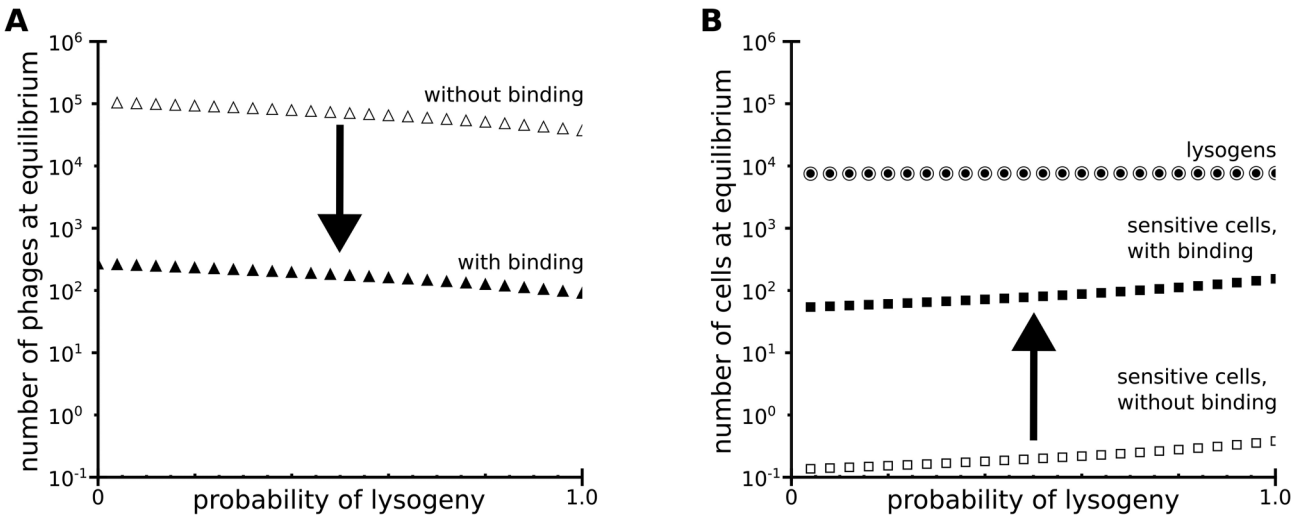

Figure 2. Nonproductive binding of phages to lysogens increases the number of sensitive cells at equilibrium, while decreasing the number of free phage. (A) The number of free phages at equilibrium decreases when binding to lysogens is included (black triangles), compared to an equilibrium with no binding to lysogens (white triangles). (B) The number of sensitive cells at equilibrium increases when binding to lysogens is included (black squares) compared to without binding to lysogens (white squares), though the number of lysogens are relatively unaffected (circles, overlapping).

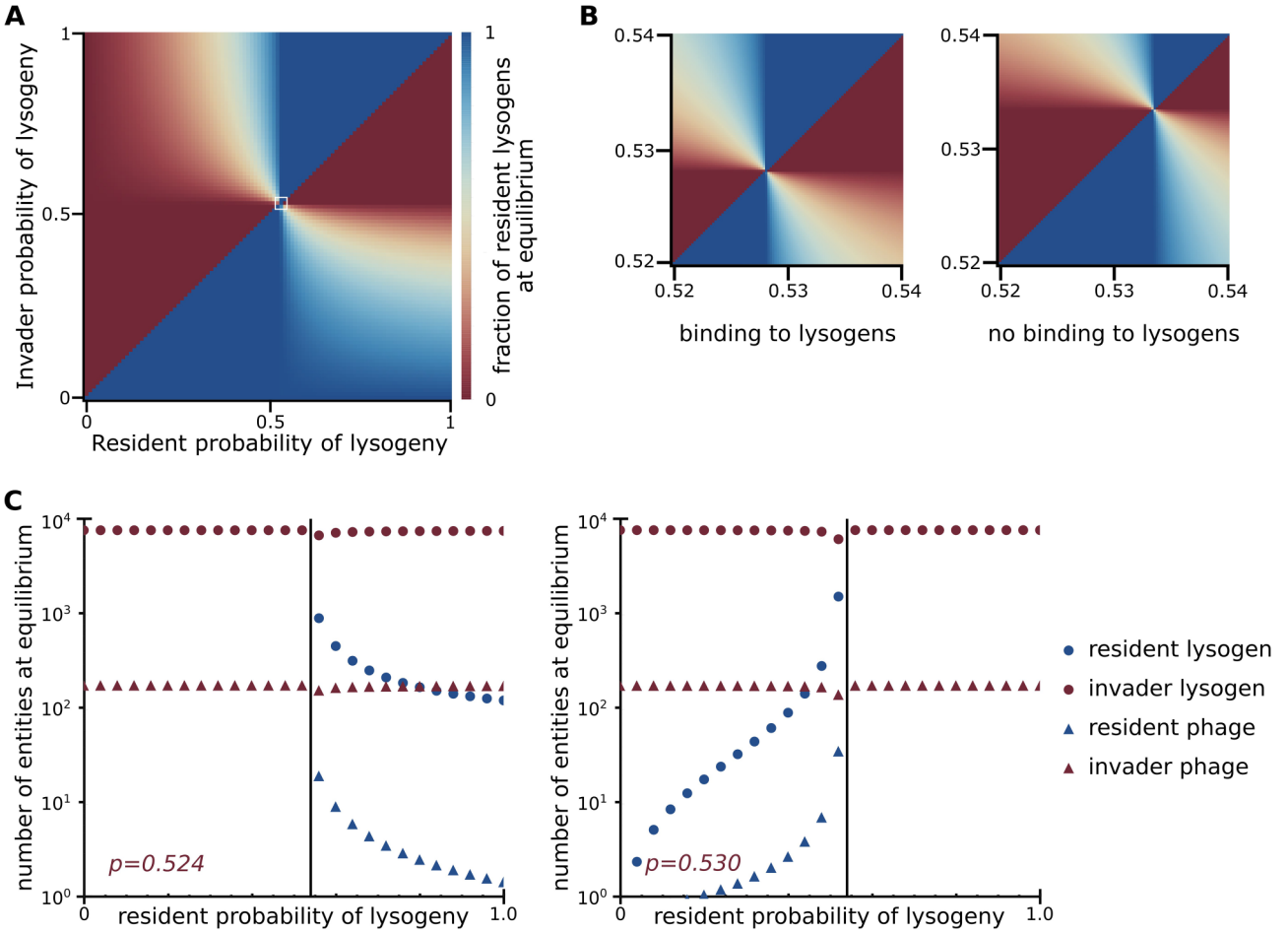

Figure 3. Invasion and invasibility in phages with fixed probability of lysogeny. (A) A pairwise invasibility plot of phages with fixed probability of lysogeny in an environment where phages bind nonproductively to lysogens. The equilibrium of the system with a single species of resident phage was solved, then a small number of invading phage and lysogens were added and the system was simulated to $t = 10^9$. The % of lysogens that are resident lysogens were then plotted. Red indicates a successful invasion. The white square indicates the section represented in panel B. (B) A zoomed-in section of the white square in panel A (left), compared to the matching area of a pairwise invasibility plot where phages do not bind to lysogens (right). C) Phages and lysogens with a fixed lysogeny rate slightly below optimal (left, $p = 0.524$) or slightly above optimal (right, $p = 0.530$) invade systems of phages with a fixed lysogeny probability at analytical equilibrium, where phages bind to lysogens. Black lines correspond to the optimal fixed lysogeny probability, $p \approx 0.527$.

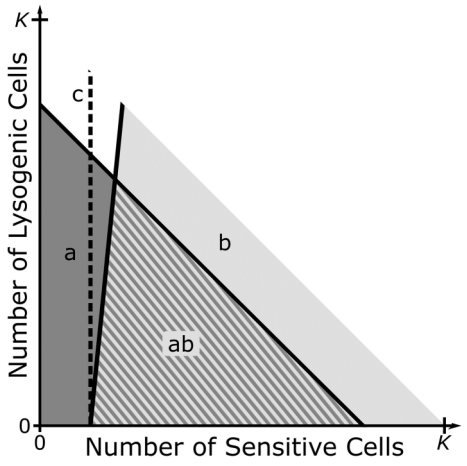

Figure 4. The invasibility of a phage-occupied system. With nonproductive phage binding, the system can be invaded by invading lysogens in the dark gray regions (a), and by invading lytic phages in the light gray regions (b), bounded by equation (7). The system cannot be invaded in the white area (c). The dotted line represents the location of the line demarcating b without nonproductive binding, representing equation (5). The graph is truncated to regions where the cell population is less than the carrying capacity *K*. Note that cell populations never reach the theoretical carrying capacity *K* due to the constant flow of the chemostat system, and region (a) is bounded by the maximum achievable population of lysogens, $K(1-\frac{i}{\tau}-\frac{\omega}{\tau})$.

as the flow rate ω increases. It also decreases as the binding rate b or burst size β increase, as under those conditions a phage burst is more likely to produce a phage that will eventually bind to a sensitive cell, increasing the effective burst size. This corresponds with the conclusion of Wahl et al. (2019), where lysis is favored if sensitive host cells can be maintained at a sufficiently high level.

When phages can bind nonproductively to lysogens, however, the ability for a lytic phage to invade additionally depends on the number of lysogens at the moment of invasion (Supplementary Material section 2.1.1), resulting in a varying threshold of sensitive cells (Figure 4) with the following equation:

$$L < (\beta - 1)S - \frac{\omega}{b} \tag{6}$$

Or, alternatively rearranged

$$S > \frac{L}{\beta - 1} + \frac{\omega}{b(\beta - 1)} \tag{7}$$

The second term in equation 7 is identical to that of lytic invasion when lysogens do not bind to phages (Equation 5). The difference lies in the additional first term, which is the ratio of lysogens to the burst size. Thus, the number of sensitive cells required for lytic invasion increases as the number of lysogens increase due to sorptive scavenging, but the impact of the number of lysogens decreases as the burst size increases. Binding rate b does not play a role in this term as the binding rate to sensitive cells and lysogens are identical, and thus cancel out.

In our model, lysogens are identical to resident lysogens other than producing a phage with a different lysogeny probability, and thus have the same growth rate as sensitive cells. Thus, lysogens can invade under most conditions where the total cell number does not exceed the carrying capacity, less the dilution and induction rate (Figure 4, Supplementary Material section 2.3).

Using invasibility as a responsive function for lysogeny

It is known that phage lysogeny probabilities are not fixed, but instead depend on a number of external factors (Herskowitz & Hagen, 1980; St-Pierre & Endy, 2008; Zeng et al., 2010; Erez et al., 2017). Instead of implementing any particular mechanism, we wished to ask the following: if a phage genome, once injected into a susceptible host, had perfect information about the external environment, what information should it respond to? and how well does it perform? Equations 6 and 7 show that, in environments with sorptive scavenging by lysogens, the number of lysogens partly determines if lytic phages can invade. This is in addition to the variables required in environments where phages do not bind to lysogens: number of sensitive cells, burst size, binding rate, and flow rate.

The molecular mechanisms by which phages can sense this information is not the focus of this work, as here we show through mathematical analysis what information *should* be sensed in order to accurately determine whether lytic invasion of an equilibrium is possible, which we suggest is beneficial for the phage to determine.

Using the equations above, we decided to implement a responsive lysogeny function where the phage undergoes lysis under conditions where lytic phages can invade, and otherwise undergoes lysogeny. In line with previous examinations of responsive functions (Sinha et al., 2017), we fix the probability of lysogeny to 1 in the regions where lytic phage cannot invade, and to 0 where lytic phage can invade, with a smooth transition fitted to the logistic function, such that the invasion-optimal responsive lysogeny function for environments with no binding (nb) to lysogens is

$$p_{nb} = \frac{1}{1 + e^{-\left(\frac{\omega}{b(\beta-1)} - S\right)}} \tag{8}$$

and the responsive lysogeny function for environments with binding (wb) to lysogens is

$$p_{wb} = \frac{1}{1 + e^{-\left(\Sigma L - \left((\beta-1)S - \frac{\omega}{b}\right)\right)}} \tag{9}$$

where ΣL is the sum of all species of lysogens in the system. We would like to note for clarity that this is not an evolutionary stable strategy, which is unable to be invaded; instead, this function maximizes its ability to invade, but does not explicitly maximize its ability to also resist invasion.

Simulations show that the phage with p_{nb} fares poorly in environments where phages bind to lysogens. It is only capable of invading systems where the resident phages are lytic or have a lysogeny probability greater than the optimal fixed probability, and even then only coexists as free phages with no lysogens (Figure 5A, left). It is also susceptible to invasion by phages with any nonzero fixed lysogeny probability (Figure 5A, right). This can be understood as a mismatch between the responsive function and the environment: the phage systematically undercalculates the decay rate of the phage in the environment as it is unable to respond to the number of lysogens, and consistently chooses lysis in environments where lytic replication is not supported.

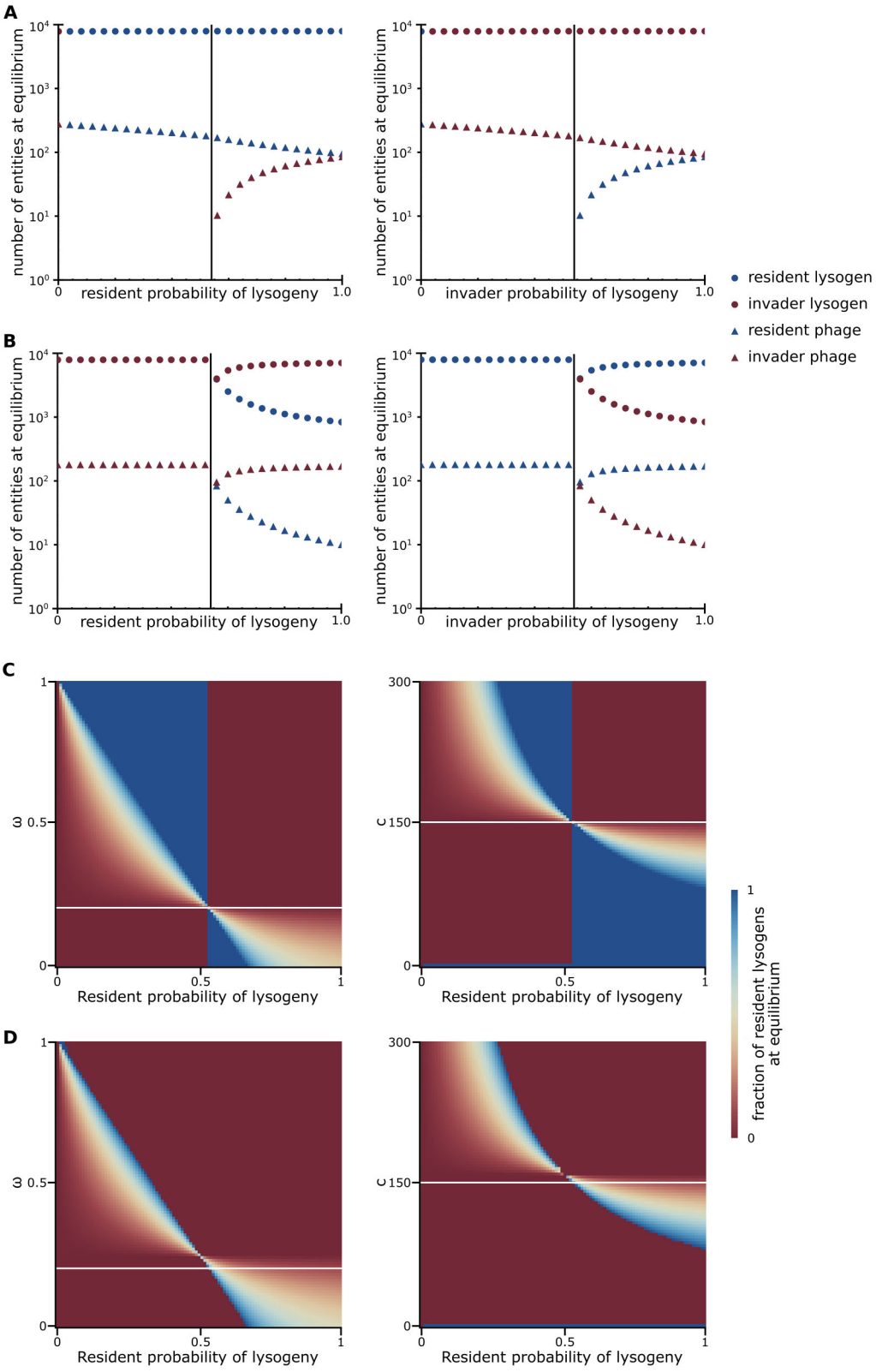

Figure 5. Invasibility plots of fixed and responsive lysogeny rates. (A) Phages and lysogens with responsive lysogeny rate that does not respond to lysogens (p_{nb}) invade systems of phages with a fixed lysogeny probability at analytical equilibrium (left), or are simulated to equilibrium and invaded by phages and lysogens with a fixed lysogeny probability (right). (B) Phages and lysogens with responsive lysogeny rate that does respond to lysogens (p_{wb}) invade a system of phages with a fixed lysogeny probability at analytical equilibrium (left), or are simulated to equilibrium and invaded by phages and lysogens with a fixed lysogeny probability (right). Black lines in A and B correspond to the optimal fixed lysogeny probability, $p \approx 0.527$.(C) Phages and lysogens with a fixed probability of lysogeny $p = 0.527$ invades a system of phages with fixed lysogeny probability at analytical equilibrium at different flow rates (ω, left) or influx of sensitive cells (c, right). (D) Phages and lysogens with responsive lysogeny rate p_{wb} invade a system of fixed lysogeny phages at analytical equilibrium at different flow rates (ω, left) or influx of sensitive cells (c, right). All systems were simulated to $t = 10^{12}$ post-invasion. White lines in C and D correspond with the parameter set (ω=0.2, $c = 150$), which are the same parameters used in A and B.

p_{nb} performs better in a matched environment where phages do not bind to lysogens (Figure S1).

On the other hand, the phage with p_{wb} fares well in environments with binding to lysogens, and can invade all non-optimal fixed lysogeny probability phage-occupied systems at equilibrium (Figure 5B, left) with a behavior similar to that of a phage with a fixed lysogeny probability slightly below optimal (Figure 3C, left). Additionally, systems occupied by phage and lysogens with p_{wb} at equilibrium fully resists invasion by phages with a fixed lysogeny probability less than the optimal fixed probability, but can still be invaded by phages with a fixed probability of lysogeny above the optimal fixed probability (Figure 5B, right). This may be due to the fact that p_{wb} is optimized for invasion when rare; when the p_{wb} phage is no longer rare, the function is no longer optimal, and appears to settle on a lysogeny probability slightly lower than optimal.

Although phages with an optimal fixed lysogeny probability can outperform those with a responsive lysogeny probability, this is strongly environment-dependent, as the optimal fixed lysogeny probability changes alongside changes to the environmental parameters (Figure 5C). The responsive lysogeny probability phages, in contrast, change their behavior in response to changes in the environmental parameters, and thereby can outperform the fixed lysogeny probability phage under a wider range of conditions (Figure 5D).

Discussion

The lysis-lysogeny decision in phages, in particular phage lambda, has been studied in great detail since the advent of molecular biology, unveiling the molecular machinery and genetic regulatory networks involved in making the fate choice between lysis and lysogeny (Ptashne, 2004). At the same time, several models have been proposed to justify the existence of lysogeny, often invoking changes in environmental conditions which shift from favoring one life strategy to another (Stewart & Levin, 1984; Maslov & Sneppen, 2015; Cheong et al., 2022).

But in order to make a decision, a system requires information. It has been shown that a number of factors can impact the lysis-lysogeny decision, such as multiplicity of infection (MOI), cell energy-growth state (Herskowitz & Hagen, 1980; Pleška et al., 2018), cell size (St-Pierre & Endy, 2008; Zeng et al., 2010) and quorum-sensing systems (Erez et al., 2017). These factors provide information about the state of the external environment, such as nutrient availability and flow rate, that the phage requires to make its decision; however, as we are limited to only known mechanisms and do not know what environmental information is important, it can be difficult to determine what information provided by these mechanisms are useful. Information received by the mechanism is additionally constrained by the physical limitations of gathering the information from inside the cell, resulting in integrating indirect information about the state of the external environment. For example, a phage genome within a cell cannot directly sense the number of phages or host availability in the environment, and must rely on indirect sources of information instead, such as the number of concurrently bound phages. Though much work has been done to examine the molecular mechanisms of how all these factors interplay in the lysis-lysogeny decision, nevertheless the question remains: what information does the system actually care about?

In our work we find that the introduction of sorptive scavenging of free phages by lysogens increases the number of sensitive cells and decreases the number of phages at equilibrium. This leads to a small decrease in the optimal fixed lysogeny probability, as equilibria with more sensitive cells can be more readily exploited by phages that tend more towards lysis. We show that the addition of sorptive scavenging by lysogens results in the invasibility of an equilibrium becoming additionally dependent upon the number of lysogens. We then found that, under these conditions, phages with a responsive lysogeny probability that responds to the number of lysogens are more capable of both invading and also resisting invasion, compared to phages that do not respond to the number of lysogens. Although the responsive strategy cannot invade the optimal fixed strategy in a given environment, it can invade any non-optimal fixed strategy in any environment, thus performing well across different environments.

Here we focus on sorptive scavenging and its effect on what information should be sensed to make the lysis-lysogeny decision, as sorptive scavenging is a general mechanism that applies to any system without superinfection exclusion, independent of the mechanism by which information is sensed. The question naturally arises, then, of how the mechanism-agnostic responsive lysogeny function compares to known biological mechanisms influencing the lysis-lysogeny decision. Temperate phages have been shown to have multiple systems known to influence the probability of lysogeny, which have been thought to provide useful information about the environment (Zeng et al., 2010; Erez et al. 2017; Silpe & Bassler, 2019).

Although not the focus of this study, a preliminary treatment comparing the responsive lysogeny function to arbitrium or the phage/cell ratio shows that the mechanistically-informed functions perform poorly in comparison to p_{wb} (Supplementary Material section 4). Both rely on the existence of a threshold (either arbitrium concentration or phage/cell ratio) to switch between lysis and lysogeny, and, similar to a fixed lysogeny probability, although an optimal threshold exists for a given set of environmental parameters, this threshold changes when environmental parameters change (Figures S2AB, S3AB, S4A). The responsive lysogeny function p_{wb} is an idealized responsive function optimized towards invasion, and, as it can directly sense the environmental parameters (such as flow rate) and species (such as number of cells) of the system, it outperforms the mechanistically-informed functions, which can only sense those parameters indirectly if at all (Figures S2C, S3C). Additionally, this may also suggest that responsiveness to phage/cell ratio and arbitrium may have evolved in non-chemostatic conditions where environmental conditions do not change, as they respond to large changes in host availability found in fluctuating environments or epidemic conditions (Berngruber et al., 2013; Doekes et al., 2021).

Integrating information from the environment to make decisions in phages is not limited to the lysis-lysogeny decision. Lysis timing is another decision that can vary based on environmental conditions (Moussa et al., 2012; Bednarek et al. 2022) and can be examined under a similar framework. Additionally lysogen induction is another decision which benefits by responding to environmental conditions,

as it has been shown that prophages can induce in response to changes in the environment (Ptashne, 2004; Bruce et al., 2021).

The effect of nonproductive binding can also impact other phage life strategies. Pseudolysogeny occurs when phages do not integrate their genome into the host, yet still persist and transmit vertically, and can become resistant to other sister phages (Mäntynen et al., 2021). It has been shown that pseudolysogeny can be MOI-dependent, with increasing MOI decreasing lysis probability (Sanchez-Martinez et al., 2025), which suggests that the nonproductive binding of phages to pseudolysogens could also reduce free phage and thus effective MOI.

Some phages can also adopt a lifestyle of productive chronic infection, where, instead of lysing the host cell, the chronically infected cell can constantly release phage particles without lysing (Mäntynen et al., 2021). Nonproductive binding by chronically infected cells, however, would reduce the total number of free phages in the environment as the number of infected cells increase, and may result in changes in budding rate to reduce the resources spent on producing phages that have a low chance of finding a susceptible host.

Our system models a continuous mass-action kinetics chemostatic environment, with a constant inflow of sensitive cells. This was chosen to model steady-state dynamics and invasion at equilibrium, as it has been previously shown that, in systems without periodic fluctuations, pure lysogeny is preferred when there is no inflow of sensitive cells (Wahl et al., 2019). Environments with a consistent inflow of sensitive cells can exist in rivers, sewage systems, or any such environment with a unidirectional flow, in addition to environments with a resistant population which loses resistance at high rates, such as under phase variation (Shkoporov et al., 2021).

Our model is not without caveats, as we used a simple model for demonstration purposes. In reality, phage infections take time to progress and do not occur instantaneously. During that time, it is possible for superinfections to occur, which would both sorptively scavenge more phages and can provide information to the phage to make its lysogeny decision. Binding of phages to these intermediate infected cells increases the decay of free phages in the environment, which thereby increases the number of sensitive cells required for lytic invasion (Supplementary Material section 5, Figure S6AB). Additionally, the longer the intermediate infected state persists, the more effective it is at reducing the number of free phages (Figure S6CD).

We also assume that lysogens have perfect immunity, that the cells do not evolve resistance, that phages, lysogens and cells all have identical decay rates, and that lysogens and cells have identical growth rates. Imperfect immunity would drive down lysogen numbers as they are predated upon, but would strongly depend on the magnitude of immunity. Additionally, imperfect immunity would provide a selection pressure towards losing the receptor (Berryhill et al., 2023) and may be a driver towards phages adopting superinfection exclusion rather than immunity. The evolution of resistance would eventually lead to the system being dominated by resistant non-lysogens, as the lysogen population is constantly being reduced by induction, unless the lysogens are able to compensate with higher growth rates. Differing growth or decay rates between species would affect how sensitive the responsive lysogeny function responds to each, but would still respond to the number of lysogens. We use concepts borrowed from adaptive dynamics to evaluate our phages, such as the assumption that mutants invade only when the system is at dynamical equilibrium (Brännström et al., 2013), which we recognize may be of limited applicability in phages as phages have a high mutation rate and can greatly vary in phenotype with small mutations.

Finally, we should acknowledge that these simulations are that of well-mixed environments, as opposed to structurally-organized environments such as biofilms and microcolonies. Phages coexist in nature with the hosts they predate upon, and in many cases their hosts form a spatial structure that impacts the dynamics and spread of phages (Abedon, 2012), but result in systems that are more complex to implement and analyze.

In conclusion, lysogens that sorptively scavenge phages from the environment protect sensitive cells from infection. This results in a decreased optimal fixed lysogeny probability as the number of sensitive cells increases, and additionally increases the number of sensitive cells required at equilibrium for lytic phages to invade. We further show that, under these conditions, phages with a lysogeny probability that responds to the number of lysogens outperform those that cannot, suggesting that it may be beneficial for a phage to sense the number of lysogens in its environment.

Supplementary material

Supplementary material is available online at *Evolution*.

Data availability

The simulation code used in this study is available at https://github.com/theguetlab/responsive-lysogeny

Author contributions

B.W. designed the system and did the mathematical analysis, coding and running the simulations. B.W. wrote the manuscript, with revisions from C.C.G..

Funding

There are no funding sources to declare.

Conflict of interest

The authors declare no conflicts of interest.

Acknowledgments

We thank Fyodor Kondrashov and Gašper Tkačik for valuable input and guidance in building the model, and Stephen Abedon as well as the two anonymous reviewers for the comments provided on the manuscript.

References

Abedon, ST. (2012) Thinking about microcolonies as phage targets. *Bacteriophage*, 2(3), 200–204. https://doi.org/10.4161/bact.22444.

Bednarek, A, Cena, A, Izak, W, Bigos, J, & Łobocka, M. (2022) Functional Dissection of P1 Bacteriophage Holin-like Proteins Reveals the Biological Sense of P1 Lytic System Complexity. *International*

Journal of Molecular Sciences, *23*(8), 4231. https://doi.org/10.3390/ijms23084231.
Berngruber, TW, Froissart, R, Choisy, M, & Gandon, S. (2013) Evolution of virulence in emerging epidemics. *PLoS Pathogens*, *9*(3), e1003209. https://doi.org/10.1371/journal.ppat.1003209.
Berryhill, BA, Garcia, R, McCall, IC, Manuel, JA, Chaudhry, W, Petit, MA, & Levin, BR. (2023) The book of Lambda does not tell us that naturally occurring lysogens of Escherichia coli are likely to be resistant as well as immune. *Proceedings of the National Academy of Sciences*, *120*(11), e2212121120. https://doi.org/10.1073/pnas.2212121120.
Berryhill, BA, & Levin, BR. (2025) Semantics Count in the Description of the Interactions Between Bacteria and Bacteriophage. *PHAGE: Therapy, Applications, and Research*,*6*, 3–4, https://doi.org/10.1089/phage.2024.0063.
Biggs, KRH, Bailes, CL, Scott, L, Wichman, HA, & Schwartz, EJ. (2021) Ecological Approach to Understanding Superinfection Inhibition in Bacteriophage. *Viruses*., *13*(7), 1389. https://doi.org/10.3390/v13071389.
Brännström, Å, Johansson, J, & von Festenberg, N. (2013) The Hitchhiker's Guide to Adaptive Dynamics. *Games*, *4*(3), 304–328. https://doi.org/10.3390/g4030304.
Brown, S, Mitarai, N, & Sneppen, K. (2022) Protection of bacteriophage-sensitive Escherichia coli by lysogens. *Proceedings of the National Academy of Sciences*, *119*(14), e2106005119. https://doi.org/10.1073/pnas.2106005119.
Bruce, JB, Lion, S, Buckling, A, Westra, ER, & Gandon, S. (2021) Regulation of prophage induction and lysogenization by phage communication systems. *Current Biology*, *31*(22), 5046–5051.e7. https://doi.org/10.1016/j.cub.2021.08.073.
Cheong, KH, Wen, T, Benler, S, Koh, JM, & Koonin, EV. (2022) Alternating lysis and lysogeny is a winning strategy in bacteriophages due to Parrondo's paradox. *Proceedings of the National Academy of Sciences*, *119*(13), e2115145119. https://doi.org/10.1073/pnas.2115145119.
Doekes, HM, Mulder, GA, & Hermsen, R. (2021) Repeated outbreaks drive the evolution of bacteriophage communication. *Elife*, *10*, e58410. https://doi.org/10.7554/eLife.58410.
Erez, Z, Steinberger-Levy, I, Shamir, M, Doron, S, Stokar-Avihail, A, Peleg, Y, Melamed, S, Leavitt, A, Savidor, A, Albeck, S, Amitai, G, & Sorek, R. (2017) Communication between viruses guides lysis-lysogeny decisions. *Nature*, *541*(7638), 488–493. https://doi.org/10.1038/nature21049.
Herskowitz, I, & Hagen, D. (1980) The lysis-lysogeny decision of phage lambda: Explicit programming and responsiveness. *Annual Review of Genetics*, *14*, 399–445. https://doi.org/10.1146/annurev.ge.14.120180.002151.
Hewson, I, & Fuhrman, JA. (2003) Viriobenthos production and virioplankton sorptive scavenging by suspended sediment particles in coastal and pelagic waters. *Microbial Ecology*, *46*(3), 337–347. https://doi.org/10.1007/s00248-002-1041-0.
Li, G, Cortez, MH, Dushoff, J, & Weitz, JS. (2020) When to be temperate: on the fitness benefits of lysis vs. lysogeny. *Virus Evolution*, *6*(2), veaa042. https://doi.org/10.1093/ve/veaa042.
Mäntynen, S, Laanto, E, Oksanen, HM, Poranen, MM, & Díaz-Muñoz, SL. (2021) Black box of phage–bacterium interactions: exploring alternative phage infection strategies. *Open Biology*, *11* (9), 210188. https://doi.org/10.1098/rsob.210188.
Maslov, S, & Sneppen, K. (2015) Well-temperate phage: optimal bet-hedging against local environmental collapses. *Scientific Reports*, *5*, 10523. https://doi.org/10.1038/srep10523.
Moussa, SH, Kuznetsov, V, Tran, TA, Sacchettini, JC, & Young, R. (2012) Protein determinants of phage T4 lysis inhibition. *Protein Science*, *21*(4), 571–582. https://doi.org/10.1002/pro.2042.
Payne, P, Geyrhofer, L, Barton, NH, & Bollback, JP. (2018) CRISPR-based herd immunity can limit phage epidemics in bacterial populations. *Elife*, *7*. https://doi.org/10.7554/eLife.32035
Pleška, M, Lang, M, Refardt, D, Levin, BR, & Guet, CC. (2018) Phage-host population dynamics promotes prophage acquisition in bacteria with innate immunity. *Nature Ecology & Evolution*, *2*(2), 359–366. https://doi.org/10.1038/s41559-017-0424-z.
Ptashne, MA. (2004) *Genetic switch: phage lambda revisited*. CSHL Press.
Sanchez-Martinez, R, Arani, A, Krupovic, M, Weitz, JS, Santos, F, & Antón, J, (2025) Episomal virus maintenance enables bacterial population recovery from infection and promotes virus–bacterial coexistence, *The ISME Journal*, *19*(1), wraf066, https://doi.org/10.1093/ismejo/wraf066.
Shkoporov, AN, Khokhlova, EV, Stephens, N, Hueston, C, Seymour, S, Hryckowian, AJ, Scholz, D, Ross, RP, & Hill, C. (2021) Long-term persistence of crAss-like phage crAss001 is associated with phase variation in Bacteroides intestinalis. *BMC Biology*, *19*(1), 163. https://doi.org/10.1186/s12915-021-01084-3.
Silpe, JE, & Bassler, BL. (2019) A Host-Produced Quorum-Sensing Autoinducer Controls a Phage Lysis-Lysogeny Decision. *Cell*, *176*(1-2), 268–280.e13. https://doi.org/10.1016/j.cell.2018.10.059.
Silva, JB, Storms, Z, & Sauvageau, D. (2016) Host receptors for bacteriophage adsorption. *FEMS Microbiology Letters*, *363*(4), fnw002. https://doi.org/10.1093/femsle/fnw002.
Simmons, EL, Bond, MC, Koskella, B, Drescher, K, Bucci, V, & Nadell, CD. (2020) Biofilm Structure Promotes Coexistence of Phage-Resistant and Phage-Susceptible Bacteria. *mSystems*, *5*(3), e00877–e00819. https://doi.org/10.1128/mSystems.00877-19.
Sinha, V, Goyal, A, Svenningsen, SL, Semsey, S, & Krishna, S. (2017) In silico Evolution of Lysis-Lysogeny Strategies Reproduces Observed Lysogeny Propensities in Temperate Bacteriophages. *Frontiers in Microbiology*, *8*, 1386. https://doi.org/10.3389/fmicb.2017.01386.
Stewart, FM, & Levin, BR. (1984) The population biology of bacterial viruses: why be temperate. *Theoretical Population Biology*, *26*(1), 93–117. https://doi.org/10.1016/0040-5809(84)90026-1.
St-Pierre, F, & Endy, D. (2008) Determination of cell fate selection during phage lambda infection. *Proceedings of the National Academy of Sciences*, *105*(52), 20705–20710. https://doi.org/10.1073/pnas.0808831105.
Wahl, LM, Betti, MI, Dick, DW, Pattenden, T, & Puccini, AJ. (2019) Evolutionary stability of the lysis-lysogeny decision: Why be virulent?. *Evolution; International Journal of Organic Evolution*, *73*, 92–98. https://doi.org/10.1111/evo.13648.
Wolfram Research, Inc. (2017) Version 11.1. *Mathematica*.
Zeng, L, Skinner, SO, Zong, C, Sippy, J, Feiss, M, & Golding, I. (2010) Decision making at a subcellular level determines the outcome of bacteriophage infection. *Cell*, *141*(4), 682–691. https://doi.org/10.1016/j.cell.2010.03.034.

Received December 5, 2024; revisions received March 5, 2026; accepted March 31, 2026
Associate Editor: Ben Ashby; Handling Editor: Jason Wolf