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MINI REVIEW

Lysogeny in nature: mechanisms, impact and ecology of temperate phages

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Viruses that infect bacteria (phages) can influence bacterial community dynamics, bacterial genome evolution and ecosystem biogeochemistry. These influences differ depending on whether phages establish lytic, chronic or lysogenic infections. Although the first two produce virion progeny, with lytic infections resulting in cell destruction, phages undergoing lysogenic infections replicate with cells without producing virions. The impacts of lysogeny are numerous and well-studied at the cellular level, but ecosystem-level consequences remain underexplored compared to those of lytic infections. Here, we review lysogeny from molecular mechanisms to ecological patterns to emerging approaches of investigation. Our goal is to highlight both its diversity and importance in complex communities. Altogether, using a combined viral ecology toolkit that is applied across broad model systems and environments will help us understand more of the diverse lifestyles and ecological impacts of lysogens in nature.

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Why study lysogeny?

Bacteria significantly alter the biosphere, affecting global biogeochemical cycles and the biology of other organisms biology (Alivisatos *et al.*, 2015), but do so under the constraints of bacteriophage (phage) infection. Such phage infections range from productive to lysogenic (see Concept Box and Figure 1a) dependent on, for example, phage genetics, host genetics, phage concentration, host physiology and environmental conditions. Temperate phages in particular can replicate either lysogenically as prophages or, instead, produce virions. Although prophages in lysogenic cycles largely have been viewed as dormant entities, both prophages and their subsequent productive cycles can affect individual cells as well as entire communities. The phenomenon of lysogeny is well known, early reviews of lysogeny date to over half a century ago (Lwoff, 1953), though mostly temperate phages infecting *E. coli* have been characterized in depth including λ, Mu, P1 or N15. In nature, phages have been detected wherever their host microbes exist (Weinbauer, 2004), with reviews focusing on total viral communities from soil, aquatic and host-associated systems (Chibani-Chennoufi *et al.*, 2004; Suttle, 2005; Sawstrom *et al.*, 2008; Srinivasiah *et al.*, 2008; Williamson, 2011; Marcó *et al.*, 2012; Reyes *et al.*, 2012; Abeles and Pride, 2014; Sime-Ngando, 2014; Virgin, 2014; Ogilvie and Jones, 2015; Zablocki *et al.*, 2016). Assessing predominant infection dynamics and associated driving factors, however, can be challenging due to difficulties in determining lysogeny abundance, diversity and ecology (Paul and Weinbauer, 2010).

Here, we complement efforts to specifically review lysogeny which have largely focused on prophage genomics and impacts of lysogeny on either microbial cells (Casjens, 2003; Brussow *et al.*, 2004; Canchaya *et al.*, 2004; Abedon and LeJeune, 2005; Fortier and Sekulovic, 2013; Hargreaves *et al.*, 2014; Feiner *et al.*, 2015; Menouni *et al.*, 2015; Davies *et al.*, 2016) or particular environments (for example, aquatic (Paul, 2008)). We aim to establish an integrative view across model systems and environments, whereas also highlighting emerging tools for the study of lysogeny in nature.

Lysogeny mechanistic diversity

Most molecular knowledge of lysogeny has been derived from a handful of *E. coli* phages, such as λ and Mu, which integrate into the bacterial chromosome via site-specific recombination (Casjens and Hendrix, 2015) or random transposition (Harshey, 2014), respectively. In contrast, other phages are maintained extrachromosomally with either circular

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Concept Box

Bacteriophage (phage):	Virus that infects a bacterial host.
Lytic cycle/infection:	Virus reproduction that destroys its host cell to release virion progeny.
Lysogenic cycle/infection:	Non-bactericidal phage infection with phage genome replication but no virion production.
Induction:	Virus infection changes from a lysogenic cycle to a productive cycle.
Chronic cycle/infection:	Generally non-bactericidal phage infection, where virions are produced and continuously released.
Productive cycle/infection:	Virus reproduction with production of virion particles.
Virulent phage:	Phage which displays only lytic cycles (no chronic or lysogenic cycles).
Temperate phage:	Phage which can undergo either virion-productive or lysogenic cycles.
Prophage:	Phage genome that replicates with its host cell while *not* generating virion progeny.
Cryptic prophage:	Prophage that has mutationally lost its ability to enter a virion-productive cycle.
Lysogen:	Bacterial cell that harbors at least one prophage.
Polylysogen:	Bacterial cell that harbors more than one prophage.
Transduction:	Virion-mediated transfer of bacterial DNA to new bacteria either with associated temperate phage genome (specialized transduction) or not in association with phage genome (generalized transduction).
Virome:	Metagenomic sequences of viral communities.

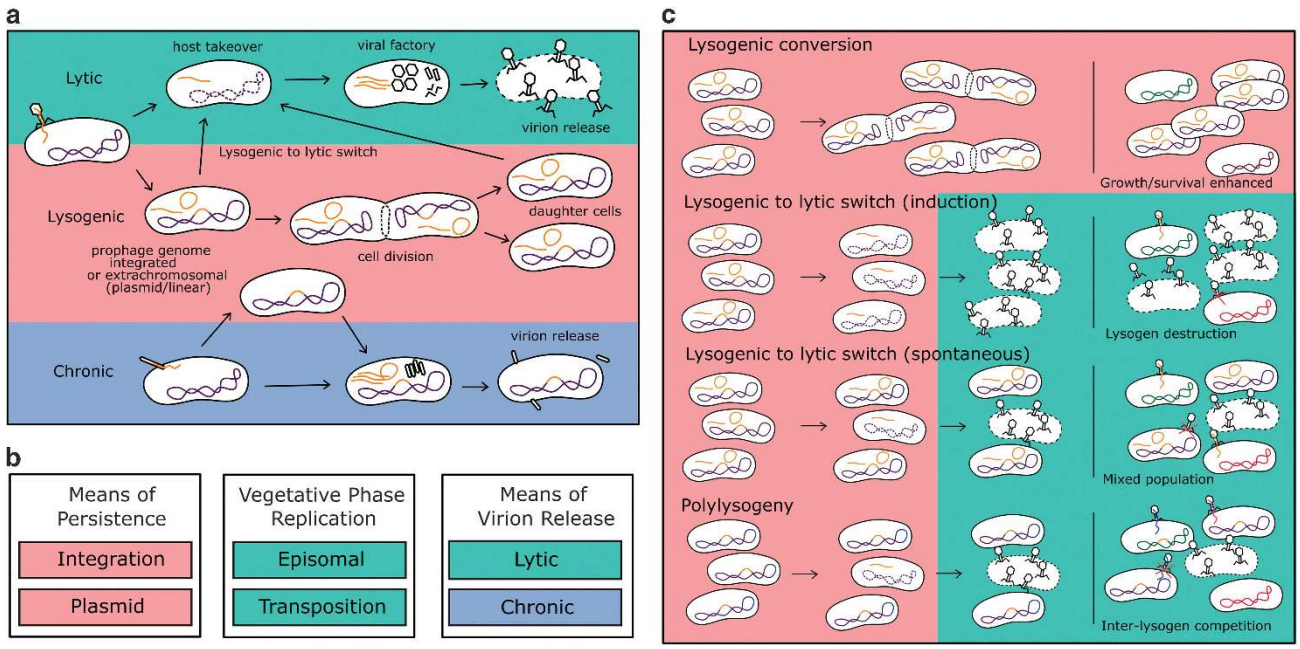

Figure 1 Modes of temperate phage infection, from cell to community. (**a**) A temperate phage can infect a cell through either virion-productive or lysogenic cycles, where it either hijacks its host's metabolism to produce new virion progeny or instead replicates its genome alongside the host without producing new virions, respectively. The production of virion particles can occur either following phage adsorption (productive cycle) or instead following a switch from a lysogenic cycle to a productive cycle (lytic or instead chronic infection cycles depending on the temperate phage). Although these are generalized dynamics of infection, details can vary with specific phage-host types, ranging from efficient to inefficient infections, where the dynamics and outcome of the infection may vary. (**b**) Summary of phage infection strategies by stage. Persistence describes the prophage stage during the lysogenic cycle, replication describes the phage-genome state during productive cycles and release refers not just to the means by which progeny phage virions transition from the intracellular to extracellular state but also the impact of productive cycles on the phage-infected bacterium (i.e., lytic but not chronic results in host-bacterium physiological death). (**c**) Implications of modes of temperate phage infection on bacterial communities. Lysogenic conversion constitutes the phenotypic effects of prophage carriage to its host cell. The lysogenic to lytic switch changes community structure by creating a mixed cell community where some lysogens are removed via lysis and the released virions can infect surrounding cells. Polylysogeny occurs when a bacterium possesses multiple prophages.

(for example, P1, (Lobocka *et al.*, 2004) or linear (for example, N15, (Ravin, 2015)) genomes. Some temperate phages, such as satellite phage P4, require other temperate phages, such as P2, to complete infection cycles (Christie and Calendar, 2016). Other temperate phages, for example, *Vibrio cholera* phage CTXphi, chronically infect their host during productive cycles and integrate during lysogenic cycles (McLeod *et al.*, 2005). Although infection details differ, lysogeny generally proceeds through three steps: (i) establishment, (ii) maintenance and also, potentially, (iii) induction of productive cycles (Figure 1). Focusing on λ as a reference, we highlight how these mechanistic factors both serve as a

knowledge baseline for further study and can contribute to lysogen ecology.

Establishment

Given evasion of host resistance mechanisms (Samson *et al.*, 2013), temperate phages 'decide' whether to produce virions (productive cycle) or instead establish lysogenic cycles as prophages. In λ, the 'decision' to enter lysogeny is driven by genetic compatibility (for example, host *attB* integration sites), host physiological state (for example, nutrient depletion increases lysogeny) and phage density (for example, higher MOIs increase lysogeny) (Casjens and Hendrix, 2015). Integration is driven via recombinases acting on phage (*attP*) and bacterial (*attB*) attachment site sequences that determine specificity (Fogg *et al.*, 2014), or prophages may integrate randomly (for example, Mu) or not at all (for example, P1).

Maintenance

Once established, integrated prophages replicate as part of the bacterial chromosome, whereas extrachromosomal prophages require genes for plasmid inheritance (for example, ParA/ParB in P1 or SopA/SopB in N15) and persistence (for example, toxin–antitoxin proteins that kill plasmid-lacking cells) (Casjens and Hendrix, 2015; Ravin, 2015). Either state has the potential to impact on host gene regulation and resulting biology, including growth rate, development and phenotype (Feiner *et al.*, 2015). In λ, maintenance is tightly regulated by its repressor, CI, via a complex genetic feedback circuit (Bednarz *et al.*, 2014). During this stage, prophages not only can alter cellular processes, but are subject to evolutionary change, with selection presumably balancing phage versus cell needs (Bobay *et al.*, 2013).

Induction

Activation of the lytic-lysogenic switch occurs either spontaneously at low frequency (10^{-8}–10^{-5} per cell for λ (Czyz *et al.*, 2001)) or as a result of external stressors such as those triggering the cell's DNA damage response (the SOS response) (Casjens and Hendrix, 2015), leading to inactivation of CI. Stressors include changes in nutrients, pH or temperature, and exposure to antibiotics, hydrogen peroxide, foreign DNA (Banks *et al.*, 2003; Mell and Redfield, 2014; Casjens and Hendrix, 2015) or DNA damaging agents (Cochran *et al.*, 1998). Alternatively, prophages can influence the induction of other phages. For example, satellite temperate phage P4 is induced via Cox, an anti-repressor encoded by temperate phage P2 (Christie and Dokland, 2012), whereas *Enterococcus* prophages pp1, pp3 and pp5 inhibit the induction of co-infecting prophages pp4 and pp6 (Matos *et al.*, 2013). This view of intracellular phage-mediated competition highlights the complexity of interactions among phages of likely ecological relevance.

Once induced, prophages replicate either episomally (for example, λ, P1, N15) or by transposition (for example, Mu). Later, virion particles assemble and are packaged with phage DNA via endonucleolytic enzymes that either cut DNA at specific sites (for example, *cos* phages) or non-specifically after filling up the capsid (for example, headful packaging by *pac* phages) (Rao and Feiss, 2015). Specialized transduction (by *cos* temperate phages) and generalized transduction (by *pac* phages generally) can differentially impact bacterial genome evolution (Rao and Feiss, 2015).

Such models of temperate phage infection (Figure 1) offer a comparative baseline for discovering variations in lysogeny in nature. For example, as observed in *Staphylococcus aureus,* temperate phage can integrate into one host genome but exist extrachromosomally in others (Utter *et al.*, 2014), or as found in *Salmonella*, be asymmetrically inherited by only one daughter cell (Cenens *et al.*, 2013a). As conditions in nature are highly variable, it is also critical to distinguish lysogeny from delayed or inefficient lytic infections (Dang *et al.*, 2015), as well as determine how natural infections can differ from those in the laboratory (Chibani-Chennoufi *et al.*, 2004). Establishment of new phage-host model systems also will be instrumental towards furthering our understanding of lysogen ecology.

Benefits and consequences of lysogeny

Temperate phages alter the biology of their hosts and, in turn, influence the surrounding community of host and non-host cells (Figure 1c). We briefly summarize four such effects, which have been previously reviewed. First, integrating prophages can engineer a host's genome (Menouni *et al.*, 2015) and help to regulate gene expression and function such that integration and excision alters cellular processes (Feiner *et al.*, 2015). Second, prophages can change cell physiology by introducing novel functions or altering pre-existing ones, such as virulence factor production, metabolism, cell development and immunity to phages (Hargreaves *et al.*, 2014). Third, through transduction, temperate phages can facilitate the transfer of bacterial DNA that potentially confer new phenotypes such as antibiotic resistance (Davies *et al.*, 2016). Fourth, induced and released temperate phages can modify bacterial communities by lysing competitor bacterial strains (Duerkop *et al.*, 2012), lysogenizing other cells (Gama *et al.*, 2013), and liberating intracellular contents for neighboring cells to use as nutrients (Nanda *et al.*, 2015).

Prophages can be 'domesticated' by losing genes, including those necessary for virion production (Wang *et al.*, 2010; Bobay *et al.*, 2014). Resulting prophage-derived genomic elements can be selectively maintained by cells should they still confer some advantage. Such cryptic prophages also can directly impact the wider ecosystem. R-type bacteriocins, which resemble phage tail-like particles, can, for example, kill neighboring competitor bacteria (Gebhart *et al.*, 2012). Phage tail-like metamorphosis-associated contractile structures in the biofilm formed by *Pseudoaltermonas luteoviolacae,* by contrast, can trigger the settlement of eukaryotic tube worm larvae to surfaces (Shikuma *et al.*, 2014), though exactly how *P. luteoviolacae* might benefit from this process is unclear. Prophage decay also can result in repetitive sequences that facilitate chromosomal insertions, creating niche-defining genomic islands. In *Cyanobacteria*, these have been hypothesized to influence expression of adjacent nitrogen stress response genes (Sullivan *et al.*, 2009). Decayed prophages can still be inducible as well as capable of lysing their host cell, as illustrated by R-type bacteriocins (Gebhart *et al.*, 2012), and their genes may re-enter the virus gene pool via recombination during co-infection with other phages (De Paepe *et al.*, 2014a).

Genetic, ecological and functional insights into lysogeny

Viral ecology has been extensively studied and reviewed, providing insights into lysogeny and its influencing factors that we synthesize here (Figure 2). *Genetically*, temperate phages have been identified in ~40–50% of microbial genomes (Canchaya *et al.*, 2003; Casjens, 2003; Fouts, 2006; Paul, 2008; Touchon *et al.*, 2016), and more recently from 21/30 phyla for which complete isolate genomes were available (Touchon *et al.*, 2016). *Ecologically*, lysogens are widespread (Chibani-Chennoufi *et al.*, 2004), occurring in terrestrial (Williamson *et al.*, 2007; Srinivasiah *et al.*, 2008), aquatic (Wommack and Colwell, 2000; Weinbauer, 2004; Suttle, 2005; Paul, 2008; Sawstrom *et al.*, 2008; Paul and Weinbauer, 2010; Sime-Ngando, 2014) and host-associated ecosystems (Reyes *et al.*, 2012; Abeles and Pride, 2014; De Paepe *et al.*, 2014b; Virgin, 2014; Edlund *et al.*, 2015; Ogilvie and Jones, 2015), though frequencies vary.

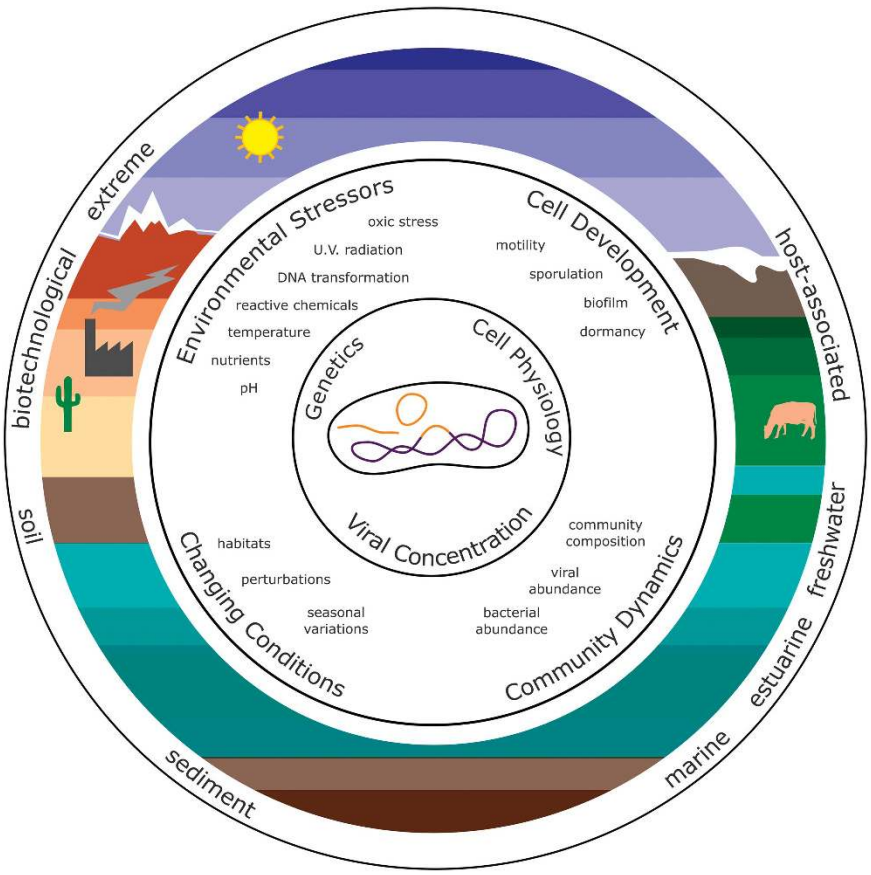

Figure 2 Ecology of lysogeny. The establishment and maintenance of lysogeny in the cell depends on the genotype of phage and host, the physiological status of the cell, and phage concentration. In nature, temperate phage-host cell interactions are influenced by multiple factors, ranging from biological (e.g., cell development and community dynamics) to environmental (e.g., factors that cause stress and environmental fluctuations). Altogether, the interplay of all of these factors may help to explain the incidence of lysogeny across different systems, including aquatic, terrestrial and microbiome-associated (e.g., as associated with humans, animals and so on).

Functionally, a paradigm of lysogeny is that it enhances phage and host survival, particularly under adverse conditions, with most data deriving from aquatic and soil environments (Paul, 2008; Sawstrom *et al*., 2008; Srinivasiah *et al*., 2008; Williamson, 2011; Sime-Ngando, 2014). Specifically, lysogen frequency generally is inversely correlated with primary microbial productivity levels during specific seasons or environments (Sawstrom *et al*., 2008). Modeling (Stewart and Levin, 1984) suggests that the lysogenic state should be favored under conditions that cause reduced host cell number and activity (for example, low productivity, low nutrients or reduced host fitness) or when viral particle decay rates are high (for example, from heat or UV exposure), as postulated in soil and aquatic environments (Sime-Ngando, 2014).

Virus-to-microbe-ratios (VMR) have been associated with lysogeny such that lower VMRs (due to, for example, high rates of virion decay and/or low virion production) may be indicative of conditions that could favor lysogeny (Williamson, 2011). VMRs vary considerably, from 1.4 to 160 in marine waters (Wigington *et al*., 2016) and between ~0.001 and >1000 in different soils (Williamson, 2011). Generally where lower VMRs occur, for example, human gut lumen (0.019 to 0.209; (Kim *et al*., 2011)) and some soils (for example, ⩾12 in wetland soils; (Williamson *et al*., 2007)), lysogeny is hypothesized to be common. Conversely, where higher VMRs occur, for example, marine oligotrophic waters and cold desert soils, lysogeny is considered to be less prevalent (Paul, 2008; Zablocki *et al*., 2016). Recent research builds on this, finding that low VMRs occurred where microbial cell numbers are most abundant (Knowles *et al*., 2016). How specific virus-host abundances fit into either the previous view of where low host cell numbers would increase lysogeny over lytic infections, to the alternative that high host cell numbers promotes lysogeny, invites renewed effort to develop experimental hypothesis-testing approaches, as exemplified by the few but important mesocosm experiments available (Srinivasiah *et al*., 2008; Pradeep Ram and Sime-Ngando, 2010).

Where to explore lysogeny next

Next-generation sequencing is beginning to map viral diversity across less-explored ecosystems, using genomes derived from viral particles (Reyes *et al*., 2012) or total microbial communities (Paez-Espino *et al*., 2016). The abundance, diversity and activity of lysogeny in many systems, however, remains underexplored.

In applied settings, understanding lytic-lysogenic dynamics may aid in improving biotechnological processes, such as in agricultural or food production, but such knowledge is in its infancy. For example, prophages are diverse among lactic acid bacteria responsible for fermentation processes such as wine (for example, *Oenococcus*) or dairy (for example, *Lactococcus* and *Lactobacillus*) (Marcó *et al*., 2012; Kot *et al*., 2014). These offer models of microbial succession during fermentations that are both ecologically and economically interesting given that prophages can be both beneficial (improving host fitness) and detrimental (lysing cells upon induction).

In host-associated systems, lysogeny studies have largely focused on microbial virulence (Brussow *et al*., 2004; Abedon and LeJeune, 2005; Fortier and Sekulovic, 2013; Hargreaves *et al*., 2014; Feiner *et al*., 2015; Davies *et al*., 2016). In humans, temperate phages appear common (Abeles and Pride, 2014; De Paepe *et al*., 2014b; Edlund *et al*., 2015; Ogilvie and Jones, 2015). In addition, infection dynamics of the human gut virome (Waller *et al*., 2014) show low host cell abundances when temperate phages are in lytic cycles, presumably lysing those hosts. Another study found increased expression of phage genes involved in lytic cycles during periodontal disease (Santiago-Rodriguez *et al*., 2015), suggesting a connection between phages and disease, though it was not confirmed that these genes were associated with temperate phages. Given the importance of microbiota in health and disease (Alivisatos *et al*., 2015), and the added consequences of the use of antibiotics, which are stressors that impact on lysogen induction (Allen *et al*., 2011), host-associated systems are ideal for exploring the implications of the lytic-lysogenic switch. Further, investigation of specific temperate phage–host interaction dynamics can reveal key players driving ecosystem change (Allen *et al*., 2011; Waller *et al*., 2014).

Across host genomes, patterns are emerging in both the types of bacteria that are commonly lysogenized and prophage diversity. For example, the detection of λ-like, P1-like or Mu-like phages varies across microbial genomes, with Mu-like and P1-like being least reported (Casjens, 2003; Fouts, 2006; Bobay *et al*., 2013; Roux *et al*., 2015b). In addition, prophages appear to predominate across some microbial phyla (for example, 74% of *Firmicutes*, 41% of *Actinobacteria* and 22% of *Cyanobacteria*), but not others (for example, 0% of *Chlamydiae*) (Touchon *et al*., 2016). Correlations between prophage frequency and bacterial growth rates, genome size and pathogenicity have been found (Touchon *et al*., 2016) and could be driven by a microbe's ecology. For example, prophages have been associated only with invasive *Staphylococcus aureus* strains (Goerke *et al*., 2009), and are absent from the intracellular pathogen, *Chlamydiae* (Touchon *et al*., 2016).

Emerging approaches to study lysogeny in nature

A combination of approaches for investigating lysogeny in bacterial isolates and complex

communities (Figure 3) can be used to assess its abundance, diversity and activity. Experimental methods for detecting lysogeny have provided foundational mechanistic and ecological knowledge, but are recognized to have methodological issues. First, they often require exposure to stressors or lysogen dilution (Paul and Weinbauer, 2010), which can have variable induction efficiencies (Braid *et al.*, 2004; Hanh *et al.*, 2015; Niu *et al.*, 2015). Second, quantifying induction is problematic as virion enumeration is challenging on field samples (Forterre *et al.*, 2013) and highly sensitive to burst size estimates (Parada *et al.*, 2006). Here, we focus on how sequencing-based methods can complement more traditional experimental approaches and help formulate hypotheses to experimentally test.

Sequencing-enabled approaches for identifying and quantifying temperate phages:
Prophage sequences can be identified from whole or draft microbial isolate genomes (Lima-Mendez *et al.*, 2008; Zhou *et al.*, 2011; Akhter *et al.*, 2012; Roux *et al.*, 2015a); theoretically from single-cell genomes (Roux *et al.*, 2014; Labonte *et al.*, 2015b); or from microbial metagenomes (Waller *et al.*, 2014; Roux *et al.*, 2015a). From viromes, temperate phages can be identified by marker genes (for example, integrases or ParA/B genes (Emerson *et al.*, 2012)); phylogenic analysis of conserved genes (for example, DNA polymerase gene (Schmidt *et al.*, 2014)); similarity to isolate phages or by cross-comparing viral and bacterial sequence datasets (Waller *et al.*, 2014); and by predicting phage/host lifestyle through *in silico* genome analysis (for example, with PHACTS (McNair *et al.*, 2012)). Such sequence-based approaches can even help identify hosts (Waller *et al.*, 2014; Hannigan *et al.*, 2015; Labonte *et al.*, 2015a,b; Edwards *et al.*, 2016) and the relative proportions of temperate phages undergoing lysogenic or lytic infections (Waller *et al.*, 2014). Prophage functionality, however, from *in silico* prediction requires experimental validation. In addition, activity can be inferred from presence in metatranscriptomes (Dupont *et al.*, 2015; Engelhardt *et al.*, 2015; Santiago-Rodriguez *et al.*, 2015) and metaproteomes (Ogilvie *et al.*, 2013) or by coupling viromics to induction experiments (McDaniel *et al.*, 2008). Although confirming activity depends on experimental induction, this latter approach revealed seasonal patterns in lysogen frequency, inversely correlated to bacterial productivity in Antarctic Ocean waters (Brum *et al.*, 2015).

Improving sequence-based and experimental characterization of lysogeny:
Sequence-based approaches can be improved with better technology to obtain (Brown *et al.*, 2014), assemble (Bankevich *et al.*, 2012) and identify

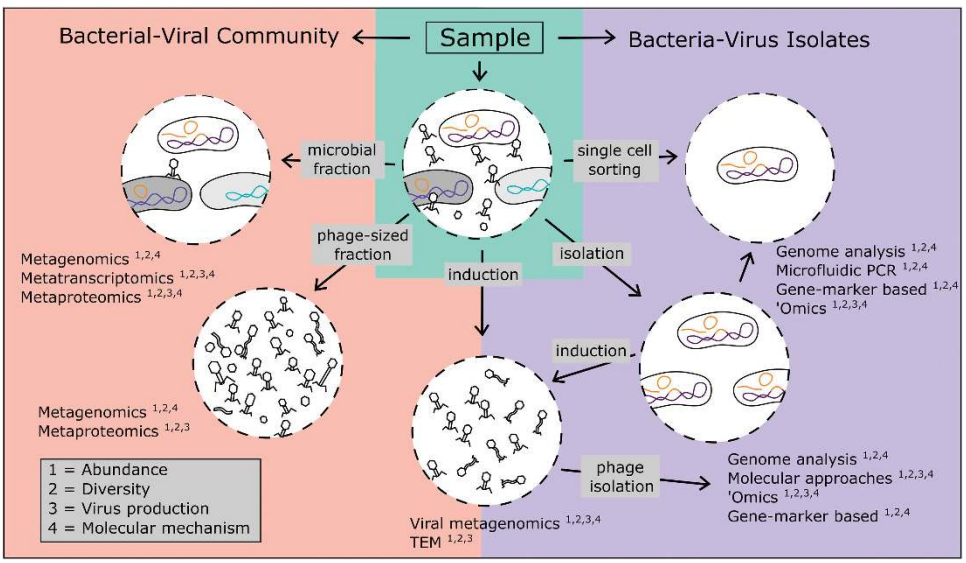

Figure 3 Approaches and methods pipeline for characterizing lysogeny. Multiple approaches to investigating lysogeny can be applied to a bacterial community either prior to induction, following induction or to isolate samples. Community samples may be divided into bacterial and viral fractions, where the DNA can be sequenced (metagenomics) and prophages analyzed bioinformatically. In addition, sequencing RNA (metatranscriptomics) and protein (metaproteomics) may provide information on abundance and activity. Treatment of samples with inducing agents (e.g., mitomycin C, UV radiation) can measure the proportion of lysogens that are sensitive to such treatment by detecting the switch from lysogenic to productive (generally lytic) cycles. Information of phage-cell interactions can be obtained by culturing and isolating lysogens from environmental samples, which can then be treated for induction and/or analyzed in detail genetically, molecularly and structurally (microscopy). Techniques such as 'omics (transcriptomics, proteomics, metabolomics) allow characterization of molecular changes during infection. When paired with single-cell resolution, infection dynamics can be followed to determine the prophage type (e.g., integrated versus extrachromosomal) and the fraction of infected and lysed cells. A combination of these approaches can inform the distribution, abundance and types of temperate phages, lysogens, and uninfected hosts, as well as increase our mechanistic understanding of the establishment, maintenance and dynamics of temperate phage infections.

temperate phages either by circumventing reference database limitations (for example, via k-mer analysis (Hurwitz *et al*., 2014)) or expanding known prophage sequence diversity (Roux *et al*., 2015b; Paez-Espino *et al*., 2016).

Experimentally, there is critical need for developing both additional experimental approaches that can help test *in silico*-derived hypotheses, and new model systems that can capture the diversity of lysogenic infections in nature. Here, methods for gene marker-based approaches are emerging for single-cell resolution including microfluidic digital PCR (Tadmor *et al*., 2011), fluorescently labeled probes (Allers *et al*., 2013), fluorescently labeled phages (Zeng *et al*., 2010)), and fluorescent reporters of prophage gene expression and genome inheritance (Cenens *et al*., 2013b). These can help discriminate between lysogeny and poorly characterized lysogenic (Abedon, 2009) or inefficiently lytic (Dang *et al*., 2015) infections. Although such methods could be improved, as discussed in (Dang and Sullivan, 2014), they nevertheless still should be helpful for characterizing lysogenic infections.

Conclusions

Temperate phages can switch between infection modes that have different but significant affects on microbial communities. Lytic cycles both kill and solubilize host bacteria, whereas lysogenic cycles impact host cells more subtly, both physiologically and genetically. Though lysogeny has been long recognized, fundamental questions nonetheless remain: (i) How do lysogen abundances change across space, time and taxa? (ii) What are the consequences and impacts on prophage-host interaction dynamics and ecosystem function? (iii) What drives these patterns? (iv) From the phage perspective, what types of prophages predominate, and why? (v) From the host perspective, why are some bacteria more prone to lysogeny than others? Numerous emerging approaches offer opportunities to develop model systems, as well as study the diverse ecological roles that lysogens have in natural microbial communities. Given these new approaches, we posit that as lytic phages have dominated the viral ecology literature to date, temperate phages should soon share the spotlight.

Conflict of Interest

The authors declare no conflict of interest.

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