

# Ocean viruses and their effects on microbial communities and biogeochemical cycles

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## Abstract

Viruses are the most abundant life forms on Earth, with an estimated  $10^{31}$  total viruses globally. The majority of these viruses infect microbes, whether bacteria, archaea or microeukaryotes. Given the importance of microbes in driving global biogeochemical cycles, it would seem, based on numerical abundances alone, that viruses also play an important role in the global cycling of carbon and nutrients. However, the importance of viruses in controlling host populations and ecosystem functions, such as the regeneration, storage and export of carbon and other nutrients, remains unresolved. Here, we report on advances in the study of ecological effects of viruses of microbes. In doing so, we focus on an area of increasing importance: the role that ocean viruses play in shaping microbial population sizes as well as in regenerating carbon and other nutrients.

## Introduction

The study of viruses of microbes has undergone a revolution in the past 20 years. What has been termed “The Third Age of Phage” [1] can be viewed more broadly as a renewal of interest in environmental viruses, and in particular in viruses of microbes [2-11]. This renewal has been spurred by advances in direct-imaging methods, sequencing technologies and bioinformatics that have revealed a previously unknown world of viral diversity in natural environments [12]. The study of viruses in the oceans has been key to many discoveries: from the finding that viruses have evolved novel lineages of key photosynthetic genes (as in cyanophages infecting *Synechococcus* and *Prochlorococcus* [13-17]) to the identification of many novel viral families that defy much of the conventional wisdom about viral life history (e.g. the discovery of “giant” algal-infecting viruses [18,19] and even viruses that exploit other viruses [20]). Altogether, it is well established that a diverse reservoir of viruses infect and lyse bacteria, archaea and microeukaryotes at the base of the ocean’s food web [2,21]. Despite the growing literature on viruses of microbes, we remain relatively poorly informed concerning

the dynamic, ecological effects of virus infection of marine microbes. In this report, we focus on the functional role of viruses within oceanic waters. In doing so, we highlight knowns, unknowns and challenges in three areas: (i) the role of ocean viruses in shaping microbial community composition; (ii) the role of ocean viruses in determining carbon and nutrient availability; (iii) modelling efforts to link viral infection of microbes with ecosystem-scale consequences.

## Viral infection and microbial community composition

Viruses, in general, and viruses of microbes, in particular, infect a subset of available hosts in any environment. The subset of hosts that a virus typically infects is narrower than the range of microbes that are typically consumed by a grazer species (e.g. a protist or zooplankton). However, there is evidence that viruses of microbes can infect hosts from different species or even different genera. For example, some cyanophages can infect different strains within the same cyanobacteria species, either *Synechococcus* or *Prochlorococcus*, as well as strains of different cyanobacterial

genera [13]. The quantitative study of the host-range of viruses of microbes is in its infancy [22-26], an issue we return to later. Successful viral infections can lead to lysis of hosts as well as the conversion of hosts into lysogens where the viral genome is integrated into that of the host, subsequently altering host physiology [2,21,27]. Lytic viral infection of microbes and its effects are our primary concerns here.

Viral lysis of microbes is thought to have direct effects on microbial community composition. Ostensibly, viral lysis should decrease the abundance of specific microbial lineages that are targeted by viral infection [28]. Estimates of bacterial-induced mortality suggest that viruses are, in some cases, as important as grazers in selectively killing microbes [29,30], whereas, in other cases, they may be the dominant source of microbial mortality [31,32]. The depletion of susceptible bacteria leads to the possibility of dynamic fluctuations in viral and microbial populations, a result predicted by simple population models [33]. Nonetheless, direct evidence for coupled oscillations between virus-microbe systems in the oceans is limited. The reasons are complex, but likely due to the fact that the emergence of new (or previously rare) viral subtypes occurs frequently and rapidly [34-37]. The changing identities of strains and their populations can make it difficult to infer the consequences of virus-microbe interactions. Hence, paradoxically, the seemingly most apparent consequences of viral-induced lysis of microbes may be hard to observe in practice. We anticipate that observations of virus and microbial abundances *in situ* via genomic and metagenomic methods, with improved time-scale resolution, will provide direct evidence for specific functional relationships between viruses and microbial hosts.

### **Viral infection and the availability of carbon and nutrients**

Virus-induced mortality of microbes has direct effects on ecosystem function. Lysis of microbes involves the release of organic carbon and other nutrients back into the environment. This redirection is known as the viral shunt [8]. The viral shunt denotes the fact that cellular materials released as particular or dissolved organic material are not directly available for utilization by organisms from higher trophic levels (e.g. plankton and fish) (see Figure 1) but are primarily utilized by predominantly heterotrophic bacteria, although some efforts have shown nutrients released in this manner to be rapidly assimilated by eukaryotic plankton [38].

Direct efforts to estimate the viral shunt are rare, with most indirectly determining virus turnover rates and from this inferring virus-mediated elemental release.

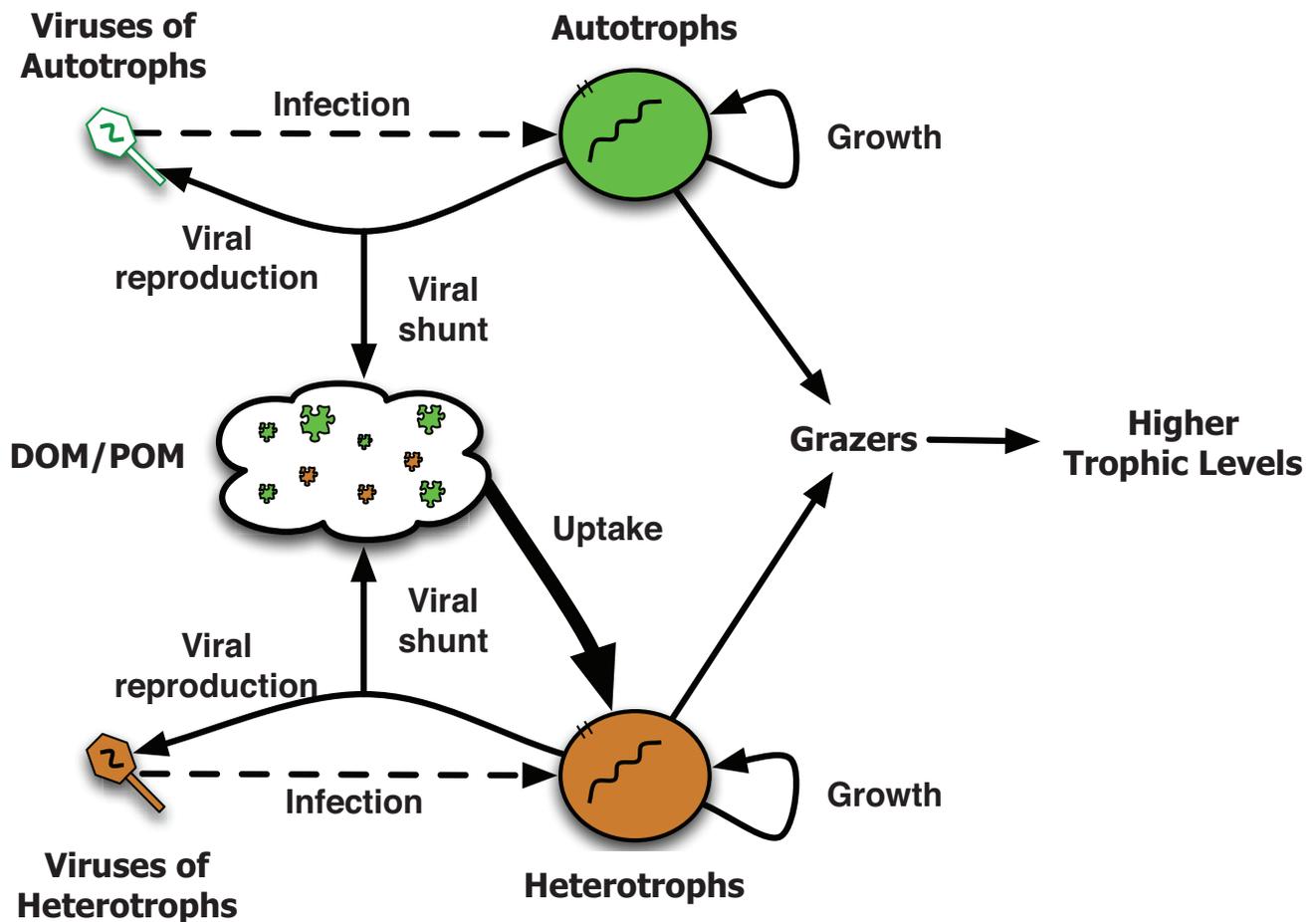
While several approaches exist to estimate virus production [39], currently favoured approaches all depend on the same steps: dilution of samples and estimates of virus reoccurrence [31]. Application of these approaches in recent years has begun to provide a broad overview of the variability of virus effects across different oceanic realms [40-43], with all observations pointing to differing constraints on virus activities in different systems.

In addition, recent evidence suggests that viral lysis of microbes changes the relative distribution of dissolved organic matter with many indirect effects in ocean ecosystems. For example, viral lysis of microbes shifts organic matter from cells into dissolved and particular organic pools. The type of organic material released in viral lysis includes a spectrum of molecules ranging from bioavailable (i.e. "labile") to recalcitrant (see Figure 2) and may be dependent as much on the location of the lytic event as the players involved [44]. In the deep ocean, the fate of virus-released organic matter remains a mystery, but this process may drive the generation of the ancient organic carbon measured by marine chemists [45]. Moreover, it is known that virus activity may drive the formation of marine snow by releasing "sticky" components from within cells [46], while at the same time disaggregating particles through cell lysis [44]. Overall, we still know little about how virus activity changes the character of dissolved organic matter, the effect of viruses on carbon distribution (i.e. fixation, respiration, mineralization and export) in marine systems, despite the potential impacts on global budgets on both short-term and geological time scales.

In addition to direct effects, the differential conversion of cellular material by viruses into a spectrum of dissolved organic material may *indirectly* affect the growth of microbial populations. An intriguing hypothesis is that heterotrophs and autotrophs may be "primed" (i.e. stimulated) by the lysis of microbes [38,45,47-51]. This includes the release of lysis byproducts that may stimulate the growth of a subset of heterotrophs [3] as well as eukaryotic auxotrophs [52]. Characterizing priming and its consequences constitutes an important area of future research, as determining the fate of carbon released from lysed cells is critical to understand how it is recycled or removed (i.e. rendered recalcitrant) from marine carbon budgets [44,45,53]. The study of nutrients may also be critical to this goal, as it has been demonstrated that the release of bioavailable nutrient elements, including N and Fe [38,54], may maintain ecosystem productivity under conditions where nutrient availability limits carbon production.

Finally, the infection of microbes also alters host metabolism, often in significant ways. For example,

Figure 1. Schematic of the viral shunt



The lysis of microbes by viruses releases cellular material into the environment. Some of this cellular material can be utilized by microbes for subsequent metabolic processes. Here, we note that available dissolved organic material (DOM) and particulate organic material (POM) is utilized primarily by heterotrophs (the thicker arrow leading downward from the DOM/POM pool). Note that many other processes are not included in this schematic, e.g. sinking out of the system, exudation during growth, light input, or the influx of inorganic carbon and nutrients. Abbreviations: DOM, dissolved organic material; POM, particulate organic material.

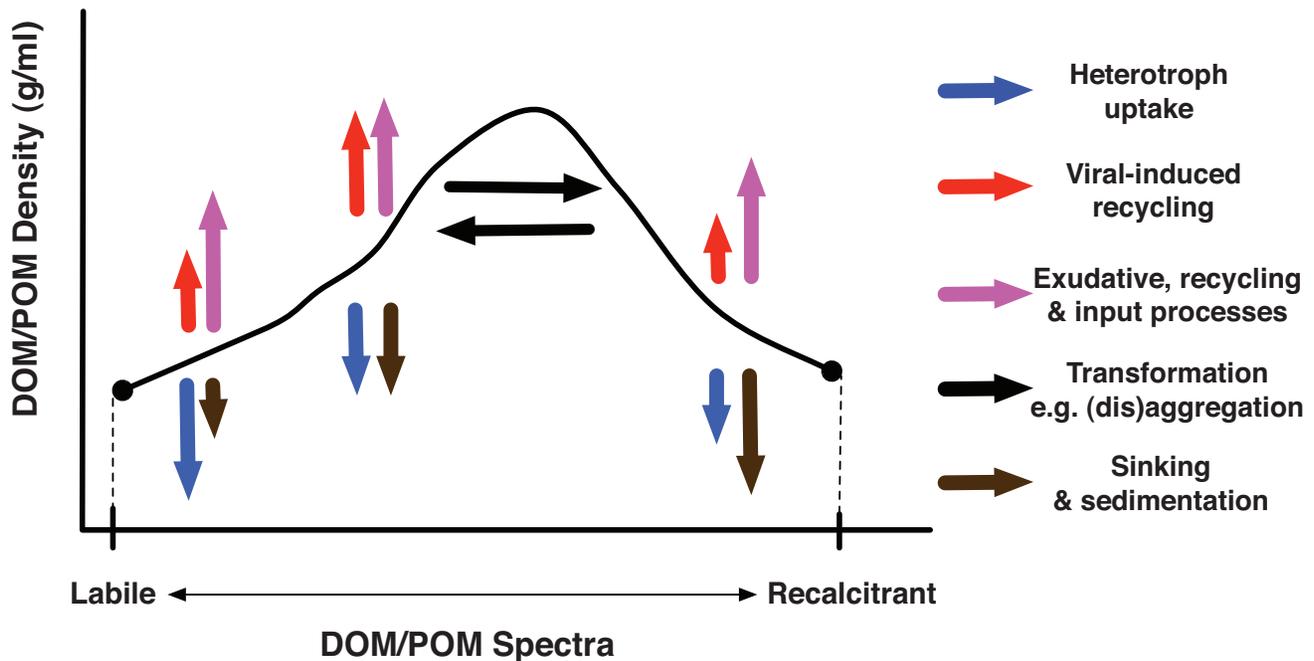
cyanophage-infecting cyanobacteria, such as *Prochlorococcus sp.* and *Synechococcus sp.*, increase the overall photosynthetic rate of microbes, presumably changing the fixation rate of carbon from the environment before lysis. Cellular-based studies have confirmed that pathways within cells can be altered at the metabolic level [55-57]. Similarly, persistent infections, such as occurs during lysogeny, can change the rate and type of utilization processes. Hence, infection can alter the behaviour of microbes, as seen from an ecosystem perspective. The net effect of such differential metabolism at the ecosystem level, however, remains largely unknown. Estimates of the contribution of lysogeny production to virus activity in marine systems remain highly variable [21,58,59]. Future work should likely consider changes in cellular

biochemistry as well as differences in cellular processes (e.g. growth efficiency, respiration and photosynthesis, etc.) between lysogens and uninfected cells. Quantifying these differences is likely to be an important component of efforts to census the overall rates at which viruses affect ecosystem functions.

#### Modelling efforts to link viral lysis with carbon and nutrient availability

Dynamic models of viral-host interactions in marine environments have, at their core, the same set of assumptions as were made for dynamics of *Escherichia coli* and associated phage in chemostats [33]. These now-classic "box" models consider how abundances of hosts, viruses and resources change with time due to the effects

Figure 2. Schematic of the role of viruses in the differential regeneration of organic matter



The release of cellular materials by viral lysis depicted in Figure 1 increases the dissolved organic matter (DOM) and particulate organic matter (POM) in the environment. Lysis also changes the abundance of distinct biomolecules. Here, for purposes of illustration, we simplify the high-dimensional configuration space of biomolecules into a one-dimensional axis. The x-axis denotes the degree to which organic material is easy to utilize by organisms (i.e. labile) vs. hard to utilize by organisms (i.e. recalcitrant). The y-axis denotes the amount of organic material across this accessibility spectrum. The vertical arrows denote how a particular process can change the availability of different organic materials, potentially in non-uniform ways. The horizontal arrows denote that some processes may convert material from one state to another without changing the total amount of material. The size of the arrows represents an estimated magnitude of a given process. We note that characterizing the space of biomolecules and the role of viruses in modifying the relative abundance of biomolecules is an ongoing challenge. There are data to substantiate the existence of horizontal and vertical arrows (e.g. [41]) but less data to substantiate the correct size of horizontal and vertical arrows. Abbreviations: DOM, dissolved organic material; POM, particulate organic material.

of resource uptake, cell division, viral-induced mortality of hosts, and viral reproduction via lysis. Extensions have taken into account a greater complexity of factors, including the possible covariation of bacterial life history traits and viral life history traits [34,35,60]. The most prominent extension to ocean systems is termed "Kill-the-Winner" [28,61], in which viruses specialize in distinct hosts and contribute to the successive decline of host strains that rise to dominance. Kill-the-Winner assumes one-to-one relationships between individual viruses and hosts. The cross-infection of viruses and hosts is more complex. For example, empirical assays of viral-host cross-infectivity reveal that viruses can infect many microbial hosts, and, similarly, microbes can be infected by many viruses [13,24-26]. A reanalysis of phage-bacteria cross-infection assays found a characteristic nested pattern [23]. The nested pattern implies there is a hierarchy of infection ability (amongst viruses) and susceptibility to infection (amongst bacteria) within the re-examined studies. Hence, a major question moving

forward is: do the predictions of Kill-the-Winner and other population ecology models change given other cross-infection assumptions? In the context of the first direct effect outlined earlier, it would be important to quantify the relationship between who infects whom and the relative abundance and survival of host and viral strains.

Perhaps the biggest impediment to predictive modelling of direct and indirect effect of viruses of microbes on microbial community composition and ecosystem function is the empirical observation that rare genotypes can rise to observable levels rapidly and frequently [62-66]. These changes may be the result of *de novo* mutation of successful genotypes as well as emergence of pre-existing, yet rare, microbes that experience changes in conditions that dramatically affect fitness. Unifying ecological and evolutionary dynamics in a single model is difficult, and most models of host-viral dynamics neglect evolution entirely. A few models are available that have begun to

assess how such evolutionary details matter. First, it has been proposed that evolutionary changes in allocation of phytoplankton to virus resistance *vs.* growth would lead to the evolution of co-limitation by hosts rather than the maximization of host productivity in a given environment [67]. However, the cost of resistance to viral infection remains largely uncharacterized in natural communities (see [68] for a laboratory study using marine cyanobacteria). Second, an evolutionary Kill-the-Winner model predicts that constant total diversity can emerge at the community level even if the identities of strains are in constant flux [69]. This model predicts that at the community scale there may be invariants for which fine-scale evolutionary details do not matter. Some empirical support for this idea comes from one study in which changes in system nutrient levels were buffered despite rapid changes in strains coevolving over a multi-month experiment [70]. Third, multiple coevolutionary models of viral-host interactions mediated by receptor resistance [71,72] and CRISPR immune defense [73] demonstrate principles under which coevolutionary-induced diversification may arise. Linking models to data and understanding when and which details matter is an issue relevant to the study of viruses of microbes and to problems in microbial ecology more generally [74].

### Viruses are everywhere, but what are they doing and how important are they?

The potential role of viruses in marine biogeochemical cycles [75,76] and the viral shunt [8] has been discussed for nearly two decades now, yet the quantitative impact viruses have on regional and global scale processes remains generally unresolved apart from estimates from a few marine virus production surveys [e.g. 32,38,40,41,77-81]. This uncertainty with respect to quantifying viral effects manifests itself in two critical ways. First, there are a number of global earth systems and climate models that integrate geophysical processes with the biology of microbes to metazoans to predict the dynamics of carbon nutrients and biodiversity [82-84]. However, the smallest biotic agents on the planet – viruses – are rarely, if ever, included in such models. Second, the most recent Intergovernmental Panel on Climate Change released its last report in 2007 noting: “The overall reaction of marine biological carbon cycling (including processes such as nutrient cycling as well as ecosystem changes *including the role of bacteria and viruses*) to a warm and high-CO<sub>2</sub> world is not yet well understood. Several small feedback mechanisms may add up to a significant one” [85]. The emphasis is ours. The assessment of quantitative effects of viruses on populations, communities and ecosystems in a form that can be integrated into large-scale models and climate change scenarios should be a major research goal.

There are many challenges to reach this goal. First, data on the quantitative effects of viruses on ecosystem processes are highly variable, and may reflect differences in collection and estimation methods in addition to natural biological variation. There is a need for increased standardization of methods (e.g. [86]) as well as the integration of existing data to relate viral interaction and effect data to environmental and geographic drivers. Second, new methods are being developed to characterize the genomes of viruses of microbes and the microbes they infect (e.g. [87]). Yet, how much do these details matter? That is, are there particular host-viral interactions, and even particular lineages or ecotypes, that are key to the flux of particular types of organic and inorganic pools? Multi-scale mathematical methods can help infer viral effects at large scale based on cellular level interactions. Finally, there is a growing emphasis on the quantification of genomic and transcriptomic diversity within ocean microbes. However, predicting ecosystem-level effects of viruses of microbes requires quantitative estimates of rates and interactions coinciding with genomic and transcriptomic surveys. We hope that future work on viruses of microbes in the oceans includes efforts to combine rates, -omics data and mathematical models in the service of answering a fundamental question: what effects do viruses have on the global earth system?

### Competing interests

The authors declare that they have no competing interests.

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