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Abstract

During the past 30 years, a vast number of articles have been published on the importance – in terms of abundance, diversity and functional roles – of viruses inhabiting the aquatic world (either marine or freshwater), which include several excellent reviews. Our knowledge, e.g. of the interactions of viruses with the living (organisms) and non-living compartments (i.e. dissolved organic matter/particles/nutrients/physical factors) in aquatic environments, has considerably increased. Furthermore, recent new ideas, concepts and technologies have shed light on host–virus interactions and the diversity of viral species and functions as discussed in this book. This chapter highlights some of these current advances in the field of aquatic viral ecology. Recently developed models and concepts will also be discussed, further emphasizing the role of defence mechanisms against viruses which appear to be important drivers in strain diversification of host species. Additionally, new environments such as anoxic and benthic sediments have received more attention and novel information has been gathered, e.g. on archaeal and RNA viruses. Interactions within entire food webs, such as with heterotrophic dinoflagellates, oysters and even cascading effects up to cyanobacteria-consuming flamingo populations represent another aspect of looking at viruses and their role in the global biosphere. The chapter also discusses knowledge gaps and proposes future research avenues.

Introduction

Viruses of microorganisms (VoMs) as found in aquatic environments consist of those infecting archaea, bacteria, or eukaryotes, the latter especially infecting algae and protists (see Chapters 7, 8, 10 [79] and 11, respectively). This chapter focuses on findings and concepts dealing with aquatic viral ecology, virus interactions with hosts, and virus diversity. It builds on research that has been summarized in older reviews as mentioned in 'General aspects of [80] aquatic viral ecology'. Although this review mainly deals with viruses of microorganisms, other viruses are also within the realm of viruses of aquatic environments. Rather than being comprehensive, this chapter focuses on key concepts along with some not fully considered research avenues.

In the first part we discuss the general aspects of aquatic viral ecology, focusing particularly on the role of viruses in aquatic ecology. Then we provide an updated outlook on aquatic viruses based on insights gleaned from recent findings. A glossary provides additional information on terms used in this chapter (Table 6.1).

General aspects of aquatic viral ecology

Since the discovery of high viral numbers as well as significant viral infection rates of microbes in aquatic environments (Bergh 1989, Suttle *et al.* 1990), it has been widely recognized that viruses are major actors for the functioning of aquatic ecosystems. Viruses have been described as 'partners' in pelagic food webs (Bratbak *et al.*, 1990), 'new players in the game' (Bratbak and Heldal, 1995), 'killers of winners' (Thingstad and Lignell, 1997; Kirchman, 2013), and 'major players' in global ecosystems (Suttle, 2007). They have also been said to 'rule the waves' (Bratbak and Heldal, 2000) as well as 'the world' (Wilson *et al.*, 2009), 'manipulate the marine environment' (Rohwer and Vega Thurber, 2009) and 'reprogram the metabolism in the sunlit and dark ocean' (Hurwitz *et al.*, 2013). Finally, viruses have been portrayed as 'the key to survival in the seas for microorganisms' (Paul, 2008) and 'catalysts of nutrients cycling' (Suttle, 2005), which 'lubricate the microbial loop' (Allen *et al.* 2008).

Table 6.1 Glossary of terms used in this chapter

Term	Explanation
Aphotic zone	Portion of a lake or ocean where there is little or no sunlight
Archaea	One of the two domains of life forming the prokaryotes
Archaeal viruses	Viruses infecting Archaea
Attached	Microorganisms attached to particles/aggregates are operationally distinguished by filtration through 0.8–1 µm filters from their so-called free-living counterparts
Autotrophs	Here used for organisms synthesizing organic matter from carbon dioxide and releasing oxygen via photosynthesis (photoautotrophs)
Bacteria	One of the two domains of life forming the prokaryotes
Bacterial viruses	Viruses infecting Bacteria; Equivalent to bacteriophages as well as phages
Bacteriophages	See Bacterial viruses
Bloom	Originally used for phytoplankton (phytoplankton bloom), which develop in spring with the onset of water stratification and enhanced light availability, and which are then followed by a decay period
Boom–bust	Description of population growth that is followed by population decline; see similarly Bloom
Copepod	Type of small crustaceans
CRISPR	Stands for Clustered Regularly Interspaced Short Palindromic Repeats and is a type of adaptive immunity used by microorganisms against viruses
Cyanobacteria	Photoautotrophic bacteria
Diatom	Major group of unicellular microalgae
Dissolved organic matter (DOM)	Fraction of organic matter that can pass through filters with a pore-size of 0.2 – 0.45-µm; the main chemically characterizable macromolecules in the oceanic DOM pool are carbohydrates, proteins and lipids although a large fraction of DOM, usually more than 50%, is not chemically not characterizable
Diversity (of species)	Described by species richness (number of species), species evenness (abundance of individual species) and degree of species differences (taxonomic relatedness of species)
DOM	See Dissolved organic matter
Eukaryotes (Eukarya)	One of the two domains of life besides Archaea and Bacteria, comprises organisms with a nucleus in their cells
Eukaryotic viruses	Viruses infecting Eukarya
Eutrophic; Eutrophic environments	Regions where inorganic and organic nutrients are available at higher supply rates than under oligotrophic (i.e. much less productive) conditions; the nutrient supply rate influences the composition of food-web structure by favouring organisms with greater competitive abilities despite higher nutrient demand
Food web	Description of the complex trophic structure of most ecosystems, where prey species may be consumed by multiple predator species and following death all species may be consumed by multiple decomposer species

Table 6.1 Continued

Term	Explanation
Food-web efficiency	The percentage efficiency of energy transfer between trophic levels
Free-living	Contrast with Attached
Grazers	Here primarily used for protists feeding on prokaryotes as well as on other protists, although note that aquatic animals also can graze on algae and protists
Growth efficiency	Ratio between growth and uptake of substrate (i.e. nutrient) as measured in the same unit, usually in terms of carbon
Heterotrophs	Organisms that consume already assimilated organic matter (grazers and heterotrophic bacteria)
Mesopelagic	Water layer between the euphotic zone where no longer sufficient solar radiation is available to allow photosynthesis and the deep water masses. Usually the mesopelagic layer ranges between 100 m and 1000 m depth.
Microalgae	Small phytoplankton, i.e. small-in-size algae
Microorganisms	Non-taxonomic term used for microscopic organisms; here used for viruses, prokaryotes and protists
Mineraliser	Organisms which can convert organic matter to inorganic nutrients; here heterotrophic bacteria and heterotrophic protists
Oligotrophic	See Eutrophic
Organic aggregates or particles	Here used synonymously with particulate organic matter
Particulate organic matter (POM)	Fraction of organic matter retained by filters with a pore-size of 0.2 – 0.45-µm; technically, (microbial) cells belong to the POM pool
Phages	See Bacterial viruses
Photic zone	Zone within bodies of water where majority of photosynthesis occurs
Phylotype	Microorganisms identified by the sequence similarity of their small ribosomal RNA subunit
Phytoplankton	Photoautotrophic plankton
Plankton	Drifting organisms; divided into virioplankton (viruses), bacterioplankton (bacteria and archaea), phytoplankton (photoautotrophic eukaryotes), and zooplankton (heterotrophic eukaryotes)
POM	See Particulate organic matter
Primary producers	Here used for organisms assimilating organic carbon from inorganic material (photoautotrophs, although chemoauthotroph primary producers also exist within aquatic environments)
Primary production	Synthesis of organic compounds from aqueous carbon dioxide (typically by photosynthesis)
Prokaryotes	Comprised of the domains Bacteria and Archaea, i.e. organisms with no nucleus in their cells
Protists	Small, single-celled, photo- and/or heterotrophic eukaryotes
Remineralization	Breakdown or transformation of organic matter into its simplest inorganic forms
Suspended matter	Roughly equivalent to POM/aggregates/particles; usually used to describe larger material; can contain significant amounts of inorganic particles
Trophic levels	Position an organisms occupies in a food web
Upwelling	Oceanographic phenomenon that involves wind-driven motion of dense, cooler, and usually nutrient-rich water towards the ocean surface, replacing the warmer, usually nutrient-depleted surface water
Viral shunt	Release of materials from organisms by viral lysis and uptake of especially the organic component of this material by heterotrophic prokaryotes
Zooplankton	Planktonic organisms which assimilate particulate organic carbon (POM), that is, rather than DOM

A consensus thus exists as to the importance of viruses in the ecology of aquatic biomes.

More specifically, it is now well established that microorganisms play a crucial role in microbial food webs and biogeochemical cycles (Pomeroy, 1974; Azam *et al.*, 1983) (Fig. 6.1). The classical concept of a grazing food chain composed of phytoplankton (primary producers), herbivorous zooplankton (primary consumers), and carnivorous zooplankton (secondary consumers, etc.) has been extended to include additional microbial processes. A key component of this extension is production of dissolved organic matter (DOM), which is released or 'exuded' from even healthy phytoplankton, but also produced in the course of 'sloppy feeding' by zooplankton. Heterotrophic prokaryotes, that is, members of domains Bacteria and Archaea, are the main users of this DOM, and they themselves are grazed upon by flagellates and ciliates, which are consumed, in turn, by meso- and macro-zooplankton. Bacterial assimilation of DOM and subsequent grazing on bacteria by larger organisms thus can return carbon that otherwise would have been lost to food webs. This grazing action also results in an enhanced remineralization of organic matter, either directly due to the conversion of organic matter to carbon dioxide and NH4 or indirectly due to the stimulation of bacterial activity as a consequence of sloppy feeding and release of labile organic matter from food vacuoles rich in N and P. These inorganic nutrients are then used by both primary producers and heterotrophic bacteria. These DOM-related pathways are collectively referred to as the 'microbial loop'.

Subsequent research has revealed that viral lysis is another important cause of prokaryote as well as phytoplankton mortality (Proctor and Fuhrman, 1990; Fuhrman and Noble, 1995; Noble and Fuhrman, 1997, Suttle *et al.*, 1990; Suttle and Chan, 1993). Viral lysis not only kills cells, particularly in the course of releasing new viral particles, but also converts those cells into DOM, consisting mainly of cell content, and Particulate Organic Matter (POM), the latter consisting mainly of cell wall fragments. This conversion prevents nutrients from reaching higher trophic levels, at least in the near term. Instead, the cellular debris is consumed by heterotrophic bacteria, generating therefore 'a viral loop' (Bratbak *et al.*, 1992) or 'viral shunt' (Wilhelm and Suttle, 1999) (Fig. 6.1B), which stimulates bacterial production and respiration (Fuhrman, 1999). Viral lysis thus 'catalyses' nutrient cycling (Suttle, 2005, 2007; Wilhelm and Suttle 1999; Weinbauer *et al.*, 2011a; Shelford *et al.*, 2012, 2014) and thereby 'lubricates' the microbial food web (Allen *et al.*, 2008).

The carbon pool found in marine DOM and POM is approximately as large as the carbon pool consisting of atmospheric CO2 (Hedges, 2002) or in all global biota (Dittmar and Paeng, 2009). Thus, the fate of carbon bound to DOM and POM (including microorganisms) is an important factor influencing the climate. One of the most significant functions of heterotrophic bacteria in the ocean

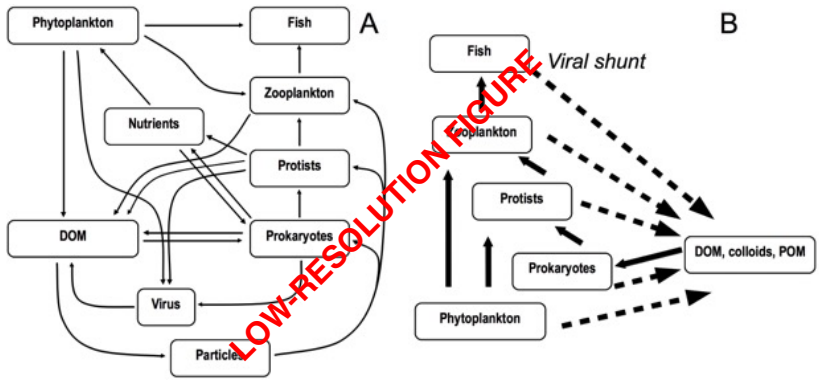


Figure 6.1 Idealized food webs. A) Simplified planktonic food web with grazing food web (phytoplankton–zooplankton), microbial loop (DOM–bacteria–protists) and viral shunt. B) details of the viral shunt and the flow of organic matter are shown (dashed lines).

is the transformation of DOM and POM into biomass, on the one hand, and into CO_2 by respiration, on the other hand. The biomass is then found again in the food web (del Giorgio and Cole, 1998).

On microscales, the microbial community is operationally structured (determined experimentally by filtration) into free and particle-attached microorganisms. Attached microorganisms are embedded within nutrient-rich organic matrices (Alldredge and Cohen, 1987) and consequently bacterial abundances and activities found in association with particles can be one or two orders of magnitude higher than in surrounding waters (Simon *et al.*, 2002). Marine snow and the plume of sinking or rising particles are – presumably as a consequence – considered to be hot spots of biogeochemical transformations, e.g. generation and removal of DOM, as mediated by microorganisms (Azam, 1998; Azam and Long, 2001; Kiørboe and Jackson, 2001). Aquatic snow also impacts local prokaryotic communities e.g. by adsorbing viral particles, which can lead to diminished pressure by viral lysis of the free-living bacterioplankton (Weinbauer *et al.*, 2009; 2011b).

The fate of most of the organic carbon generated by primary production in the upper ocean, i.e. carbon fixing CO_2 via photosynthesis, is remineralization to CO_2. A small fraction of the fixed carbon, however, is not remineralized but is instead stored for millennia as 'recalcitrant' DOM (not easily biodegradable by prokaryotes). Recently, the concept of the 'microbial carbon pump' has been proposed as a conceptual framework that addresses this biogeochemical issue (Jiao *et al.*, 2010).

Likewise, metabolic balance, which is the ratio of primary production to community respiration (P/R ratio), is critical for determining whether the ocean is globally heterotrophic (in this case, gaining energy from organic carbon) or instead autotrophic (converting inorganic carbon, i.e. CO_2, to organic carbon) in terms of net trophic production. That is, whether more CO_2 is generated via cellular respiration versus fixed via processes such as photosynthesis. The P/R ratio, in other words, determines whether the ocean is globally retentive or a net source of carbon (del Giorgio and Duarte, 2002). In distinguishing these contrasting scenarios, viruses seem to play an essential role.

Virus interactions with hosts

Viruses interact with their hosts most prominently in terms of either productive or latent infections (see Chapter 1). Hosts, however, also can [81] resist viral infection through various means. The consequences of viral infection generally involve production of new virions and modifications of the host cell, the latter being often fatal as in the case of virus-induced cell lysis. In addition, viruses can carry non-viral DNA that can become incorporated into susceptible cells (transduction).

General lifestyles

When a virus infects its host cell, it takes over its metabolism. New viral nucleic acids and capsids are assembled and packaged together into new virions. Finally, in most instances the infected cell lyses and the virions are released into the environment; these viral particles can then further re-infect other hosts. These subsequent infections of new hosts can be described epidemiologically as secondary infections (Abedon 2015). Furthermore, the cell wall is fragmented by this lysis and cellular contents are spread into the surrounding environment. These viruses are called lytic (prokaryotes) or virulent (eukaryotes). Other viruses, called 'temperate' for viruses of prokaryotes or 'latent' for viruses of eukaryotes, can, depending upon circumstances, either follow the lytic/virulent model or become integrated into the host genome as prophages/proviruses. They then replicate together with their host genome until induced by agents (chemicals, environmental conditions, etc.) into lytic cycles or, for some viruses, chronic cycles. Chronic infection, in which viruses either bud or are otherwise extruded out of host cells without killing those cells, remain scarcely documented for aquatic viruses. Pseudolysogeny, e.g. a phenomenon when only a fraction of the infected cells produce free virions (e.g. Abedon 2009), is also rarely found in aquatic virology literature and poorly understood in general.

Even when viruses are in a lysogenic cycle, proviruses have been shown to express transcriptional regulatory and repressor-like proteins (Paul, 2008). These proteins are hypothesized to suppress unneeded metabolic activity to help host survival in unfavourable environments. Conversely, host metabolic/physiologic status can affect (i) viral production through the modification of the latent period, the burst size and the number of infected

cells, and (ii) the viral life cycle more dramatically, e.g. by leading viruses to enter the lysogenic cycle during times of host physiological stress. Changes in environmental conditions can also alter viral dynamics and replication cycles (Wommack and Colwell, 2000; Weinbauer, 2004). Recent evidence has shown the importance of host cell physiology in lifestyle decisions (Maurice *et al.*, 2011; Palesse *et al.*, 2015).

Viral infection and host resistance

Using a variety of different strategies, hosts can defend themselves against viral infection (for a review on these strategies against prokaryotic viruses, see Hyman and Abedon, 2010). Here, we present a few examples related to the aquatic environment. Viral infections can be avoided directly by production of a variety of specific enzymes such as the CRISPR-associated endonuclease, Cas. Alternatively, cells can change, reduce, or eliminate cell surface receptors, physiologically or evolutionarily, to block viral adsorption and thereby entrance, replication, and subsequent release (Labrie *et al.*, 2010; Thomas *et al.*, 2012). Host cells can also develop indirect strategies to escape viral infection by controlling their size, abundance, and growth rate to reduce encounter rates with viruses. This likely is the strategy used by SAR11, what probably is most bacterial group in the ocean (Morris *et al.*, 2002). It has been proposed that SAR11 is so successful because of its small cell size and the low growth rates as resistance mechanisms (so-called K-strategy) (Kirchman, 2013; Zhao *et al.*, 2013). Resistance can also take place during the change of the life cycle in algae (called metagenesis), as in the case of eukaryotic coccolithophorid phytoplankter *Emiliana huxleyi*, which can be either haploid (one chromosome) or diploid (two chromosomes). Only the latter form is susceptible to viral attack (Jacquet *et al.*, 2002; Frada *et al.*, 2008). Lysogeny, which can be interpreted as a survival strategy of viruses living at low host density or slow metabolism, can confer immunity against homologous viral infection or replication (Weinbauer and Rassoulzadegan, 2004; Fuhrman, 1999).

Tested viruses generally have been found to be able to develop solutions which allow them to fend off host anti-viral systems (Samson *et al.*, 2013). For example, advances in CRISPR-Cas studies have shown that phages can evade the CRISPR-Cas immune system by various mechanisms (Deveau *et al.*, 2008; Sapranauskas, 2011; Semenova *et al.*, 2011; Bondy-Denomy *et al.*, 2013; Seed *et al.*, 2013). Other examples of viral mechanisms of evasion of host defences are known, and evading such defences is an important means by which viruses can modify their host ranges (see e.g. Hyman and Abedon, 2010).

Despite the documented give-and-take between viral-resistance mechanisms and viral means of overcoming those mechanisms, resistance to viral infection does not appear to be a dominant process in the environment (Fuhrman, 1999; Weinbauer 2004). This could be the result of a physiological cost related to resistance, which may cause disadvantages in the competition for resources when compared to non-resistant cells. For example, there is evidence for the concept of a cost of resistance (CoR) which is now widely accepted as an explanation for limitations on bacterial resistance to viral infections (Lennon *et al.*, 2007, 2008; Våge *et al.*, 2012, 2013). In this concept, it is assumed that there are two basic organism strategies: types not investing in resistance (low CoR) and types strongly investing into resistance (high CoR). This concept was related to the growth rate of hosts and to their life strategy. Fast-growing hosts and/or hosts possessing large cells, which have been described as 'r-selected', concur with low CoR (no investment in resistance, hence allowing for fast growth) and these hosts consequently are more susceptible to infection and lysis. K-selected hosts, i.e. slow-growing and/or small cells, have a high CoR and are less susceptible to infection (Suttle, 2007; Pagarete *et al.*, 2013). The cost of some defence systems, however, have also been considered as relatively low.

Quorum-sensing, host resistance and defence

Barrangou *et al.* (2012) suggested that CRISPR-Cas based host defence might be involved in the control of quorum-sensing signal regulatory cascades. Quorum sensing (QS) is a cell-density-dependent intercellular communication mechanism that is widespread in both prokaryotic and eukaryotic microorganisms (Kleerebezem *et al.*, 1997; Whitehead *et al.*, 2001; Nickerson *et al.*, 2006; Spraque *et al.*, 2006), which frequently occurs at high cell density (Fuqua *et al.*, 2001), and which can even

be involved in cross-domain communication (e.g. Bacteria–Eukaryota; Hughes and Sperandio, 2008; Pacheco and Sperandio; Hartmann and Schikora, 2012). Cells can produce QS signal compounds (e.g. N-acyl homoserine lactones, autoinducer-2, etc.) to self-regulate their population size by auto-inducing a variety of functional genes in response to environmental stresses and adaptation (Whitehead *et al.*, 2001). Viral lysis is one of the QS-induced phenotypes and the promoting/triggering of viral lysis (prophage induction) through QS has already been detected for some bacteria (Ghosh *et al.*, 2009).

Recently, quorum-sensing has also shown to be involved in phage defence in *E. coli*, where moderately reducing the number of virus-receptor molecules on cell surfaces caused a dramatic reduction of infection rates (Høyland-Kroghsbo *et al.*, 2013). These findings support the hypothesis that virus–host interaction in cells (lysis/host defence) might be regulated by QS. It is noteworthy that the QS signal compounds have also been detected in water (e.g. wastewater; Feng *et al.*, 2013), and in waterborne bacteria such as cyanobacteria (Sharif *et al.*, 2008), macroalgae (Kim *et al.*, 2007) and *Vibrio harveyi – V. harveyi* quorum sensing-controlled bioluminescence is believed to be responsible for the 'milky seas' phenomenon in the ocean (Miller *et al.*, 2005; Nealson and Hastings, 2006).

Placing viral lysis and host resistance in a context of QS network regulation by hosts could help to provide answers to some pertinent questions. Firstly, the boom–bust pattern (indicative of 'Killing the Winner' KtW) for viral populations are often observed even when there are no massive blooms occurring within environments, i.e. when total bacterial abundance remains roughly stable (Chow and Fuhrman, 2012; Pagarete *et al.*, 2013; Zhong and Jacquet, 2014). This can be explained within the KtW hypothesis, where viral lysis controls the competitively fast-growing r-selected populations (Thingstad, 2000; Weinbauer, 2004; Suttle, 2007) in response to environment changes (e.g. nutrient availability), thus preventing bloom formation by the winner of the competition for nutrients. Since the maintenance of constantly elevated defences is costly, Høyland-Kroghsbo *et al.* (2013) have hypothesized that some bacteria have additionally developed mechanisms to estimate the risk of phage infection and to adjust their growth and defence strategies accordingly. Recently, three homologues of bacterial genes from the accessory gene regulator of QS systems has been detected in a *Clostridium* phage genome (phiCDHM1; Hargreaves *et al.*, 2014). This is the first time that QS genes have been reported in a phage genome and the discovery suggests that phages might influence their bacterial hosts or neighbour bacterial populations in novel ways (Hargreaves *et al.*, 2014).

Virus-mediated gene transfer, gene transfer agents, virus and non-virus genes

Viruses, along with other mobile genetic elements (e.g. plasmids, transposons and integrons), allow the transfer of genes among and between organisms in aquatic ecosystems (Frost *et al.*, 2005). The process is called 'transduction' and consists of viruses picking up DNA from one host and transferring that DNA to another host. In generalized transduction, viruses randomly acquire host DNA during DNA packaging or encapsulation, while in specialized transduction proviruses excise specific parts of host DNA, ones found adjacent to the proviral insertion site, when entering a lytic cycle. Foreign DNAs carried to and injected into recipient cells can either be digested or recombined with homologous regions of recipient chromosome resulting in exchange of genetic material. Thus, the overall effect of transduction could be to homogenize gene sequences among virus-susceptible host populations. For example, Chiura (1997) could demonstrate that phages isolated from marine bacteria could repair amino acid deficiencies even in *E. coli*. This suggests a capacity of gene transfer towards a broad range of bacterial hosts. Mounting evidence from (meta) genomic studies has shown that viruses constitute an important genetic reservoir, or gene bank, and revealed that viral particles not only contain their own genes but also a high number of host-derived genes. These include genes involved in host virulence, photosynthesis or nucleic-acid metabolism (Desnues *et al.*, 2008; Rohwer and Thurber, 2009; Clokie *et al.*, 2011). As described above, even quorum-sensing related genes were also discovered in a *Clostridium* phage genome.

Gene transfer agents (GTAs) are phage-like elements involved in horizontal gene transfer (Lang and Beatty, 2007; Lang *et al.*, 2012). They integrate genetic material into a recipient chromosome for

replication and are released from host cell by lysis, similar to phages, and they are probably originally derived from phages (Lang *et al.*, 2012). Nevertheless, GTAs (i) do not carry genes that allow their own propagation (i.e. GTA encoding genes); (ii) bear insufficient DNA to encode particle-structure proteins, and (iii) carry random pieces of host genomes. Four genetically unrelated GTAs have been identified in bacteria and archaea so far (Lang *et al.*, 2012). It has been reported that genes encoding RcGTAs are found in most marine systems (Biers *et al.*, 2008). The same study also showed that these GTAs are mainly produced by marine bacteria and move genes between species of Alphaproteobacteria.

[82]

Other possible gene transfer entities include bacteriophage-like particles (BLPs) and membrane vesicles (MVs). BLPs are elements similar to GTAs (e.g. with a tailed phage morphology, packaging host DNA randomly), except for the fact that no gene transfer has yet been witnessed. In the case of PBSX-BLP of *Bacillus subtilis*, the particles kill cells that do not harbour the BLP, conferring a selective advantage for those carrying the BLP (Lang *et al.*, 2012; Wood *et al.* 1990). Membrane vesicles, by contrast, are small (roughly the size of viruses), lipidic elements which are secreted by cells and which harbour different types of DNA, including host chromosomal, plasmid, and even viral DNA (Biller *et al.*, 2014; Gaudin *et al.*, 2014). Membrane vesicles therefore could be considered to be another indirect method for the horizontal gene transfer of host and viral DNA (Chiura *et al.*, 2011; Velimirov *et al.*, 2011). Furthermore, all the gene transfer elements cited above are difficult to distinguish from true viruses in environmental samples during enumeration using classical methods such as EFM (Forterre *et al.*, 2013).

In addition to transduction, host DNA released by viral lysis could be transferred to other organisms through uptake of environmental genetic material, i.e. natural transformation, and this constitutes another, although indirect, mechanism of the virus-mediated gene transfer (Fuhrman, 1999; Weinbauer, 2004). Uptake of exogenous cellular DNA released from viral lysis through transformation is not necessarily a host-species specific process but can also spontaneously occur between two distinct hosts, or even between prokaryotes and eukaryotes (Dunning *et al.*, 2007; Keeling and Palmer, 2008). Filée *et al.* (2008, 2009) detected bacterial-like genes in genomes of phycodnaviruses and mimivirus that infect protists. This resident bacterial DNA was acquired several times during successive acquisition events. The authors proposed that the host (or a host symbiont) of a giant virus (see Chapter 11) has provided both the necessary source of bacterial DNA (from host grazing of bacteria) and the cell compartment that enables this DNA to encounter actively replicating viruses. This bacterial DNA could have been incorporated into eukaryotic algae through transformation and thereby packaged by phycodnaviruses during replication (generalized transduction). Some studies have shown that virus-like particles in seawater and hot springs have been involved in gene transfer between the three cellular domains (Archaea, Bacteria and Eukaryota), but the nature of the particles remains unknown (Rohwer and Breitbart, 2009).

Viral infection and virus-mediated host mortality

Viral lysis is associated with death of the lysed cell and is one of the most significant ecologically functional roles of viruses. For example, it was shown that virus-mediated cell death is involved in the termination of phytoplankton blooms (Bratbak *et al.*, 1993; Tarutani *et al.*, 2000; Jacquet *et al.*, 2002). Estimations of virus-induced mortality rates, which are assumed to be associated with virus-induced cell lysis, indicate that viral lysis also controls phytoplankton biomass in non-bloom forming species (Brussaard *et al.*, 1996; Evans *et al.*, 2003; Gastrich *et al.*, 2004; Nagasaki *et al.*, 2004; Tarutani *et al.*, 2000; Baudoux *et al.*, 2006). These estimations of virus-induced cell mortality have revealed that viruses, through top-down processes, can control host population size, especially through regulation of the fastest growing taxa.

It is well established that viruses are a major cause of mortality of prokaryotes (the most abundant organisms on earth), which on average are as important as grazing by protists (Fuhrman and Noble 1995, Weinbauer, 2004; Pradeep Ram *et al.*, 2014). For example, a recent study of 11 freshwater lakes confirms that the mechanisms of prokaryotic production regulation varied with sampling depth from grazing being more important in the euphotic zone and viral lysis being more important in the aphotic zone (Pradeep Ram *et al.*,

2013). In the euphotic zone of 19 freshwater lakes (French Massif Central), the temporal shift in viral life strategy was controlled by the availability of phosphate and chlorophyll concentrations (thus, influencing prokaryotic growth): high concentrations (stimulating growth) favoured lytic cycles and low concentrations (causing low growth) favoured lysogenic cycles (Pradeep Ram *et al.*, 2014). In natural environments without bloom episodes, viral lysis could account for approximately 20–40% of the daily loss of bacterial biomass in surface waters of oceans (Suttle, 1994), although a range of 0 up to 100% has been reported (Wilhelm and Matterson, 2008; Danovaro *et al.*, 2010).

Viral infection of phytoplankton and virus-mediated population control has been studied extensively in the past two-to-three decades (Brussaard 2004). A recent interesting finding indicates that *Microcystis* cyanophages infection occurs in a diel cycle, which may depend on the light cycle (as previously proposed by Suttle, 2000) (Kimura *et al.*, 2012). Diel cycles of lysis have also been demonstrated in bacterioplankton (Winter *et al.*, 2004).

Population dynamics and diversity

The temporal dynamics of virus and host populations have often been studied by investigating potential correlation patterns in culture model systems (e.g. Marston and Salée, 2003; Clasen *et al.*, 2013) or in the environment (e.g. Mühling *et al.*, 2005; Sandaa *et al.*, 2008; De Corte *et al.*, 2010; 2012; Zhong *et al.*, 2013). The approach of seeking potential correlation patterns has provided some robust results in culture model systems and has been used to test ecological hypotheses. The most frequently used model system to examine the outcome of virus–host interactions has been *Synechococcus* and associated cyanomyoviruses. By monitoring the temporal dynamics between *Synechoccocus* and cyanomyoviruses, studies have shown that the abundance of the two communities are coupled, suggesting bloom-bust patterns occurring over a time scale of days to weeks (Marston and Salée, 2003; Clasen *et al.*, 2013). Using the same model system, a rapid diversification of the *Synechococcus* host (Marston *et al.*, 2013) and its co-occurring viruses (Marston and Amrich, 2009) has been demonstrated. By using the qPCR approach to quantify cyanomyoviruses and FCM to enumerate the picocyanobacteria, Sandaa and Larsen (2006) detected a coupling between the two communities in Norwegian costal seawater across a year-long cycle, which suggests viral control over cyanobacterial abundances. In contrast, only weak (or lack of) correlations could be detected in the oligomesotrophic Lake Bourget (Lake Bourget) and [83] the oligotrophic Lake Annecy (Zhong *et al.*, 2013), except for the spring period in Lake Bourget, where the relationship between the two communities was obvious.

Other methods have included fingerprinting (e.g. T-RFLP, DGGE, RAPD) in studies between T4-like viruses and their bacterial hosts (Chow and Fuhrman, 2012; Needham *et al.*, 2013; Pagarette *et al.*, 2013; Zhong *et al.*, 2014; De Corte *et al.*, 2010, 2012; Chow *et al.*, 2013). The T4-like myoviruses have been shown to exhibit seasonal dynamics and inter-annual recurrence from the examination of monthly samples over a two- to three-year study period (Chow and Fuhrman, 2012; Pagarette *et al.*, 2013; Chow *et al.*, 2013). Some phylotypes displayed boom–bust patterns, abundance oscillation, or persistence that could be related to shifts in either environmental parameters or host dynamics. In Norwegian coastal seawater, the dynamic pattern of total *Synechococcus* cyanobacterial communities could be related to several OTUs of T4-like virus, which dominated the myoviral community and whose importance differed with time (Pagarette *et al.*, 2013). Needham *et al.* (2013) worked on samples taken daily over a time series of 78 days and examined at the same time the community structure of bacteria using RISA. They found a connection between myoviruses and potential hosts (i.e. OTUs from *Actinobacterium*, *cyanobacterium*, and members of SAR11 and SAR 86) over the scale of days. Furthermore, Chow *et al.* (2013) analysed the protist community using primers targeting the 18S RNA gene. They found that (i) virus–bacteria relationships were more cross-linked than protist–bacteria relationships in network association analysis (using Cytoscape), suggestive of an increased taxonomic specificity in virus–bacteria relationships, and (ii) bacteria–virus relationships showed a stronger positive correlation than bacteria–protist relationships on a monthly and seasonal scale. This in turn is suggestive of a more important viral role in controlling bacterial abundance in the ocean than protistan grazing. Winter *et al.* (2010) could demonstrate a co-variation of viral and

prokaryotic community structure over a seasonal scale in the deep sea.

A few studies have provided experimental evidence that viruses can affect microbial community composition (Weinbauer and Höfle, 1998; Suttle *et al.*, 1990; Winter *et al.*, 2004; Hewson and Fuhrman, 2006; Sandaa *et al.*, 2009). For instance, increasing viral concentrations through the addition of viral concentrates induced changes in the composition of marine primary producers including cyanobacteria (Suttle *et al.*, 1990). Incubating a freshwater bacterial community with and without the viral community from the same sample, Weinbauer and Höfle (1998) detected changes in abundance and growth rate of bacterial populations as well as in the community composition. Meunier and Jacquet (2015) recently reached the same conclusion by artificially increasing or decreasing viral concentrations in lake samples. The virus-mediated host community structuring could be due to the direct lysis of specific host species. Weinbauer and Rassoulzadegan (2004) suggested that the mass release of cellular materials during cell lysis could also change the composition and bioavailability of organic materials and nutrients and thus change of the microbial community. Both quantity and composition of the material released by viral lysis affects microbial community (Suttle, 2007). Evidence has shown that cellular material released by viral lysis can indeed affect bacterial community composition (Riemann *et al.*, 2009; Holmfeldt *et al.*, 2010).

Virus–host coevolution

Using a *Synechococcus* and cyanomyoviruses model system to examine the outcome of virus–host interactions, a significant diversification in *Synechococcus* (Marston *et al.*, 2013) and its co-occurring viruses (Marston and Amrich, 2009) has been demonstrated, suggesting coevolution, that is, changes and counter changes in the genetic make up of host and viruses. Marston and Amrich (2009) revealed a significant diversity of cyanomyovriuses within a single *Synechococcus* strain, observing that viral isolates shared an average nucleotide identity of 99.3–99.8% after examining different myoviral maker genes. This diversity was believed to have been generated by point mutations, homologous recombination within a host strain, and intragenic recombination between different cyanomyovirus strains. Microdiversity among closely related viral isolates has the potential to influence the population dynamics of viruses and hosts (Marston and Amrich, 2009), and could influence overall rates of infection and viral-induced host mortality (Wilmes *et al.*, 2009). These results indicate that coevolution (in virus–hosts co-incubation) may contribute to the generation and maintenance of *Synechococcus* and viral diversity and thereby influence virus-mediated mortality of these key marine bacteria (Marston *et al.*, 2013). Thus, virus–host interactions can generate and maintain diversity within host and viral populations by exerting selective pressure on the host for viral resistance and on the virus to overcome host resistance (Andersson and Banfield, 2008; Wilmes *et al.*, 2009).

Recently, Sun *et al.* (2012) exposed a host (*Streptococcus thermophilus* DGCC7710) to a phage (phage 2972) to which the host had no resistance. After 1 week of co-culture, they examined the genomes of both viruses and host. They found newly incorporated CRISPR spacers in *S. thermophilus* DGCC7710 and recently acquired single nucleotide polymorphisms (SNPs) in phage 2972. These spacers were variable short regions in CRISPR loci, which were originally acquired from a virus and thus conferred to the host as a means of resistance to viral infection through the CRISPR-Cas immune system. Sun *et al.* (2012) suggested that the acquisition of immune elements (spacers) following phage exposure led to a genetically diverse population with multiple subdominant strain lineages. They also suggested that CRISPR-based virus-resistance can be associated with major resistance-linked viral diversity purging events that can re-direct evolutionary trajectories of both host and phage populations.

Indirect and unexpected interactions

Phage–host interactions can also have indirect as well as unexpected and even surprising effects on the food web (Miki and Jacquet, 2008). This was initially found to be the case when it was shown that viruses can potentially stimulate primary production, counteracting mortality due to grazing to the point of tipping the status of a phytoplankton population from declining numbers to growth (Staniewski and Short, 2014). It has also been shown that *Synechococcus* growth is probably dependent on regenerated nutrients, following the

lysis of heterotrophic bacteria (Weinbauer *et al.* 2011).

Grazing has been reported to stimulate viral infection of bacterioplankton (Weinbauer *et al.*, 2003, 2007; Jacquet *et al.*, 2007), although it should lower infection rates since it competes with viruses for prey (e.g. microbial cells) and grazers probably consume infected cells (Simek *et al.*, 2001). The virus-mediated effects in the upper levels of the food chain (grazing food chain; Fig. 6.1) may be variable. One example is preferential grazing by the heterotrophic dinoflagellate *Oxyrrhis marina* on virus-infected *Emiliania huxleyi* (Evans and Wilson, 2008). In this experimental study, grazing rates of *O. marina* were observed to increase in the presence of virus-infected *E. huxleyi* prey. On a large scale this would direct more carbon, nitrogen, and phosphorus into particulate forms, making it available via grazing to higher trophic levels (see Fig. 6.1). Another experimental study has provided evidence of an indirect impact of bacteriophages on bloom-forming microalgae via phage-induced lysis of algae-killing bacteria (Cai *et al.*, 2011). In this study, a lytic phage isolated from an algicidal bacterium that specifically kills the toxic dinoflagellate, *Alexandrium tamarense*, was observed to trigger algal growth by reducing the abundance of the bacterium and hence reducing the algicidal effect.

Virus-induced effects cascading up the food chain can have even more unexpected results. In a recent field study, cyanophages were shown to affect an African flamingo population in a bottom-up cascade, i.e. from the base to the top of the food web (Peduzzi *et al.*, 2014). In the alkaline-saline Lake Nakuru (Kenya), an important feeding site of the Lesser Flamingo (*Phoeniconaias minor*), cyanophage infection led to a breakdown of the main food source, the cyanobacterium *Arthrospira fusiformis*. This resulted in a dramatic reduction in flamingo abundance, indicating that viral infection at the very base of a food chain can affect the distribution of end consumers.

These different examples raise the question of how aquatic ecosystems would even function were they free of viruses. One scenario would be that primary production would slow down, resulting in much less photosynthesis and thus much less oxygen production. Hence, there is the hypothesis (see also 'General aspects of aquatic viral ecology') that viral lysis overall promotes nutrient cycling, production, and diversity in aquatic systems.

Interactions with environmental factors

In this section we focus on interactions between viruses and the physicochemical environment, including parameters of climate change, such as global warming and ocean acidification.

Interactions with dissolved organic matter

As discussed above, in planktonic food webs viral lysis products are shunted away from the grazing food chain and the microbial loop (referred to as the 'viral shunt'; Wilhelm and Suttle, 1999). Viral lysis products can be efficiently utilized by heterotrophic prokaryotes, thereby again entering the food web. The net effect is that lysis detours bacterial production away from higher trophic levels such as protists and ultimately converts organic matter into inorganic nutrients (Wilhelm and Suttle, 1999; Haaber and Middelboe, 2009; Pollard and Ducklow, 2011). Recent culture-based experiments with marine microorganisms showed that phage infection alters both host metabolism and lysate composition (Ankrah *et al.*, 2013; Sheik *et al.*, 2014). In the Northern Baltic Sea, virus-mediated cell lysates accounted for a substantial fraction of the bacterial carbon and phosphorus demand (Holmfeldt *et al.*, 2010).

The release and consumption of D-amino acids, whose origin is attributed mainly to the remains of bacterial peptidoglycan, is also anticipated to be a result of viral lysis (e.g. Azúa *et al.*, 2014). Another study also suggests the rapid use of viral lysis products after relieving phosphorus limitation (Motegi *et al.*, 2015). In an experimental study by across marine environments, the decrease of bacterial growth efficiency was explained by virus-induced conversion of bacterial biomass into dissolved organic carbon (Motegi *et al.*, 2009). More experiments with seawater cultures and the addition of monomeric and polymeric substrates revealed that bacterial communities grown under substrate-rich conditions are less subject to viral attacks, thus supporting the notion that supplies of dissolved organic matter affect the magnitude of bacteria-virus coupling in marine environments

(Motegi and Nagata, 2009; Motegi *et al.*, 2015). An increase of respiration by viral lysis of bacteria, hence a stronger conversion of DOC into CO2, was also reported for the Australian Bremer River (Pollard and Ducklow 2011). A previous article has already provided an overview of other significant studies on this virus-DOM coupling (Jacquet *et al.*, 2010). Nevertheless, comprehensive studies on the significance of the viral shunt in aquatic systems are strikingly scarce, particularly for flowing inland waters (Peduzzi and Luef, 2008; Peduzzi, 2015).

Interactions with particulate organic matter

The viral ecology of organic and inorganic particles in aquatic systems has been previously comprehensively reviewed (Weinbauer *et al.* 2009). Some important conclusions from that review and new information are included in the following compilation. Quality, size and age of particles and aggregates as well as the exposure time of viruses to aggregates apparently are the most important factors regulating viral abundance (Kernegger *et al.*, 2009). Importantly, particles (mainly with organic constituents) appear to play a role as viral scavengers or reservoirs rather than viral factories (Weinbauer *et al.* 2009; Peduzzi 2015). Moreover, adsorption of viruses to suspended matter can stimulate the growth of the free-living prokaryotic community, e.g. by reducing viral lysis by displacement of viruses to the particulate (attached) fraction (Peduzzi and Luef, 2008; Weinbauer *et al.*, 2009, 2012). In addition, inorganic particles, such as clay and calcite, as another type of suspended matter, can also remove free-living viral particles in aquatic environments (Clasen *et al.*, 2008; Brussaard, 2004). In an Amazonian floodplain lake, flood pulses and the resulting turbidity were found to affect viral and host abundance (Barros *et al.*, 2010). Streams and rivers are often particle-rich environments, which create microscale patchiness for microorganisms. It has been estimated that up to 35% of the viruses are associated with suspended matter in water of the Danube River (Luef *et al.*, 2007; 2009). The generation of more comprehensive studies has been hampered by the complicated techniques required to reasonably enumerate particle-associated viruses (see Peduzzi, 2015). Moreover, it remains unclear to what extent viruses are truly attached to the matrix of the particles or distributed in the pore water of suspended matter and aggregates (Weinbauer *et al.*, 2009).

A specific type of suspended particle is black carbon (soot), which has both anthropogenic and non-anthropogenic origins (Weinbauer *et al.*, 2012). Significant amounts of this material, originating from the incomplete combustion of biomass and fossil fuels, enter aquatic systems via atmospheric deposition; river-runoff can transport significant amounts of this material into the ocean (and into lakes). Black carbon strongly absorbs both organic carbon and microorganisms. In experiments, addition of black carbon to seawater resulted in immediate (20–30 min) adsorption of 10–20% of the bacterial and viral abundance (Weinbauer *et al.*, 2012; Cattaneo *et al.*, 2010). A higher percentage of viruses, when compared to bacteria, were found attached to these particles, suggesting a negative effect on overall viral biomass. The experimentally observed increased bacterial production after black carbon addition could, to some extent, be due to lowered bacterial mortality stemming from reduced viral lysis (Weinbauer *et al.*, 2012). This has also been demonstrated in experiments (Malits *et al.*, 2015). Embedding bacteria into the matrix of black carbon, however, could also cause reduced infection, e.g. by 'hiding' receptors (Cattaneo *et al.*, 2010).

Viruses can also influence the formation of organic aggregates. For example, viral lysis of bacterio- and phyto-plankton may influence the formation process and stability of algal flocs (Weinbauer *et al.*, 2009). In an experimental study, the formation of fewer but larger suspended aggregates was shown to result from elevated abundances of viruses (Peduzzi and Weinbauer, 1993). The export of such diatom-derived material into the deep sea has been termed 'viral shuttle' and could be an import viral role in the ocean besides the viral shunt which rather enhances nutrient recycling (Sullivan *et al.*, 2017). A more recent experimental study reported that significant changes in the particle size distribution occurred primarily within the size range of relatively large particles (> 4 μm), likely as a result of the aggregation of smaller-sized particles originating from host microbial lysis. In a marine spring phytoplankton bloom experiment, organic micro-aggregates with attached prokaryotes were observed to form under turbulent conditions, but seemed to be reduced in the presence of viruses.

This suggests that turbulence and viruses play a significant, previously neglected role in shaping particle aggregation (Maltis and Weinbauer, 2009). Viral lysis of bacteria and subsequent particle dynamics generated large variations in the particle size distribution over a broad size range on timescales from hours to a few days (Uitz *et al.*, 2010).

Overall, aggregates are more scavengers of viruses than sites of release of viruses into the water surrounding the particles (Weinbauer *et al.*, 2009). There are also examples, however, where aggregates serve as viral factories rather than as viral traps (Bettarel *et al.*, 2015). During aggregation, virus-trapping could predominate, while during dissolution, virus-release could become more dominant. Also, whether aggregates are already saturated with viruses (either from attachment or viral production within the particle), will influence the net outcome between trapping and release.

Finally, attached viruses can be transported with aggregates, either horizontally by floating particles or vertically by sinking particles (e.g. Weinbauer *et al.*, 2009). Viruses from sinking particles enter the sediments.

Physicochemical factors and climate change

Abiotic factors may impact viruses directly by causing viral decay, or indirectly by affecting host growth or physiology, thus affecting viral production rates. The influence of different physical factors in the environment, such as temperature, oxygen, light availability or salinity has been investigated (Weinbauer, 2004; Brussaard, 2004; Cissoko *et al.*, 2008; Bettarel *et al.*, 2011). An interesting experimental study regarding the mixing of freshwater and seawater in estuaries demonstrated that production rates of freshwater viruses sharply declined after seawater addition, followed by a rapid (within 48 h) recovery of viral populations. Conversely, marine viruses were not significantly affected by mixing with freshwater (Cissoko *et al.*, 2008). It is assumed that viruses can rapidly respond to dramatic shifts in the abundance of bacterial hosts and community composition, and that these hosts may suffer from osmotic shock (Bonilla *et al.* 2009).

A study on the effect of oxygen on microbial and viral populations was conducted in a deep productive freshwater reservoir by Pradeep Ram *et al.* (2009). The frequency of infected bacterial cells was found to be lower in the anoxic (no oxygen present) than in the oxic zone (saturated with oxygen), caused by forcing from thermal stratification. On average, viruses were responsible for 23% loss of bacterial production in the oxygenated surface waters, but only for 9% in deep anoxic waters. In this study the viral influence on heterotrophic bacteria in the anoxic zone was remarkably low compared to other studies (Pradeep Ram *et al.*, 2009). Another study dealt with the viral community structure in the Eastern Tropical South Pacific oxygen minimum zone (Cassman *et al.*, 2012). The virus-to-microbe ratio fluctuated in the oxycline and declined in the anoxic zone to less than one. The number of viral genotypes declined from 2040 at the surface to 98 in the oxycline; only <5% of genotypes were shared between surface and anoxic core viromes. Thus, the viral community was characterized by fluctuations in abundance, taxa and diversity across the oxygen gradient, and it appeared that the reduction in oxygen coincided with a shift to unique viral genotypes in the anoxic core.

Another important physical factor influencing microbial processes is light. Some viral infections of phytoplankton in the ocean have been found to prevent a shutdown of photosynthesis by the host, e.g. as defence mechanism, in infected cells and allow it to continue and provide the energy needed for virus replication (Mann *et al.*, 2003). Other studies have demonstrated that viruses themselves are sensitive to UV-radiation (Suttle and Chen, 1992). Along a salinity gradient near the Pearl River estuary (South China Sea), viral decay rates were found to be significantly correlated with the UVA diffuse attenuation coefficient. UV-radiation increased the viral decay rates by ca. 30%, which decreased bacterial mortality, thus mitigating the inhibitory effects of UV-radiation on bacteria (Yuan *et al.*, 2011).

In flowing waters, environmental variability is especially large and clearly driven by the dynamic hydrology (Peduzzi, 2015). The high degree of spatial heterogeneity in such systems, e.g. backwaters with often lake conditions, also plays a role (Peduzzi and Luef, 2008; 2009; Jacquet *et al.*, 2010; Ma *et al.*, 2013). For example, in a river–floodplain system of the Danube and in an Amazonian floodplain lake, viruses, together with their microbial hosts, were found to be influenced in a complex manner by turbidity and hydrodynamics (Peduzzi and Luef, 2008; Barros *et al.*, 2010).

The effect of global warming on viral and host communities was experimentally studied in microcosm experiments in two contrasting Arctic marine systems (Lara *et al.*, 2013). Viral numbers, bacterial abundance and overall system production increased significantly and influenced the lytic/lysogenic decision. This showed that increases in temperature stimulate heterotrophic microbial biomass and activity, and viral lysis contributes to the increase of the DOM pool in the water column. In the review of Danovaro *et al.* (2010) on the effect of climate change on marine viruses, it was concluded that there will likely be direct and indirect consequences on viruses, including cascading effects on biogeochemical cycles, food webs, and metabolic balance of the ocean. Discussing a range of case studies, evidence was found that marine viruses interact actively with current climate change and they are considered to be a key biotic component able to influence the oceans' feedback on climate change. The limited number of data prevents incorporation of virus-related processes into current climate models on the necessary spatial and temporal scales at which climate change scenarios would respond and interact with this important compartment of the biosphere. This calls for focused research priorities and long-term data sets to enhance our knowledge about the role of aquatic viruses in the present climate change scenario (Peduzzi, 2016).

Ocean acidification is mainly due to the uptake of anthropogenic CO_2 from the atmosphere. Although the effect on microorganisms has been questioned, clear evidence has been presented that there is an effect (Liu *et al.*, 2009; Weinbauer *et al.*, 2011c). Larsen *et al.* (2008) investigated, in a mesocosm study, the effect of elevated pCO_2 on the viral community composition using flow cytometry and showed that 'high-fluorescence viruses' were stimulated while the other viral groups were not altered. Clearly the abundance of EhV (viruses infecting *Emiliania huxleyi*) decreased at elevated pCO_2 (1050 µatm). This indicates changes in the viral community composition. Evidence for moderate effects of ocean acidification of viral abundance and dynamics has been presented for the EPOCA ocean acidification experiment in Svalbard (Brussaard, 2008). This is likely due to indirect effects such as changes in host composition and activity. So far, direct effects on viruses have not been investigated.

Virivory

Consumption of viruses in the course of grazing by protists has been demonstrated in only a restricted number of studies both from marine (Suttle and Chen, 1992; Gonzales and Suttle, 1993) and fresh waters (Manage *et al.*, 2002; Bettarel *et al.*, 2005). There is no doubt that bacteria are the principal constituent in the diet of heterotrophic nanoflagellates (HNF) in most or all aquatic ecosystems (Sanders *et al.*, 1992; Sherr and Sherr, 1994; Pernthaler 2005) but, on some occasions, viruses also can contribute to HNF nutrition or at least flagellates could be responsible for part of the decay of viral particles. Indeed, protozoa may benefit from grazing on viruses by (1) removing viruses as competitors with protozoa for bacteria and (2) obtaining additional nutrients from viruses, although the nutrient content of viruses in and of itself would be insufficient for protozoa to persist.

New and poorly studied environments or viral groups

Benthic and anoxic environments

The largest benthic ecosystem on earth, the deep-sea benthos, has revealed extremely high viral production worldwide (Danovaro *et al.*, 2008). These authors reported that viral infections can be responsible for the abatement of up to 80% of prokaryotic heterotrophic production, and they also observed a virus-induced prokaryotic mortality increasing along with depth. Beneath a depth of 1000 m, viral lysis is by far the most important mortality factor of the benthic prokaryotic heterotrophic production, indicating the important role of viral lysis in global biogeochemical cycles. This is supported by more recent evidence regarding ongoing production of viruses in deep subsurface sediments (Engelhardt *et al.*, 2013). Within a comprehensive set of globally distributed subsurface sediments (some core samples more than 300 metres below surface; mbsf), enormous numbers of viruses (up to 10^9 per ml) indicated their potential as a controlling factor for prokaryotic mortality in the marine deep biosphere. Even in the oldest sediments, microbial communities were suggested to be capable of maintaining viral populations, indicative of an ongoing viral production. Thus, viruses

are likely independent indicators for microbial life in the marine deep biosphere.

The morphological diversity and community structure of benthic viruses of a deep, permanently anoxic freshwater lake revealed unique and novel putative viruses (Borrel *et al.*, 2012). Communities at the surface (–10 cm) could be discriminated from those at intermediate depths (–27 cm) or deeper (–40 cm) layers. Unusual morphotypes, new in freshwater systems, were detected, some of them resembling dsDNA viruses of hyperthermophilic and hyperhalophilic Archaea. Also, oxygen-reduced zones of the water column appear to harbour specific viral communities. For example, associated with the Eastern Tropical South Pacific oxygen minimum zone, the number of genotypes ranged from 2040 at the surface to only 98 in the oxycline (Cassman *et al.*, 2012). Within the oxygen minimum zone viromes, only 4.95% of genotypes were shared between surface and anoxic viromes. From the sampled DNA sequences within the oxygen minimum zone, more than 97.8% were novel. In this study, the viral community of the oxygen minimum zone was characterized by fluctuations in abundance, taxa and diversity across the oxygen gradient, displaying a shift to unique viral genotypes in the anoxic layer.

The atmosphere and aquatic environments

An unexplored ecosystem is the atmosphere, which is probably the 'last frontier of biological exploration on earth' (Rothschild and Mancinelli, 2001), together with the deep biosphere. Due to the few reports available, it remains unclear what fraction of the virus-like particles are microbial viruses. In a study conducted on air-samples collected from Korea, authors reported viral numbers ranging between 1.7×10^6 and $4.0 \times 10^7/m^3$ (Whon *et al.* 2012). Genomic analysis suggested that the majority of the collected viral particles were plant and animal viruses, although sequences belonging to *Inoviridae* and *Microviridae* were also found (see Chapter 7). Another study on the Caribbean atmosphere on St. John Island (Virgin Islands, USA) enumerated 18.1 to 213/m^3 VLPs during clear weather conditions and following an African desert dust-event, respectively (Griffin *et al.* 2001).

Given the high abundance of microorganisms in the euphotic zone of oceans, one would expect that aerosolization transports viruses into the atmosphere with microbes that migrate with winds and rains. In fact, viruses infecting the phytoplankton species *Emiliania huxleyi* (e.g. EhVs) can spread through the air, leading to widespread algal die-offs. Sharoni *et al.* (2015) showed, indeed, that EhVs can be conveyed long distances and transmit infection to the remote locations of coccolithophore blooms. Aquatic environments can therefore be a source of viruses (and microorganisms) of the atmosphere and conversely they can be deposited from the atmosphere into aquatic environments. Hence, the investigation of the atmosphere is likely to be of major interest, in some cases, towards better understanding of host-virus dynamics and/or the distribution and traffic of some microorganisms around the globe.

Concepts and models

Lytic viruses are believed to have consequences on at least two ecologically relevant levels. One is related to viral effects on diversity and population/community structure and dynamics. The other is related to the biogeochemical consequences of diverting the flux of energy and material away from the predatory transport towards higher trophic levels. This energy and material instead is returned to non-organism aspects of environments as small particles and dissolved organic material via the viral shunt (Fig. 6.1), or instead these biogeochemical processes influence the export of organic matter into the deep sea (biological pump).

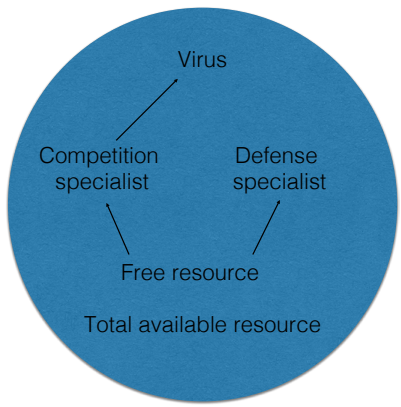
Viral control of host diversity

Several concepts have been introduced in attempts to capture essential aspects of host–virus interactions. Included in such a collection are the concepts of 'Red Queen dynamics' (Clarke *et al.*, 1994), 'Killing the winner' (KtW) (Thingstad and Lignell, 1997; Thingstad, 2000), 'Seed bank' (Breitbart and Rohwer, 2005), 'The king of the mountain' (Giovannoni *et al.*, 2013) and also 'The Cheshire cat escape strategy' (Frada *et al.*, 2008). These concepts [84] emphasize different aspects of host–virus interactions such as the potential for rapid antagonistic coevolution, the coexistence of hosts with competition versus defence strategies, and existence of a background reservoir from which dominating viruses can be selected. Although all these aspects

are likely to be present, it has proven to be remarkably difficult to obtain solid experimental evidence needed to transform many of these concepts from their status as ideas into quantitative working tools for virus ecology. This is the case even when worked out in a mathematical form such as KtW (Winter *et al.*, 2010).

The KtW concept was, in its original form, based on steady-state arguments (e.g. Thingstad, 2000) where the 'winner' (competition specialist) is the best competitor for nutrients or DOM that would 'win' in the absence of a selective loss such as from viral lysis. In the latter case, the defence (against viruses) strategist can 'win' (Fig. 6.2). The use of the KtW concept is somewhat confused as it is applied in both a dynamic version (e.g. Avrani *et al.*, 2016) and in its original steady-state (e.g. Thingstad, 2000) version. The conceptual difference is important since the 'winner' in the dynamic version is the most abundant host, killed by viruses and then replaced by another 'winner' host. In the steady-state version it is the fastest growing host, i.e. the one that would become dominating if its abundance was not controlled by lytic viruses.

Pagarete *et al.* (2013) recently used a dynamic version to explain boom–bust patterns in microbial populations and/or viruses in nature when there is no massive bloom. Here KtW was used to describe successive waves of competitively successful microbes (fast growing), which are decimated by viral infection and then replaced by defence specialists, fostering a dynamic and diverse system.



[92] **Figure 6.2** Schematic of the general structure of the 'killing-the-winner' hypothesis. Redrawn from Winter *et al*. (2010).

This fits quite well with the seed-bank hypothesis (Breitbarts and Rohwer, 2005) stating that (i) only a few members of viruses may be abundant at any given time, most of them being rather rare and forming a potential bank-population for recruitment; and (ii) viruses preying on their hosts move from the bank to the active fraction through viral production, and the previously abundant and active fraction enter back into the bank, thereby resulting in a change of the dominant types of microbial species. Recently, such dynamics and concepts were also applied for ssDNA viruses inhabiting alpine lakes (Zhong *et al.*, 2015).

The basis for both versions of KtW is that the lytic action of viruses depends largely on the probability of contact with the host (Fuhrman, 1999; 2009). In the dynamic version this makes the most abundant hosts most vulnerable. In the steady-state version, host-abundances are constrained by the steady-state requirement for their viruses: For a virus population to persist, its host population must be abundant enough to allow on average one of the viruses released per cell in a lytic event to find and successfully infect a new host before it is destroyed. Viral abundance on the other hand is constrained by the steady state requirement for the host, i.e.; hosts must divide as fast as the sum of their losses, usually assumed to be the sum of grazing and viral lysis. Since loss to viral lysis can increase with viral abundance, this links viral abundance to host activity (as in steady-state higher infection rates have to be balanced by faster host growth), rather than to host abundance. This means that the apparently plausible inference that abundant viruses belong to abundant hosts is not necessarily true. The original steady-state KtW (Thingstad and Lignell, 1997; Thingstad, 2000), has recently been refined by introducing trade-offs between competition and defence (Våge *et al.*, 2013) and strain-specificity of viruses (Thingstad *et al.*, 2014).

The introduction of a trade-off between competition and defence links the growth and loss sides for the host. As an increased defence means a reduction in the probability that a host–virus collision will lead to a successful infection, the consequence is that in steady-state conditions a higher host population is needed for defence strategists to sustain a viral population. KtW models with trade-off thus predict slow-growing defence strategists to be dominant. Experimentally reducing viral abundance in

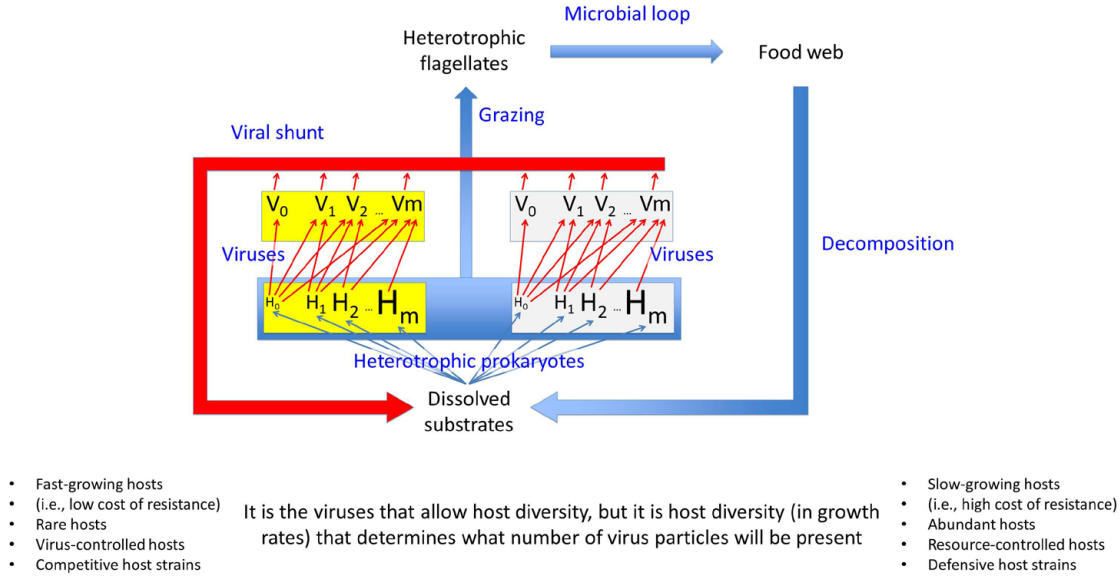
such a system would lead to positive net growth in rarer but faster-growing, otherwise virus-controlled parts of the community, while little effect would be expected in the dominant, virus-resistant part. This is seemingly consistent with experiments where previously rare host species have been observed to become dominant when viral abundance is reduced (Bouvier and delGiorgio, 2007; Cram *et al.*, 2016).

Another intriguing perspective following from this line of reasoning is that dormancy, i.e. the high proportion of low-activity cells of heterotrophic prokaryotes found in aquatic systems (e.g. Malmstrom *et al.*, 2004) could be a consequence of the need for cost-expensive defence, rather than a sign of lack of suitable nutrients. Dominance of low-activity individuals in the prokaryotic community should thus perhaps be seen more as a consequence of 'having closed the gates to keep the enemy out' rather than a result of 'there is no food out there' (Thingstad *et al.*, 2014).

Attempts to compare the KtW with experimental data have assumed that host groups would correspond to data with a resolution at 16S rDNA level, i.e. data that resolve the host community to a kind of species-level. Repeated isolation of individuals of a prokaryote 'species' from the same environment has, however, led to the concept of a core genome characterizing the 'species', but with other genomic regions being highly variable between strains. These variable regions have been suggested to play a central role in viral defence (Rodriguez-Valera *et al.*, 2009). A related discovery is how host–virus interaction matrices for isolates from natural environments can be reshuffled to reveal a nested structure (Jover *et al.*, 2013). Since arms-race dynamics are likely to lead to nested interaction matrices (Thingstad *et al.*, 2014; Haerter *et al.*, 2014), the different lines of experimental evidence converge to suggest that prokaryote population dynamics in natural systems is a blend of two fundamentally different types of dynamics: A traditional ecological dynamic, where species invade, compete and are grazed or lysed, and an evolutionary arms-race dynamics, where each host species develop successively defensive strains.

Interestingly, the incorporation of such a concept of strain diversification into a KtW-model can explains the apparent paradox suggested by Weinbauer (2004). The paradox is that in simple laboratory co-cultures of viruses and prokaryotic hosts, the cultures rapidly become dominated by resistant hosts and have a low virus-to-host ratio, while natural seem to have high virus-to-host ratios, i.e. viral abundance is higher than host abundance. Using a model which includes strain diversification, the paradox disappears. In the chemostat analysis of Thingstad *et al.* (2014), the cost of resistance creates an accumulating difference in growth rates between the original, undefended strain, and new increasingly defensive, and therefore slower growing strains. In the chemostat, an immune strain has to grow with the dilution rate; a faster growing but susceptible strain has to have a virus population size large enough to grow at a rate which exceeds the dilution rate. In an early state of the arms race with a small cost of resistance (CoR), only a few virus types are therefore needed to maintain the chemostat equilibrium. As the arms race progresses and differences in growth rates increase, the steady state in the chemostat will be characterized by more and more viruses needed to balance the increasing difference in growth rates between hosts. The natural situation described in the 'Weinbauer paradox' (Thingstad *et al.*, 2014) is thus explained by this model as the mature state of such an arms race with a high virus to host ratio (see also Fig. 6.3).

The consequences of strain diversification, for viral control of prokaryote diversity, is quite profound. The original version of the KtW concept suggested a viral top-down control of the abundance of each 'species', where defensive ability would be the major factor determining abundance of individuals in each host species. With strain diversification, abundance within a species becomes the combined function of how many strains the species can establish and the abundance of individuals within each of these established strains. Since the establishment of strains is a competitive feature, and the abundance of individuals within a strain increases with defences, a species needs a low trade-off between competitive and defensive abilities in order to become abundant (Thingstad *et al.*, 2014). Developing a better conceptual understanding of these mechanisms is central to settling the debate of whether the bacterium SAR11 has become the world's probably most abundant organism due to its competitive or due to its defensive abilities, or perhaps due to its ability to combine the two (Zhao *et al.*, 2013).



[93] **Figure 6.3** Killing-the-winner model with strain-specific viruses. V, viruses; H, hosts; n, number of viral strains; m, number of host strains. In this model (adapted from Thingstad *et al*. 2016), prokaryote community size (blue box) is top-down controlled by grazing from heterotrophic flagellates shunting material through the microbial loop while each prokaryote species (yellow and violet) is split into strains through antagonistic host-virus arms races sending material through the viral loop. Host strains are arranged left to right from fast-growing non-defensive to slow-growing (high CoR) defensive within each species; virus strains from specialists to generalists. At steady state, the host community becomes dominated by defensive, slow growing strains. In this model, host diversity at species level becomes a function both of host competitive abilities (how many strains it can establish) and host defensive abilities (how many individuals there are per strain). Partitioning between the microbial and viral shunt depends on the difference in growth rate between strains within species and thus on CoR.

When both mechanisms, i.e. the price paid for an increase in resistance (CoR) and the ratio between the price paid and the competitive ability gained (trade-off), are incorporated into models, speculations on the consequences of the many different resistance mechanisms which have been described becomes more meaningful. For example, a modification of porin proteins, which are required for nutrient uptake, could lead to a large difference in CoR between successive host strains. In another example, a CRISPR-based defence system would require a high running and maintenance cost, that may be high at the species level; however, the price for adding new recognition sequences would be low and this could result in a low CoR for strain diversification.

Food web function

An obvious consequence of diverting energy and material into the viral shunt is that a smaller fraction of total primary production reaches higher trophic levels. This could lead to the conclusion that viral lysis in the microbial part of the food web should have a negative influence on production at higher trophic levels. However, there are two ways in which viruses could reduce this higher-level production, either by decreasing transport to higher levels (viral shunt, Fig. 6.1) or by increasing total primary production, since nutrient that are recycled could be used instead by phytoplankton. Therefore, part of the virus effect is an increase of the nutrient content in the photic zone, while another part is a reduction of the production at higher trophic levels and reduced export of organic material into the aphotic zone. How these two effects are balanced depends on factors such as where in the food chain export occurs, e.g. as sinking aggregates originating from phytoplankton debris or as faecal pellets from copepods. Another factor is how organisms are mixed between nutrient-rich and nutrient-poor water layers, such as by currents and turbulences or vertical migration of copepods. A recently published

model study (Weitz *et al.* 2015) contains such mixing effects and therefore predicts that viruses would reduce export (by reducing net import). Overall, the relative importance of the mechanisms with the viral shunt and the link to the « viral shuttle » is poorly constrained and likely also depends on factors such as season (phytoplankton bloom or not) and system productivity (oligotrophic vs eutrophic).

Biodiversity and ecosystem functioning

Issues involving viruses are usually only poorly discussed within the framework of ecological concepts developed for plants and animals. The combination of topics discussed in 'Viral control of host diversity' and 'Food web function' could constitute the basis for a mechanistic concept combining biodiversity with ecosystem functioning, thus linking the study of viral ecology to the different traditions of general BEF (biodiversity and ecosytem functioning) research (see, for example, Duffy, 2009 and references therein). For example, an experimental study with surface seawater and with different viral abundances indicates that bacterial host diversity is maximized when bacterial productivity and disturbance (virus infection/production) are balanced (Motegi *et al.*, 2013). Bacterial diversity was related in dome-shaped patterns to the ratio of viral-to-bacterial production, with highest bacterial diversity at intermediate ratios. Thus, bacterial production and virus-induced mortality may interactively affect bacterial diversity in seawater. These results are similar to patterns often found for studies on plants and animals (intermediate disturbance hypothesis) and suggest common patterns of diversity for viruses, microorganisms, plants and animals.

Conclusions

This review, on the accumulation of information on research of viruses in aquatic systems during the last decade(s), reveals – not unexpectedly – that the development of new techniques and the adaptation of existing techniques (see Chapter 15) has been a main driving force in this progress on viral research. Major advancement has been made in research on gene transfer, host resistance, population dynamics, and coevolution of viruses and hosts. Viral biodiversity has benefited enormously from the 'Omics' area. Metagenomics (see Chapter 5) has revealed that the diversity of viruses is larger than the diversity of cells in aquatic systems. This opens a new research avenue and quest, since the identity of the vast majority of this diversity (>> 90% of the sequences) remains unknown: both viruses and their hosts remain unidentified and the functions of obtained sequences remain obscure. Pioneer data on the metabolomics of isolated virus–hosts systems are available revealing exciting insights into virus–host interactions; the extension to the environment (*in situ*) and communities (community metabolomics) is a task for the years to come. [87]

Progress has also been made in other ways. Research during the last decades has resulted in the perception that viruses (and microorganisms) are much more tightly related and intertwined with (multi)cellular life, food webs and the inorganic environment than previously anticipated. Unexpected direct interactions such as viral predation on viruses (viriophages) and indirect interactions such as cascading trophic effects through the food web have been found. Considering the vast unknown diversity of viruses, one can expect that that the understanding of the biocomplexity of such interactions has only just begun. Many environments such as organic aggregates, anoxic waters and sediments or the interactions with the environment such as physicochemical influences on viral communities *in situ* or the effect of viruses on the cycling of nutrients and organic matter *in situ* remain poorly studied. [85]

Progress has also been made in our concepts on the role of viruses in food webs and biogeochemical cycles and this has resulted in improved models on the interactions of viruses with their hosts. While viral lysis can be detrimental at individual and population levels, viral infection seems now to be a key factor explaining how the large cellular diversity is sustained in aquatic systems and how geochemical cycles of elements such as C, N and P are controlled.

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[88]

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Part III

Diversity of Viruses of Microorganisms