

Impact of external forces on cyanophage–host interactions in aquatic ecosystems

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Abstract Cyanobacterial (algal) blooms have by convention been attributed to the excessive level of nutrients from pollution and runoff, which promotes the rapid growth and multiplication of cyanobacteria or algae. The cyanophage (virus) is the natural predator of cyanobacteria (the host). The aim of this review is to unveil certain pressures that disrupt cyanophage–host interactions and the formation of cyanobacterial blooms. This review focuses principally on the impact of greenhouse gases, ozone depletion, solar ultraviolet radiation (SUR) and the role of recently discovered virophages, which coexist with and in turn are the natural predator of phages. The key findings are that the increase in SUR, the mutation of cyanophages and cyanobacteria, along with changing nutrient levels, have combined with virophages to impede cyanophage–host interactions and the resultant viral infection and killing of the cyanobacterial cell, which is a necessary step in controlling cyanobacterial blooms. Consider this a ‘call to action’ for researchers interested in corrective action aimed at evolving aquatic ecosystems.

Keywords Aquatic ecosystems · Bacteriophage · Cyanobacteria · Cyanophage · Greenhouse gases · Harmful algae blooms · Ozone · UV · Virophage

Introduction

Cyanobacteria

Cyanobacteria, (known as blue-green algae, ‘BGA’) are strictly prokaryotes, or bacteria that obtain their energy through photosynthesis. These microorganisms are resilient predecessors of all higher oxygenic phototrophs, which use light as their main source of energy and can be found in self-sustaining, nitrogen-fixing communities the world over, from Antarctic glaciers to the Sahara desert (Whitton and Potts 2000). Throughout the terrestrial north and south Polar Regions, they form benthic mats and films at the bottom of lakes, ponds and streams (Schirrmeister et al. 2011). It has been determined that multiple interacting physical, chemical and biological factors lead to the formation of cyanobacterial harmful algal blooms (cyanoHABs) (Fristachi and Sinclair 2008).

Causes of cyanobacterial blooms

Cyanobacterial blooms occur when the cyanobacteria replicate faster than they are consumed by natural processes. Early research focused on the causal effect of nutrients from chemical pollution on cyanobacterial growth, whereas recent events suggest a more complex explanation must be considered.

The bloom, often many inches thick, usually floats to the surface, especially near the shoreline and in warm, slow-moving waters that are rich in nutrients from fertilizer runoff or septic tank overflows.

It was originally assumed that cyanobacteria required the high phosphorus (P) and nitrogen (N) concentrations in which they thrived. This assumption endured even though cyanobacterial blooms often occurred when concentrations

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of dissolved phosphate were quite low (Mur et al. 1999). A low ratio between N and P concentrations may in fact favour the development of cyanobacterial blooms (Mur et al. 1999). A comparison between the optimum N:P ratios for eukaryotic algae (16–23 molecules N:1 molecule of P) with the optimum rates for bloom-forming cyanobacteria (10–16 molecules N:1 molecule P), shows that the ratio is lower for cyanobacteria (Schreurs 1992). Cyanobacteria have been found to store enough phosphate to perform two to four cell divisions, which corresponds to a four- to 16-fold increase in biomass (Mur et al. 1999).

A variety of other nutrient sources such as iron, silica or carbon can also play an important role in affecting algal bloom formation. The iron-rich dust influx from large desert areas such as the Sahara is thereby also thought to play a role in causing harmful algal blooms (HABs) (Walsh et al. 2006).

In addition, the impact of zebra mussels has been reported to cause an increase in the biomass of cyanobacteria (Raikow et al. 2004). The recent discoveries regarding the effects of the invasion by dreissenid mussels *Dreissena polymorpha* and *Dreissena bugensis* on cyanoHABs in lakes with moderate nutrient levels suggest the need for a re-evaluation of the role of nutrient enrichment as the overarching driver of harmful phytoplankton blooms in freshwater systems (Raikow et al. 2004).

Economic and environmental impacts of cyanoHABs

CyanoHABs have been documented to impact water quality through production of compounds affecting taste and odor (Carmichael 2008). Selected species within about 40 genera can produce potent toxins that can cause chronic, acute or even lethal poisoning to wild or domestic animals as well as humans (Carmichael 2008).

CyanoHABs can have significant economic impacts due to human health threats along with their negative impact on aquaculture, recreation and tourism. The economic losses in the USA associated with HABs are estimated to exceed \$1 billion over the next several decades (Bushaw-Newton and Sellner 1999; Kalluri 2008).

Cyanophages

Bacteriophages (phages) are described as viruses that infect bacteria. The term ‘cyanophage’ describes the virus that infects ‘cyanobacteria’ (Fuhrman 1999; Suttle 2005). Cyanophages are typically DNA-containing viruses (Weinbauer and Wilhelm 2011). Most phages, at least in the surface ocean, belong to three phage groups of the tailed phages. Sequence analysis and isolation of viruses showed that some viruses have a cosmopolitan distribution, whereas others seem to have a more restricted geographical range (Weinbauer and Wilhelm 2011).

Cyanophages at work

It has been discovered that cyanophages behave differently under nutrient rich conditions than they do when starved of nutrients. Their behaviour may also be altered through the introduction of chemical treatments.

Phages have several potential replication cycles. The two most dominant are the lytic (virulent) and the lysogenic (temperate) cycles. The lytic cycle is typically considered the main method of viral (phage) nucleic acid replication and synthesis of virus encoded proteins resulting in the destruction of the infected cell and the release of newly-formed phages from the lysed (destroyed) host cell. The lysogenic cycle is the phenomenon in which a bacterium is infected by a temperate or dormant phage, the viral DNA is integrated in the chromosome, becoming a part of the host cell and replicated along with the host chromosome for many generations, coexisting as opposed to lysing the host cell (Todar 2012). Thus the bacterium acts as a carrier or host of the dormant virus that awaits the opportunity to be elevated to a lytic state.

In both cases the virus/phage replicates using the host DNA machinery, but in the lytic cycle, the phage is a separate molecule to the host DNA (Todar 2012). For prokaryotes in the ocean, it has been suggested that in nutrient-rich waters (characterized by a high abundance of hosts) lytic phages dominate, whereas in nutrient-poor waters lysogeny dominates (Weinbauer and Wilhelm 2011).

The isolation of the LPP-1 virus in 1963 has led to the first serious attempt to use disease-causing agents in controlling algal populations (Safferman 1973). This has opened an era of increased interest in the biological interactions underlying algal pathology.

Although the effect of cyanophages on the mortality of cyanobacterial communities is likely to be variable, current estimates suggest that cyanophages are responsible for the removal of approximately 3 % of marine *Synechococcus* on a daily basis (Whitton and Potts 2000) and about 1–3 % of marine *Synechococcus* spp. contained mature phages (Proctor and Fuhrman 1990). Others have estimated that cyanophages may be responsible for ca. 5–14 % of cyanobacterial mortality on a daily basis (Suttle and Chan 1994).

Fuhrman and Suttle (1993) and Suttle (1994) showed that up to 20 % of heterotrophic bacteria and up to 51 % of cyanobacteria are destroyed daily through viral lysis. While it has been difficult to obtain accurate in situ estimates of virus-induced host mortality (Suttle 2005), some studies report that viruses may be responsible for up to 70 % of the daily mortality of marine bacteria and phytoplankton (Proctor and Fuhrman 1990; Suttle et al. 1990; Wommack and Colwell 2000).

Attempts to induce lysis in lysogens after various physicochemical treatments were also reported (Bisen et al. 1986). During lytic infection, lysogenic associations were clearly demonstrated in filamentous and unicellular cyanobacteria but the ecological implications of lysogeny remain unexplored (Suttle 2000).

Cyanophages effect on the microbial food chain

Through the process of infecting and lysing their hosts, these viruses convert both macronutrients (P and N) as well as micronutrients (e.g., iron) from particulate forms to dissolved forms that are then available for actively growing phytoplankton and bacteria to consume (Suttle 2005; Weinbauer and Wilhelm 2011). This has the net effect of regenerating nutrients and maintaining biomass in the euphotic zone as otherwise matter and energy would be passed to higher trophic levels and lost from the food web via sinking (Fuhrman 1999).

Recently, Haaber and Middelboe (2009) reported that the degradation of *P. pouchetii* lysates was associated with significant regeneration of inorganic N and P resulting in $148 \mu\text{g N l}^{-1}$ and $7 \mu\text{g P l}^{-1}$, corresponding to 78 and 26 % of lysate N and P being mineralized to NH_4^+ and PO_4^{3-} respectively. Their results showed that the turnover of viral lysates in the microbial food web was associated with significant N and P mineralization, supporting the view that viral lysates can be an important source of inorganic nutrients in marine systems.

Using cyanophages to control cyanHABs

The keys to using cyanophages in the control of HABs lies in the understanding of the cyanophage–host interactions, the reactivation of dormant (lysogenic) viruses and the morphology of the cyanobacteria in aquatic ecosystems.

There are various biological methods and control strategies for HABs which have been identified and used in various parts of the world (Sigee et al. 1999; Foflonker 2009; Jassim et al. 2010) but it is not known the extent to which these can be applied to particular HAB species in specific environments or habitats (Drabkova and Marsalek 2007). Among these methods is the use of cyanophages which commonly occur in marine and freshwater aquatic environments (Suttle et al. 1990). They play an important role in determining the cyanobacteria during the season (Phlips et al. 1990; Suttle and Chan 1994; Sigee et al. 1999; Castberg et al. 2001) and they also replicate rapidly while tending to be host-specific.

The use of viruses to control cyanobacterial blooms was first reported by Safferman and Morris (1964). Viral infection has also been appreciated for its role in influencing the population dynamics of phytoplankton (Phlips

et al. 1990; Suttle and Chan 1994; Sigee et al. 1999; Suttle 2000; Castberg et al. 2001). The sudden decline of the cyanobacterial biomass accompanied by the cyanophage occurrence has also been reported in eutrophic lake water (Gons et al. 2002).

There are a few recent studies dealing with the possible control of cyanobacterial development by viruses (Tucker and Pollard 2005; Yoshida et al. 2006). There are however many problems that make the use of viruses difficult in practice. This is due to the rapid appearance of resistant host mutants (Cannon et al. 1976), changes in the cyanobacterial cell envelope that prevent phage adsorption (Padan et al. 1967) and the effect of environmental factors which all contribute to the complexity and unpredictability of cyanophage–cyanobacterial interactions in the field. Furthermore, the isolation and the cultivation of cyanophages from natural sources are time consuming and problematic for producing large amounts of active inoculums (Sigee et al. 1999).

The role of cyanophages in cyanobacterial populations

There is growing body of evidence pointing toward an important role for cyanophages in the dynamics of cyanobacterial populations. The studies of Phlips et al. (1990) and Castberg et al. (2001) involved using cyanophages to infect and kill four common bloom-forming species of cyanobacteria *Lyngbya birgei*, *Anabaena circinalis*, *Anabaena flosaquae*, and *Microcystis aeruginosa*. Nevertheless, the concept of using cyanophages in the control of cyanobacteria had not received widespread attention up to that point.

As previously stated, an important consideration in the potential use of cyanophages as biocontrol agents is the rapid appearance of phage-resistant mutants (Cannon et al. 1976; Waterbury and Valois 1993; Suttle and Chan 1994; Sigee et al. 1999). This is a natural phenomenon that always occurs in the bacteriophage biology (Stewart et al. 1995) and it was also reported that cyanophages are capable of entering into a lysogenic relationship with their hosts (Bisen et al. 1986). Moreover cyanophages are sometimes so obligate (host-specific) that they are often unable to infect different genetic strains of the same host species (Waterbury and Valois 1993). Even after the decline of a particular cyanobacterium by viruses, it can be easily replaced by other cyanobacterial species (Van Hannen et al. 1999).

A recent study concluded that resistance to co-occurring cyanophages has been reported for natural communities of *Synechococcus* spp.; however, little was known about the nature of this resistance (Stoddard et al. 2007) or the role of cyanophages to control cyanobacteria (Weinbauer and Rassoulzadegan 2004) especially in lakes (Tucker and Pollard 2005).

There is a need to consider factors that influence cyanophage attachment, infection, and lysis of their host, alongside the physical and chemical parameters that drive cyanobacterial growth and production (Tucker and Pollard 2005).

Effects of nutrients and external factors on the cyanophage–host interactions in aquatic ecosystems

Research has suggested that phosphate rich environments may provide a boost to the effectiveness of the viral infection cycle, thereby helping to consume cyanoHABs rather than simply causing them, as previously assumed. Two main factors appear to affect the level of cyanobacteria:

1. the heterogeneity of cyanobacterial population distributions (Anderson et al. 1993), and
2. the human activities being undertaken (HARRNESS 2005).

It is now accepted that human activity has a eutrophic effect on bodies of water, characterized by an abundant accumulation of nutrients that support a dense growth of cyanobacteria and other organisms, the decay of which provides more available nutrients to the food chain and yet depletes the shallow waters of oxygen.

It is noteworthy that the nutrient phosphate was found to have a peculiar chemical function within cyanophage nucleic acid. There are many reports which have clearly indicated that nutrient availability is responsible for the switch between lysogeny and lytic production in both marine and freshwater environments, where phosphate was also found responsible in cyanophage genotype disappearance (Wilson et al. 1996). In other words, whether a lytic cycle or lysogenic cycle is operated depends upon the nutritional status or the presence of any pathogenic condition to which the bacterium is susceptible (Singh et al. 2012).

As far as the replication of the DNA is concerned, the lytic phase relies on its own genes that are used for replication inside the host. These genes are accountable for the initiation of replication and may even include a new DNA polymerase (Singh et al. 2012). Cells raised in nutrient rich media have higher concentration of the host global regulator RNase III, which leads to elevated rates of expression of the protein N, favoring lytic growth (Wilson et al. 2002). In carbon-starved cells, on the other hand, RNase III and consequently N concentrations are low. Under these conditions N translation is repressed. This reduction of N concentration would reduce Q protein expression to a level that provides more opportunity for lysogenic response (Singh et al. 2012).

It was tentatively suggested that lysogenic viruses were induced to the lytic state following phosphate addition into the phosphate-limited enclosures. These results indicate that prophage induction may occasionally be phosphate limited or respond to increases in phosphate concentration, suggesting that phosphate concentration may modulate the lysogenic response of natural population (Williamson et al. 2002).

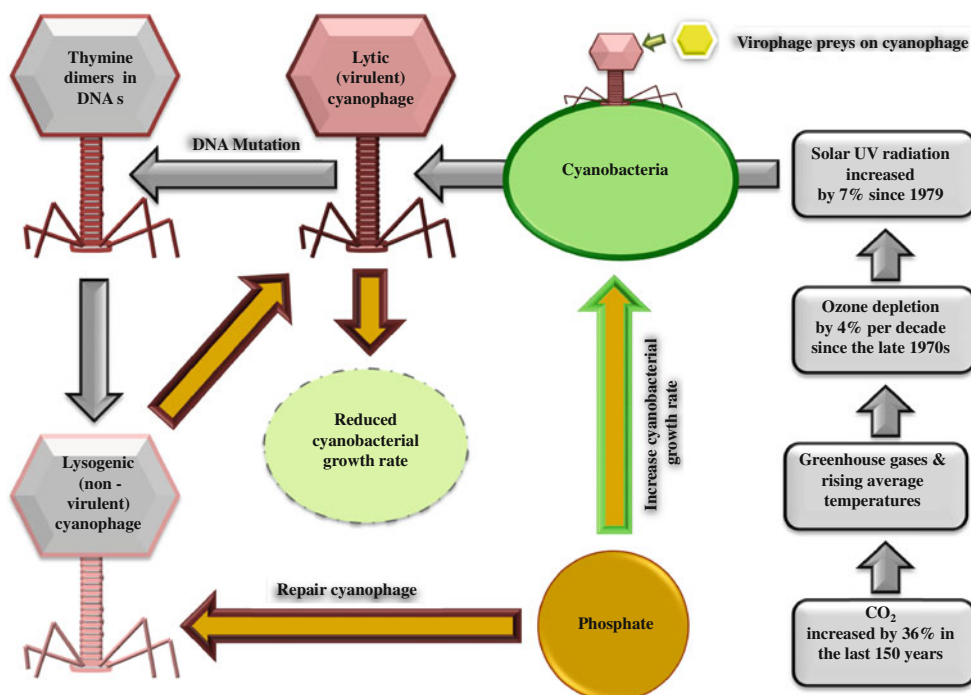
The results of Wilson et al. (1996) suggested that cyanophages established lysogeny in response to phosphate-depleted growth of host cells. They compared the proportion of infected cells that lysed under phosphate-replete and deplete conditions. This study revealed that only 9.3 % of phosphate-deplete infected cells lysed in contrast to 100 % of infected phosphate-replete cells.

The results of Gons et al. (2002) have also shown that a significant cyanobacterial lysis invariably occurred under nutrient replete conditions. It has been suggested that in nutrient-rich waters, lytic cyanophages dominate, whereas in nutrient-poor waters, lysogenic viruses dominate (Weinbauer and Wilhelm 2011). Similar results were also reported for T4 phage in which the phosphate has abolished the anti-phage activity of the platinum complexes (Pedersen et al. 1985). Obviously these data support the concept that the phosphate status of the cyanobacterial cell will have a profound effect on the eventual outcome of cyanophage–host interactions (Wilson et al. 1996).

Apparent from these findings, there is a contradiction which arises as follows: on one hand and according to conventional wisdom, an excessive level of phosphate in aquatic environments will promote the rapid growth and multiplication of cyanobacteria, causing the cyanoHAB. On the other hand, phosphate should also support the efficacy of the cyanophage infection in the cyanobacteria thus causing increased cyanobacterial lysis and the resultant release of newly-formed cyanophages (Fig. 1) to lyse (kill) an increasing number of cyanobacterial cells. This natural control cycle should contribute to the disappearance of the cyanobacterial bloom.

It is worth mentioning that lysogeny can also be induced to a lytic cycle by pollutants (Jiang and Paul 1988). It has also been reported that mitomycin C, and heavy metals such as copper and cadmium can induce the release of lytic cyanophages in marine water (Sode et al. 1997; Williamson et al. 2002; Lee et al. 2006). There is evidence to suggest that seasonal changes can also cause the prophage to enter a lytic cycle thus leading to the disappearance of cyanobacterial blooms (Gons et al. 2002; Williamson et al. 2002). The factors influencing lytic and lysogenic cyanophage infection in a natural microbial community include: depth of the water column, temperature, solar radiation, pH, cation (+ve ion) concentrations, salinity, seasonal variations and microbial community (Wommack and Colwell 2000; Ortmann et al. 2002; Singh et al. 2012).

Fig. 1 Abiotic and biotic factors that regulate cyanophage–cyanobacteria interactions and their influence on the mechanism of cyanobacterial growth and bloom formation in aquatic ecosystems



Several recent studies revealed that cyanophages dsDNA, infecting marine cyanobacteria, such as *Prochlorococcus* and *Synechococcus*, appeared to carry a much richer cache of metabolic genes than other phages like the pentose phosphate pathway (Millard et al. 2004) and phosphate acquisition (Sullivan et al. 2005). Such genes have been termed ‘auxiliary metabolic genes’ (Breitbart et al. 2007) because they are thought to provide supplemental support to the phage in key steps of host metabolism, thereby fostering a more successful infection.

From the study of Weinbauer and Wilhelm (2011), it appears that these cyanophage-encoded photosynthesis genes force the infected host cell to extend photosynthesis until shortly before cell lysis. They concluded that this likely increases the energy available within the infected cell, allowing a maximum number of new cyanophage particles to be produced. Thus, viruses interfere with host functions in a much more sophisticated way than previously thought. The latter conclusion suggests the strategy used by cyanophages for directing host metabolism and resulted from the analysis of cyanophage genome, as supported by the evidence (Suttle 2005).

The effect of solar ultraviolet radiation (SUR)

Cyanobacteria are the Earth’s oldest known oxygen-evolving photosynthetic microorganisms and they have had a major impact in shaping the earth’s atmosphere and biosphere. Their long evolutionary history has enabled cyanobacteria to evolve under anoxic conditions. They adapt well to environmental stress, including exposure to

SUR and temperature extremes, as well as scarce or abundant nutrients (Paul 2008). There is a synergy between nutrient loading and hydrological regimes made more favorable for cyanoHABs by climate change (Paerl et al. 2011).

The Intergovernmental Panel on Climate Change (IPCC) (2001) concluded that the Earth is warming, thus influencing many physical, chemical and biological processes (Walther et al. 2002). These environmental changes may also have caused alterations to adaptive or maladaptive cyanophages and their ability to lyse their target cyanophage. The following hypothesis, illustrated in Fig. 1, is based on analysis and synthesis of reports published in peer reviewed/scholarly journals. It postulates upon the impact of anthropogenic carbon dioxide emissions, ozone depletion and increased SUR on the cyanophage–host interaction in marine and freshwater environments. This hypothesis describes the potential effects of the various combinations of changing chemical, biological and physical factors on cyanophage–host interactions in aquatic environments.

The evidence of ozone depletion and increase in SUR

Since large-scale industrialization began around 150 years ago, the anthropogenic carbon dioxide (CO₂) emissions (i.e. emissions produced by human activities) originating from combustion of carbonaceous fuels, principally wood, coal, oil, and natural gas (The Habitable Planet 2012) has contributed to the increase in CO₂ in the atmosphere from 280 to 390 ppm in 2005 and it is projected to increase to

almost 700 ppm by the end of the twenty-first century (IPCC 2007). This has contributed directly to rising temperatures through the resultant depletion of the ozone layer (Paul 2008).

Nitrous oxide (N_2O) is a greenhouse gas that causes ozone depletion. When compared to CO_2 , N_2O has 310 times the ability per molecule of gas to trap heat in the atmosphere (Marchal et al. 2011). A study by of Crutzen et al. (2007) suggested that the amount of N_2O release attributable to agricultural nitrate fertilizers has been seriously underestimated. In fact, atmospheric levels of N_2O have risen by more than 15 % since 1750 (IPCC 2007).

The halocarbons and chlorofluorocarbons (CFCs, the chemical substance used in refrigerators, air conditioners and solvents) contribute the largest percentage (80 %) to the 2005 climate forcing, in which the chlorine released by CFCs reacts with ozone and destroys the ozone layer (Marchal et al. 2011). Based on their long lifetime, CFCs will still make a significant contribution and most likely the largest ozone-depleting substances contribution, to halocarbon climate forcing at the end of the twenty-first century (Peter 2011).

In general, the anthropogenic emissions of CO_2 and other gases (methane, tropospheric ozone, halocarbon gases, and N_2O) involved in this process are the fundamental cause of the greenhouse effect and have driven and will continue to have significant effects on ozone depletion (Peter 2011).

The decreasing levels of stratospheric ozone which acts as earth's natural sunscreen by shielding the surface from damaging SUR, has increased ultraviolet (UV) exposure over the last 30 years (Science News 2010). Reductions of up to 70 % in the ozone column observed in the austral (southern hemispheric) spring over Antarctica and first reported in 1985 (Farman et al. 1985) are continuing (Thompson et al. 2011) and it is forecast that without intervention, as much as 17 % of the global-average column ozone will be destroyed by 2020 with 67 % possibly destroyed by 2054 in comparison to 1980 (Newman et al. 2009).

Of the three categories of solar UV radiations, only UV-A (320–400 nm) and UV-B (290–320 nm) are able to penetrate Earth's atmosphere. Thus, these two types of UV radiation are of greatest concern to humans, especially as depletion of the ozone layer causes higher levels to reach the planet's surface (Clancy 2008). The genotoxic potential of UV is linked to its ability to provoke direct DNA damage. The damage caused by UV-B includes direct formation of thymine dimers or other pyrimidine dimers and double-strand DNA breakage (Miyamura et al. 2011).

The continuing degradation of the Earth's ozone layer by atmospheric pollutants has generated concern about the impact of increased solar ultraviolet-B radiation (UV-B) on

aquatic ecosystems (Vincent and Roy 1993; Sinha and Häder 2002). The southern hemisphere tends to have more SUR exposure because of the ozone hole, so significant increases in UV-B can be expected at the surface over Antarctica during the summer (Newman et al. 2009; McKenzie et al. 2011). The SUR levels have gone up by some 6 % on average since 1979 and are projected by some estimates to increase to 650 % by 2065 in mid-latitude cities (Newman et al. 2009; Cimitile 2011; McKenzie et al. 2011).

The impact of SUR on cyanophage–host interactions

These viruses are very vulnerable to several stressors when occurring in the water column (Wilson et al. 1996; Fredrickson et al. 2003; Sommaruga 2003; Clokie and Mann 2006) and sun light plays a key role in all phases of the cyanophage life cycle. SUR also affects viruses negatively by reducing their infectivity (Garza and Suttle 1998). Virus inactivation rates are about 10 times higher in sunlight than in the dark (Sinton et al. 2002; Sabah A. A. Jassim unpublished data). Thus sunlight is well established as an agent of viral mortality (Clokie and Mann 2006).

On the other hand, cyanophage communities tolerate damage by solar radiation better in summer than in winter (Garza and Suttle 1998). This is probably due to cyanobacterial biomass increase during the summer months and may be due to high concentrations of dissolved humic substances and detritus particles allowing only very shallow UV penetration in lakes (De Haan 1993). This may provide a safe haven to cyanophages allowing them to avoid solar radiation. Detectable cyanophage production does not occur during daytime (Garza and Suttle 1998) probably due to the significant amount of UV-B on the water surface (Newman et al. 2009). Therefore, light dependent phage adsorption might serve to trigger a wave of infection following dawn with release of progeny phage around dusk where cyanophages were found to reach a maximum abundance after midnight (Clokie and Mann 2006).

Suttle and Chen (1992) have shown that virus infectivity was very sensitive to solar radiation and in full sunlight, decay rates were $0.4\text{--}0.8\text{ h}^{-1}$. Even when UV-B radiation was blocked, rates were as high as 0.17 h^{-1} . Calculations suggest that in clear oceanic waters exposed to full sunlight, most of the virus decay, averaged over a depth of 200 m, would be attributable to solar radiation. When decay rates were averaged over 24 h for a 10 m coastal water column, loss rates of infectivity attributable to sunlight were similar to those resulting from all other processes combined. They concluded that since sunlight destroys infectivity more quickly than virus particles, a large proportion of the viruses in seawater are probably not infective (lysogenic).

UV radiation has been demonstrated to damage cyanophages (Asato 1976). Significant amounts of UV-B (290–320 nm) and UV-A (320–400 nm) radiation, which directly and indirectly damage DNA, penetrate to considerable depth in seawater (Suttle and Chen 1992). This has the potential to cause wide-ranging effects, including mutagenesis in aquatic microorganisms (Vincent and Roy 1993). It also plays an important role in the destruction of viral particles and the decrease in viral infectivity and viral attachment to host cells (Suttle and Chen 1992; Wommack and Colwell 2000; Liao et al. 2010). This will eventually lessen the survival rates of viruses and thus reduce their influence on the host cell (Suttle and Chen 1992; Vincent and Roy 1993).

It is well known that UV-B photons harm the DNA molecules of living organisms in different ways. The UV-B component of solar radiation is directly absorbed by viral DNA, resulting in the formation of cyclobutane pyrimidine dimers (CPDs) (Hader and Sinha 2005). It is widely accepted that these photoproducts prevent the replication of DNA, hence affecting virus infectivity. Loss of viral infectivity after exposure to SUR seems to be mainly caused by damage to the viral genome, although indirect damage to the capsid has also been suggested to result in inactivation (Wommack and Colwell 2000; Liao et al. 2010).

Like in many other planktonic groups, different viruses appear to have different tolerance towards SUR (Kitamura et al. 2004). The difference in sensitivity between viral nucleic acid types occurs because the most common lethal photoproducts of UV are pyrimidine dimers, particularly thymine dimers (Friedberg et al. 1995), resulting in transcription errors when the DNA replicates (Wommack and Colwell 2000; Clancy 2008). Since DNA but not RNA contains thymine, DNA-containing viruses are generally more sensitive to damage by UV than RNA-containing viruses (Murphy and Gordon 1981). In one common damage event, adjacent thymine bases bond with each other, instead of across the “ladder”. This “thymine dimer” makes a bulge and the distorted DNA molecule does not function properly (Svobodova et al. 2012).

In general, sunlight or more specifically, SUR acts as the principal natural virucide in the environment by chemically modifying viral genetic material (Lytle and Sagripanti 2005). Viral nucleic acid plays a crucial role in the absorption of UV radiation and in virus inactivation (Lytle and Sagripanti 2005). In this regard, a mathematical technique was used to quantify how the biological impacts of SUR exposure will affect life, in which a 7 % increase in UV yielded a 4.8 % increase in damage to DNA (Science News 2010; Fig. 1).

Kellog and Paul (1982) found that the degree of UV damage of some marine vibriophages was negatively

correlated with the G + C content and suggested that the increase of thymine dimer targets increases their sensitivity by reducing their ability to repair the damage, a hypothesis previously proposed for bacteria by Singer and Ames (1970). The DNA damage may be repaired after infection takes place using the host repair mechanisms (Weinbauer and Wilhelm 2011), especially for viruses possessing double-stranded nucleic acids (Lytle et al. 1972).

Homologs of these repair genes were found in very diverse viruses such as the T4 phage infecting *Escherichia coli*, algal virus infecting the symbiotic algae *Chlorella* and herpes simplex virus (Lytle et al. 1972; Weinbauer and Wilhelm 2011). The infectivity of phages can also be restored inside bacteria, either through a specific host-repair-machinery (photoreactivation) (Wilhelm et al. 1998a) or by a virus encoded repair system (Shaffer et al. 1999). Thus, different repair mechanisms or efficiencies may also explain the variability observed in virus inactivation rates.

The potential recovery of viruses makes it difficult to predict the overall effect of SUR in this interaction (Sommaruga 2003). Moreover, the inactivation-recovery process is further complicated by the fact that the physiological status of bacteria can be also impaired by SUR (Wilhelm and Smith 2000). On the other hand, the light-dependent repair mechanism of bacteria seems to be crucial to restore the infectivity of natural aquatic viruses (Wilhelm et al. 1998a, b).

This may predict that mutation linked to the increase of SUR can also occur in cyanophages DNA (Fig. 1). Obviously, DNA-mutating UV radiation also has some impact on cyanobacterial DNA, whereas, cyanobacteria are sensitive to UV light and would be affected by its increase (Sinha et al. 1999). In parallel to this, it is reasonable to expect some changes to have occurred in cyanobacterial cells due to the increase in SUR over recent decades, preventing a cyanophage–host infection. Prevention of cyanophage adsorption in marine cyanobacteria was also reported (Sigee et al. 1999; Stoddard et al. 2007). The most common mechanism appears to be an alteration of host surface receptors which reduces or eliminates the ability of phages to attach to the host cell and establish an infection (Xu et al. 1997; Bohannan and Lenski 2000; Stoddard et al. 2007).

There is also an increased incidence of lysogenic cyanophages in marine and freshwater environments (Bisen et al. 1986; Suttle 2000). Lysogeny in the unicellular cyanobacterial species has been documented experimentally in natural environments through prophage induction and the process of lysogeny is unique to certain marine unicellular cyanobacterial strains (McDaniel et al. 2002, 2006). A considerably large number of marine cyanobacteria, isolated from different parts of the world harbored

lysogenized cyanophages (Ohki 1998; Ortmann et al. 2002).

Effect of biological factors and Sputnik viroplage

The significant biological factors for modeling in situ cyanophage–host interaction were investigated in oligotrophic, eutrophic and mesotrophic environments (Wommack and Colwell 2000). It appears that larger viroplankton populations are found under conditions of high bacterial productivity. Thus, it is not surprising that the abundance of aquatic viruses is closely correlated with the abundance and activity of bacterioplankton.

The correlation between the influence of biological factors on cyanophage and cyanobacteria in different aquatic environments was also studied (Wommack and Colwell 2000). It appears that freshwater ecosystems contain high concentrations of algae and cyanobacteria where increases in phytoplankton biomass result in more algal viruses. In lacustrine systems (lakes), the short-term relationship between viruses and bacteria is negative, which in effect obscured the dependence of viral abundance on bacterial abundance in the small data set (Wommack and Colwell 2000).

The positive correlation between chlorophyll α concentration and viral direct counts in the lakes supported the significant correlation found between bacterial production and viroplankton abundance (Maranger and Bird 1995). In essence, a high phytoplankton biomass in the lakes was associated with a more productive bacterial community, resulting in increased viral abundance (Wommack and Colwell 2000).

Recently discovered, the Sputnik viroplage is a satellite virus that inhibits replication of its target phage and thus acts as a parasite of that virus. Virophages coexist with and in turn are the natural predator of phages. They hijack giant virus DNA in order to replicate and often deform phage/virus particles, making them less infective in diverse marine environments (La Scola et al. 2008; Monier et al. 2008; Sun et al. 2010; Fischer and Suttle 2011).

There are several genes that are related to Sputniks in an ocean-sampling data set, so this could be the first of a new, common family of viruses (Raoult et al. 2004). These giant virus and Sputnik virophages could have major effects on ocean nutrient cycles and they could also be major players in global systems (Monier et al. 2008; Pearson 2008).

In March 2011, the Organic Lake viroplage, which preys on viruses that attack algae (Yau et al. 2011) was discovered in the salty Organic Lake in Antarctica. It was found that virophages stimulate secondary production through the microbial loop by reducing overall mortality of the host and increasing the frequency of cyanobacterial blooms during polar summer light periods.

These viroplage signatures were also found in neighboring Ace Lake (in abundance) and in two tropical lakes (hypersaline and fresh), an estuary and an ocean upwelling site. These findings indicate that virophages regulate host–virus interactions, influence overall carbon flux in Organic Lake and play previously unrecognized roles in diverse aquatic ecosystems (Yau et al. 2011).

The only explanation of why such viruses evolve may be that Antarctic lakes have long cycles of daylight and darkness and a decrease in phycodnavirus cell killing caused by virophages may be essential for maintaining stability of the microbial food web (Yau et al. 2011). It is well known that cell killing by viruses has a major impact on ocean ecology. By regulating virus-induced cell lysis, virophages might also have a major effect on aquatic ecology; therefore, much more work is required to understand viroplage diversity and their role in the changing global ecosystem.

Conclusion

Over the last 50 years, there are many reports in peer reviewed journals and newspapers indicating a global increase in the incidence, duration and intensity of cyanoHABs. These have by convention been attributed to the excessive level of the nutrients phosphate and nitrogen as well as carbon, iron and silica, which promote the rapid growth and multiplication of cyanobacteria in aquatic environments. There are several studies which have shown that phosphate in particular, supports the efficacy of the cyanophage infection in the cyanobacteria. Thus it is reasonable to expect an excessive level of phosphate to stimulate the cycle of cyanobacterial lysis and the resultant release of newly-formed cyanophages to lyse (kill) an increasing number of cyanobacterial cells, thereby contributing to the disappearance of many cyanoHABs. Clearly the role of phosphate, as well that of other nutrients, to restore cyanophage infectivity on cyanobacteria in diverse aquatic environments needs further consideration and investigation.

Up until now, the key reasons for not using cyanophages in the control of cyanoHABs lies in the limit of the current understanding of cyanophage–cyanobacterial interactions, including cyanophage propagation and biokinetics. The difficulty of collecting and isolating cyanophage samples from cyanobacteria rich sites and the inability to reactivate dormant (lysogenic) cyanophages in aquatic ecosystems have been other challenges. The rapid appearance of cyanobacterial mutants, resistant to infection, along with the effect of changing environmental forces may be other factors. Researchers are studying these effects and discovering means to overcome these obstacles. Experimentation is

prescribed on gene modification and other less invasive means of controlling, strengthening, adapting, breeding and designing phages to increase infectivity and effectiveness. Scientists are uncovering new possibilities in cyanophage technology for protecting the environment as well as a multiplicity of uses for biocontrol and rapid detection of cyanobacteria in marine and freshwater environments.

Over the last few decades, there have been increases in greenhouse gases, coupled with the depletion of the ozone layer and the corresponding increase of SUR. These factors have been overlooked for their role on cyanophage–cyanobacterial interaction in aquatic environments. Research published over the last decade on changing environmental conditions has demonstrated how these factors have induced mutations in the highly adaptive cyanophage DNA. These mutations have led to the increase of lysogenic cyanophages coupled with a corresponding reduction of lytic cyanophages. Thus similarly evolved cyanobacteria can escape the lysis induced by cyanophages and replicating without this natural predator, they contribute to the increasing incidence of HABs worldwide.

The more recent discovery of virophages, that coexist and prey on phages, hints of many more as yet undiscovered cyanophages and supports the hypothesis regarding their influence in the global proliferation of cyanoHABs (Fig. 1). Clearly, the discovery of virophages and their impact on marine life is far more significant than previously imagined. Thus as additional virophages are discovered, it will be important to also document their impact upon aquatic ecosystems and global HABs.

Over the last 20 years, phage biotechnology, relied upon for many decades in the former Soviet Union, has emerged as an important tool to control many environmentally and medically significant bacterial pathogens. New technologies can now be used to select and replicate the most effective phages from environmental samples in order to enhance the virility of the resultant pool of phages. This should also be a useful tool in controlling cyanobacterial growth rates and thus cyanoHABs in marine and freshwater environments.

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