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Are phytoplankton population density maxima predictable through analysis of host and viral genomic DNA content?

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Phytoplankton:virus interactions are important factors in aquatic nutrient cycling and community succession. The number of viral progeny resulting from an infection of a cell critically influences the propagation of infection and concomitantly the dynamics of phytoplankton populations. Host nucleotide content may be the resource limiting viral particle assembly. We present evidence for a strong linear correlation between measured viral burst sizes and viral burst sizes predicted from the host DNA content divided by the viral genome size, across a diversity of phytoplankton:viral pairs. An analysis of genome sizes therefore supports predictions of taxon-specific phytoplankton population density thresholds beyond which viral proliferation can trim populations or terminate phytoplankton blooms. We present corollaries showing that host:virus interactions may place evolutionary pressure towards genome reduction of both phytoplankton hosts and their viruses.

INTRODUCTION

Phytoplankton photosynthesis accounts for approximately half of global primary production and is therefore a dominant component of carbon cycling (Falkowski & Raven, 1997). Lytic viruses can constrain the extent of phytoplankton blooms and impose strong selective pressures on their community structure and diversity (Bratbak et al., 1993; Muhling et al., 2005). Furthermore, these viruses and phage influence nutrient cycling in oceans and lakes by causing the release of dissolved organic matter from cells into the water (Gobler et al., 1997), thereby pre-empting the biogenic carbon pump (Fuhrman, 1999).

Phytoplankton population growth rates and cell densities are several orders of magnitude lower than those of the enteric heterotrophic bacterial model taxa upon which much of our current understanding of host:virus interactions is based. In bacterial model systems growing under rich nutrient conditions, the length of time from infection to lysis, known as the latent period, as well as the burst size, or total number of viral particles released per host cell, are tightly regulated and are presumably optimal for a given host:virus interaction. The triggering of lysis appears to involve environmental or physiological sensing (Young, 1992). The rate of viral production and the burst size varies widely with cellular physiology (Hadas et al., 1997). Genetic adaptation can also shift the latent period and the optimal burst size. For instance, when host densities are extremely high, a mutant T4 virus having a shorter latent period and a reduced burst size can out-compete a wild-type virus with longer latent period and larger burst size (Abedon et al., 2003). Rapid lysis may thus confer an advantage, in spite of a lower burst size, when the time required for a virus to encounter a new host is short in relation to the length of the lytic cycle.

Lytic cycles and burst sizes of viruses of both prokaryotic (Mackenzie & Haselkorn, 1975; Wilson et al., 1996) and eukaryotic phytoplankton (Bratbak et al., 1993, 1998) are influenced by host physiology, though apparently to a lesser extent than for viruses infecting laboratory heterotrophic bacterial cultures. Further, while theoretical models predict that high *Synechococcus* densities can drive the selection of populations of viruses with shorter lytic cycles and smaller burst sizes (Mann, 2003), generally low or fluctuating host population densities would challenge the effectiveness of this selection in nature.

In this study, we consider the relation between the molecular resources of phytoplankton hosts and the requirements of viruses that divert and harvest those resources. Physiological plasticity doubtlessly influences the ecology of phytoplankton:virus interactions and may contribute to some of the variation encountered in the emergent statistical correlations we find. For the purpose of modelling these interactions, however, we make the assumptions that under most field conditions a large burst increases viral success and that burst size is limited by host resources.

Viruses invariably depend on host resources for their propagation. Host resources include amino acids, cell volume, nucleotides, energy and reducing equivalents, and translation capacity (polymerases, ribosomes and cofactors), which are diverted toward viral genome and capsid synthesis. Of these resources, amino acids do not likely limit the maximum burst, since viral particles have a high nucleic acid to protein ratio and host protein pools are generally in excess of the total viral protein released upon lysis (calculations not presented). Although cell volume might become limiting in certain cases (Brussaard et al., 2004), phytoplankton host cell volume is usually in excess of the volume occupied by virus and phage particles

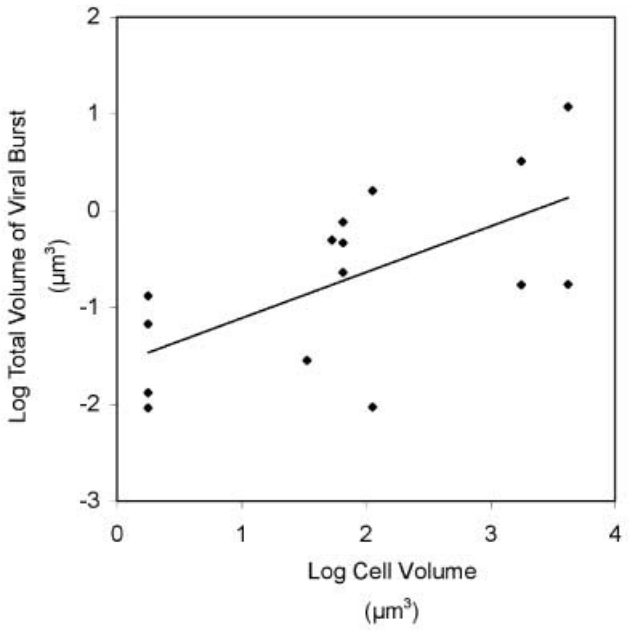

Figure 1. Plot of total volume of viral burst (μm^3) (volume of viral particle x number of viruses) versus host cell volume (μm^3). Data were log transformed. $y=0.475x-1.584$, $R^2=0.389$.

prior to lysis, and shows only a weak correlation with viral burst size (Figure 1).

Nucleotide availability, however, may constrain viral production in phytoplankton hosts, particularly during growth under low nutrients when the host nucleotide pool represents a limited resource that is not readily replenished through biosynthesis. Paul et al. (2002) noted a strong correlation between the size of the host genomes of some marine cyanobacteria and the burst size of their cyanophage viruses, expressed in nucleotide equivalents. A host genome size/viral burst size trade-off in cyanophages is also supported by Sullivan et al. (2003), who showed that the majority of phage isolated using a *Synechococcus* strain as a host were the large Myoviridae, while isolations using *Prochlorococcus* MED4, a host strain with a smaller genome, yielded almost exclusively small Podoviridae. Other *Prochlorococcus* host strains with genome sizes intermediate between *Prochlorococcus* MED-4 and *Synechococcus* yielded both Podoviridae and Myoviridae.

MATERIALS AND METHODS

We sought to address whether host nucleotide content could generally limit viral bursts in marine phytoplankton

Table 1. *Nucleic acid contents, observed and predicted burst sizes for a range of algae and viruses*. dsDNA viruses unless otherwise noted.*

Host organism	Habitat	Cell volume (μm^3)	Host genome (nucleotides/ haploid cell)	Virus	Virus type	Viral genome (nucleotides per virus)	Burst—reported	Burst—predicted**
Synechococcus WH7803	Marine	1.8	4.74×10^6	S-PM2	Cyanomyovirus	392560	41	24
Synechococcus WH7803	Marine	1.8	4.74×10^6	P60	Cyanopodo-virus	95744	81	99
Microcystis aeruginosa NIES-298	Freshwater	35	9.60×10^6	Ma-LMM01	Cyanomyovirus	320000	85	60
Micromonas pusilla	Marine	1.8	4.93×10^7	MpV	Phycodnavirus	400000	85	123
Micromonas pusilla	Marine	1.8	4.93×10^7	MpRNAV-01B	Reovirus (dsRNA)	51000	490	966
Chlorella NC64A	*P. bursaria* endo-symbiont	53	7.76×10^7	PBCV-1	Phycodnavirus	661488	138	117
Chaetoceros salsugineum	Marine	115	2.39×10^8	CsNIV	Circovirus? (ssDNA)	7002	325	34147
Phaeocystis globosa Pg-I	Marine	65	3.83×10^8	PgV Group I	Phycodnavirus	932000	248	411
Phaeocystis globosa Pg-I	Marine	65	3.83×10^8	PgV Group II	Phycodnavirus	354000	369	1083
Phaeocystis pouchetii AJ01, AJ10	Marine	65	4.02×10^8	PpV	Phycodnavirus	970000	475	414
Emiliania huxleyi	Marine	115	4.40×10^8	EhV	Phycodnavirus	824000	620	534
Heterosigma akashiwo	Marine	1766	3.89×10^9	HaV-01	Phycodnavirus	588000	770	6612
Heterosigma akashiwo	Marine	1766	3.89×10^9	HaRNAV	Marnavirus (ssRNA)	8587	21000	452728
Heterocapsa circularisquama	Marine	4187	1.66×10^{10}	HcV-01	Phycodnavirus	712000	2120	23327
Heterocapsa circularisquama	Marine	4187	1.66×10^{10}	HcRNAV	Unassigned (ssRNA)	4400	12200	3774745

*, see Materials and Methods for data sources and treatments; **, host genomic nucleotides/viral nucleotides.

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systems. We therefore conducted an extensive search of the relevant literature, genomic databases, and genome size determinations. Among the approximately 38 known viruses infecting algae and cyanobacteria, we were able to compile accurate determinations of host and viral genome sizes along with viral burst sizes for 15 pairs, including viruses with double-stranded (ds) DNA, ssDNA, dsRNA or ssRNA genomes (Table 1).

Algal genome sizes were derived from either complete genome sequence data or nuclear DNA content estimates. Viral genome sizes were derived from either complete genome sequences or estimates derived from electrophoretic separations of viral nucleic acids. Burst sizes were derived from either indirect estimates from dilution-to-extinction assays of infectivity (Suttle, 1993) or direct counts done with flow cytometry or transmission electron microscopy (TEM). Whenever possible, we used direct count estimates, since viral burst size estimates based on infectivity can underestimate viral particle numbers (Van Etten, 1983; Cotrell & Suttle, 1995). The majority of burst size data reports from the literature were not accompanied by full data sets or statistical analyses. In most instances, ranges of burst sizes were reported. We therefore plotted either the mean values (when provided) or the midpoints of the ranges, as estimates of central tendency for burst size. Alternate plots using maximum and minimum burst estimates did not substantially alter the correlations observed (data not shown). Data were log transformed prior to plotting to better accommodate a four order of magnitude range of values for burst size, and to minimize excess influence on regression plots from large viral bursts relative to small bursts, as determined using SYSTAT (Systat Software Inc., Richmond CA).

Data sources—genomes and burst sizes

The following section outlines the data sources and relevant information for each of the host:virus pairs, listed in order of increasing host genome size:

Synechococcus WH7803/SPM2 phage

Host genome: genome size estimate. (http://www.genoscope.cns.fr/externe/English/Projets). We multiplied the genome size by two, as WH7803 carries an average of two copies of its genome per cell (Binder & Chisholm, 1995).

Viral genome: dsDNA. Complete sequence (Mann et al., 2005).

Burst data: two values reported, for phosphate deplete culture and phosphate replete culture. Burst size determined by dilution-to-extinction and plaque assay for infectious particles (Wilson et al., 1996).

Synechococcus WH7803/P60 phage

Host genome: as above.

Viral genome: dsDNA. Complete sequence (Chen & Lu, 2002).

Burst data for this podovirus were not available. As a proxy, we used a single estimate for viruses infecting *Synechococcus* in the Gulf of Mexico (Garza & Suttle, 1998).

Microcystis aeruginosa/Ma-LMM01

Host genome: genome size estimate from the Institute Pasteur (N Tandeau de Marsac http://www.people.vcu.edu/~elhaij/cyanonews/V16/GenomeProjects.html).

Viral genome: dsDNA. Complete sequence (Yoshida et al., 2006).

Burst size: range of values reported (Yoshida et al., 2006).

Micromonas pusilla/MpV

Host genome: cellular DNA content estimate (Veldhuis et al., 1997).

Viral genome: dsDNA. Estimate (Waters & Chan, 1982).

Burst size: range of values reported (Waters & Chan, 1982).

Micromonas pusilla/MpRNAV-01B

Host genome: as above.

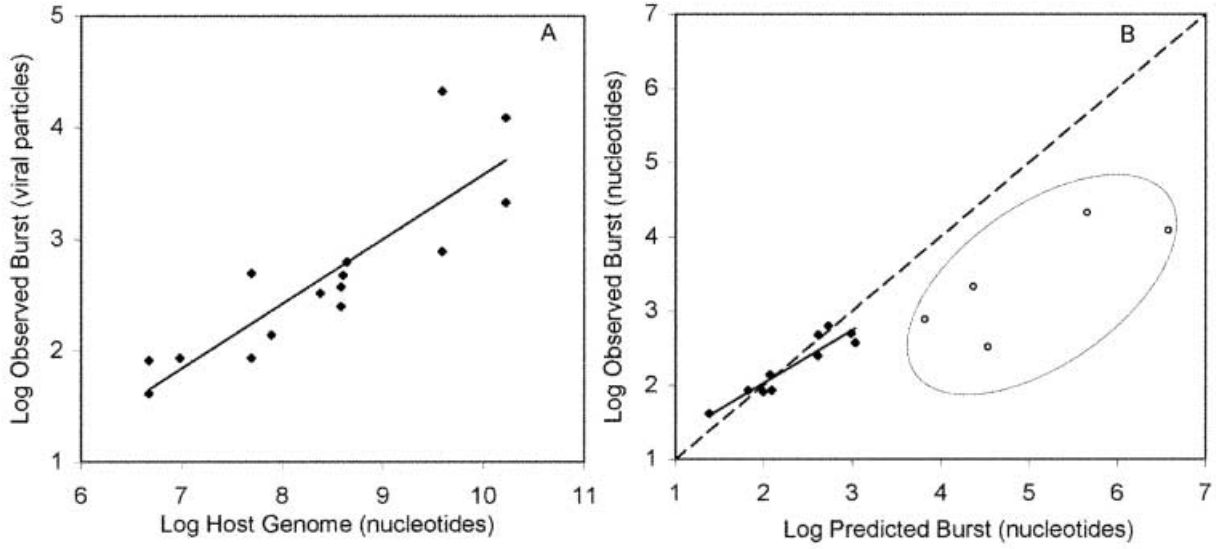

Figure 2. (A) Plot of observed viral burst size (particles per host cell) versus host genome size (nucleotides) for a range of algal/viral pairs. Data were log transformed. $y=0.580x-2.221$, $R^2=0.753$; and (B) plot of observed viral burst size (particles per host cell) versus predicted burst size (host genome nucleotides/viral genome nucleotides). Points circled represent an independently plotted subset of host/virus pairs characterized by a large host genome and/or a small viral genome. Data were log transformed. The dashed line indicates a hypothetical plot of slope 1.0. $y=0.704x+0.623$, $R^2=0.871$.

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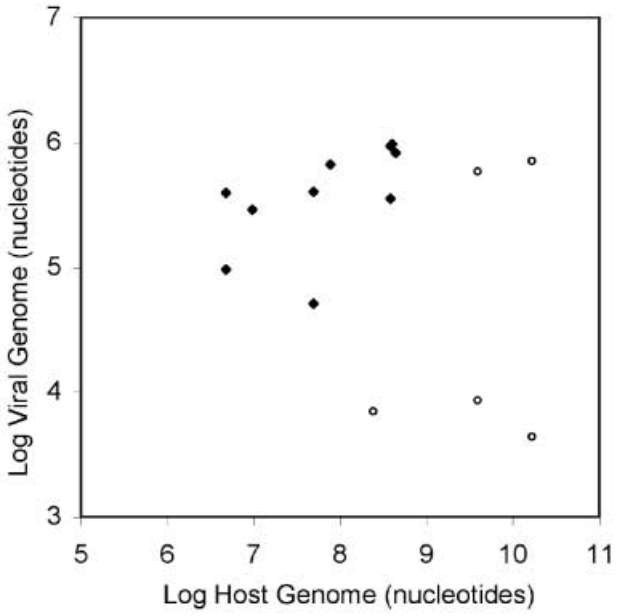

Figure 3. Plot of viral genome size versus host genome size, in nucleotides. Data were log transformed. Open circles indicate a subset of host/virus pairs characterized by a large host genome and/or a small viral genome (data points from the same pairs circled in Figure 2B).

Viral genome: dsRNA. Estimate by electrophoresis (Brussaard et al., 2004).

Burst size: range estimated by both flow cytometry and microscopy (TEM) (Brussaard et al., 2004).

Phaeocystis pouchetii AJ01 and AJ10/PpV01

Host genome: as a genome size was not found for this particular strain, we used an average DNA content for a number of *Phaeocystis* strains (Veldhuis et al., 1997).

Viral genome: dsDNA. Estimate (Jacobsen et al., 1996).

Burst size: range estimated by electron microscopy (TEM) (Jacobsen et al., 1996).

Phaeocystis globosa PgI/PgV Groups I and II

Host genome: as a genome size was not found for this particular strain, we used an average, haploid, 1C DNA content for a number of north European *Phaeocystis* strains, which ranged from 0.20 to 0.22 pg per cell (Vaulot et al., 1994).

Viral genome: dsDNA. PgV Groups I and II genome sizes, estimated by pulsed-field gel electrophoresis, are mean values for six isolates (Badoux & Brussaard, 2005).

Burst size: burst sizes for each of six viral isolates from Groups I and II were determined by flow cytometry using *P. globosa* PgI as the host strain. (University of Groningen, Netherlands) as a host (Baudoux & Brussaard, 2005).

Emiliania huxleyi/EhV

Host genome: genome size estimate (Joint Genome Institute, http://www.jgi.doe.gov/sequencing/DOEmicrobes.html).

Viral genome: dsDNA. Estimated by pulsed-field gel electrophoresis (Castberg et al., 2002).

Burst size: determined by flow cytometry; mean value reported (Castberg et al., 2002).

Chlorella NC64A/ PBCV-1

Host genome: estimated by gel electrophoresis (Higashiyama & Yamada, 1991).

Viral genome: dsDNA. Complete sequence (http://greengene.uml.edu/analysis/analysis.html).

Burst size: range estimated by dilution-to-extinction and plaque assay for infectious particles (Van Etten et al., 1983). We used a burst size reported for dark-grown cells—roughly 50% of the burst size in the light.

Heterosigma akashiwo/HaV-01

Host genome: cellular DNA content estimate (Han et al., 2002).

Viral genome: dsDNA. Estimate (Nagasaki & Yamaguchi, 1997).

Burst size: single value reported estimated by dilution-to-extinction and confirmed by direct counts using electron microscopy (TEM) (Nagasaki et al., 1999).

Heterosigma akashiwo/HaRNAV

Host genome: cellular DNA content estimate (Han et al., 2002).

Viral genome: ssRNA. Complete sequence (Lang et al., 2004).

Burst size: estimated by flow cytometry (Lawrence et al., 2004).

Chaetoceros salsugineum/CsNIV

Host genome: estimate of cellular DNA content based on that of the slightly larger *Chaetoceros muelleri* (Veldhuis et al., 1997).

Viral genome: ssDNA. Complete sequence (Nagasaki et al., 2005).

Burst size: single value reported estimated by dilution-to-extinction (Nagasaki et al., 2005).

Heterocapsa circularisquama/HcV-01

Host genome: conservative estimate of cellular DNA content based on that of the smaller *Heterocapsa pygmaea* (Triplett et al., 1993).

Viral genome: dsDNA. Estimate (Tomaru & Nagasaki, 2005, conference abstract— 4th Algal Viral Workshop).

Burst size: range estimated by dilution-to-extinction (Nagasaki et al., 2003).

Heterocapsa circularisquama/HcRNAV

Host genome: as above.

Viral genome: ssRNA. Complete sequence (Tomaru et al., 2004).

Burst size: range estimated (Tomaru et al., 2004).

RESULTS AND DISCUSSION

Viral burst size correlates poorly to host volume

In order to address the question of whether viral burst size is generally limited by the capacity of host cells to contain viruses, we compared viral burst volumes, expressed in terms of the total volume of the viral particles released, to host cell volumes for 15 viruses infecting a wide range of algal taxa (Figure 1). The correlation of viral burst to host volume was weak (R^2=0.389), suggesting that while cell volume might in certain cases limit burst

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size, other variables are likely more important. In particular, cell size itself correlates with genome size in phytoplankton (Shuter et al., 1983).

Viral burst size correlates to host genome size

When burst size was instead plotted against host genomic size, for the same 15 virus/phytoplankton host pairs (Figure 2A), we found a stronger correlation (R^2=0.753). To generate a correlation explicitly predicting burst sizes, we plotted observed burst sizes against a predicted burst size, estimated as the host genomic nucleotide content divided by the viral nucleotide content (Figure 2B). This predicted viral burst size assumes that all host genome nucleotides are converted to viral particles, that no net nucleotide biosynthesis contributes to the viral assembly, and that RNA nucleotides do not contribute significantly to the viral assembly. These assumptions are based on host–viral systems evolved under relatively low nutrient conditions where the host genomic nucleic acids represent a resource not readily replenished through biosynthesis.

For ten viruses that infect hosts containing 5×10^8 nucleotides of genomic DNA or less, we found a strong correlation (R^2=0.871) between the observed and predicted viral burst size, over a range from 10^1 to 10^3 viral particles per cell. The slope of 0.704 ±0.096 (95% confidence interval for slope, 0.483 to 0.926) suggests that host DNA content is a primary predictor of viral burst size in nucleotide equivalents. Host RNA contents vary widely with metabolic state (Dortch et al., 1983) and we therefore excluded RNA pools from our analysis. The contribution of host RNA to viral synthesis could explain some of the variation between our predicted and reported bursts. The remaining five data pairs represent large host genomes plotted independently on the same figure and discussed later.

For the cyanophages Cyanomyoviridae S-PM2 and Cyanopodoviridae P60, which both infect *Synechococcus* WH7803, we initially predicted burst sizes on the basis of one genome copy per host cell. The predicted burst of 12 for S-PM2 was lower than the 22 to 45 observed in nutrient-replete media (Wilson et al., 1996). The predicted burst of 50 for P60 was also lower than the 81 cited for bacteriophage in marine environments (Garza & Suttle, 1998). A probable source of this discrepancy is the multiple genome copies found in cyanobacteria, with *Synechococcus* WH7803 typically carrying between one and three copies (Binder & Chisholm, 1995). Doubling the genome copy number in our calculations for *Synechococcus* WH7803 eliminated the discrepancy. A similar correction was applied to the cyanobacteria *Microcystis aeruginosa*, which resulted in a predicted burst for phage Ma-LMM01 of 66, within the observed burst range of 50 to 120 (Yoshida et al., 2005).

Another explanation for observations of larger burst sizes than predicted from the host genome size is that alternate nucleotide sources, including RNA pools, may be exploited during cyanobacterial infections. While Wilkner et al. (1993) showed that host nucleic acids are the major source of phage nucleotides, *de novo* nucleotide synthesis during phage development might also contribute to phage production. Many cyanobacteria/cyanophage systems have an obligatory requirement for illumination during infection (MacKenzie & Haselkorn, 1972). The presence of the critical photosynthesis gene, *psbA*, in the genomes of some cyanophage supports the premise of preserving photosynthesis during infection (Mann et al., 2003), which may provide energy required for nucleotide synthesis. Although some cyanophage also carry thymidylate synthase and ribonucleoside reductase genes that allow them to harvest nucleotides from host RNA pools, these genes would not enable full virally-directed *de novo* nucleotide synthesis. Furthermore, viral harvest of the highly modified nucleotide pools from ribosomal or transfer RNA would require tight temporal regulation to avoid blocking translation of viral proteins, while the messenger RNA pool is quantitatively small.

Within the eukaryotic phytoplankton, observed bursts of viruses infecting the prymnesiophyte algae *Phaeocystis pouchetii* (Jacobsen et al., 1996) and *Emiliania huxleyi* (Bratbak et al., 1993; Castberg et al., 2002) are close to predicted bursts. Observed bursts for two different viruses of *Phaeocystis globosa* (Baudoux & Brussaard, 2005) are lower than predicted. We await more precise genome and burst data for another prymnesiophyte, *Chrysochromulina ercina* and its virus CeV (Sandaa et al., 2001). For viruses infecting the prasinophyte *Micromonas pusilla*, 123 particles/cell are predicted for the dsDNA virus MpV compared to an observed burst size of 70 to 100 (Waters & Chan 1982). A prediction of 966 particles/cell for the dsRNA virus MpRNAV also infecting *Micromonas pusilla* is somewhat higher than the observed burst sizes of 460 to 520 (Brussaard et al., 2004).

The five data points plotted independently (Figure 2B) represent eukaryotic hosts generally found under higher nutrient conditions and having DNA contents that are apparently in excess of viral needs. Dinoflagellate genomes can be several-fold larger than the human genome, yet the HcRNAV (Tomaru et al., 2004) and HcV (Nagasaki et al., 2003) viruses, which infect the dinoflagellate *Heterocapsa circularisquama*, release smaller bursts than predicted by our model (Figure 2B), apparently lysing their dinoflagellate hosts prior to exhausting the genomic nucleotide resources. Similarly, the burst sizes for HaRNAV (Lawrence et al., 2004) and HaV (Nagasaki et al., 1999), infecting the raphidophyte *Heterosigma akashiwo*, are smaller than those predicted by host genomic nucleotide content. A host genome size cut-off of around 5×10^8 nucleotides, above which nucleotides are unlikely to limit burst size, may apply to large phytoplankton hosts such as dinoflagellates, raphidophytes and diatoms. Such a threshold is an estimate rather than a rigorous predictor, since the small genomes of viruses such as CsNIV, HaRNAV or HcRNAV may also release them from a host nucleotide content constraint, while still achieving bursts larger than 10^3 particles/cell. CsNIV, a single-stranded DNA virus of just 7002 nucleotides that infects the diatom *Chaetoceros salsugineum* (Nagasaki et al., 2005) generates bursts that are only 0.2% of that predicted based on the the host genome of 2.4×10^8 nucleotides, below the suggested 5×10^8 nucleotide cut-off. A plot of viral genome size versus host genome size (Figure 3) shows a bias, among the smallest viruses, toward large hosts, suggesting that the cellular physiology of larger hosts perhaps better supports viral propagation from reduced viral genomes.

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In the event that a virus encounters a relative bounty of host nucleic acid resources, other factors may place ceilings on viral proliferation. For example, evidence for autocatalytic cell death in phytoplankton, analogous to apoptosis in multicellular organisms, has led to speculation that viral attack can trigger such programmed cell death (PCD) (Bidle & Falkowski, 2004) to limit viral progression. The virus may respond by triggering lysis before host DNA has been fully exploited, to abandon a cell that is dying, rapidly sinking, or otherwise limiting viral success.

Departures from unity of the ratio between host genome size and viral nucleotide plunder hint at an arms race between the host and the virus, particularly for the protist taxa examined. One divergence occurs when predicting the burst size of PBCV-1, a virus with an exceptionally large genome that infects *Chlorella* endosymbionts of *Paramecium bursaria*. Infection with PBCV-1 in the light generates bursts of between 200 and 350 (Van Etten et al., 1983), roughly twice the 117 predicted based on recycling of genomic DNA pools. PBCV-1, however, encodes a set of nucleotide synthesis enzymes that enable it to generate nucleotides *de novo*, actually increasing the DNA content of infected cells several fold (Van Etten, 2003). PBCV-1 may thus overcome the limitation imposed by their host genome size, allowing production of more genome copies in a single burst. Infection of *Chlorella* in the dark yields bursts that are half those generated in the light, suggesting that photosynthesis supplies energy and reductant for nucleotide synthesis, so that the lower virus yields in the dark more closely reflect our expected correlation with host genomic nucleotides.

Predicting population thresholds

We can use burst sizes and host densities to predict thresholds for proliferation and bloom collapse. Mann (2003) states a key equation describing host:virus interactions:

$$kBPV = DV \tag{1}$$

where k=contact rate (cm^{-3} d^{-1}); B=burst; P=host population (cells·cm^{-3}); V=viruses (particles·cm^{-3}); D=virus decay rate (d^{-1}). k is estimated as $4\pi RCf$, where R=host radius (cm); C=diffusion constant of virus particle; f=proportion of contacts leading to an infection. A simplifying assumption of this equation is that all viral particles are infective, whereas the actual fraction of infective particles may be 20–50% (Cottrell & Suttle, 1995; Van Etten, 2003).

Viral burst size and host density directly influence viral concentrations and contact rates, and are therefore significant components in models of phytoplankton mortality. When virus–host contact rates reach a given threshold, virus or phage particles rapidly accumulate, often leading to the collapse or trimming of a host population back below a critical density (Nagasaki et al., 1994; Wommack & Colwell, 2000; Sandaa et al., 2001).

A restatement of the Mann (2003) equation, cancelling virus particles cm^{-3} from both sides, shows that the host population threshold required for viral proliferation is directly proportional to the viral decay rate and inversely proportional to the burst size and the contact rate:

$$P = D/(B \cdot k). \tag{2}$$

Host:virus pairs generating burst sizes from 10^1 to 10^3 particles per cell fall under our hypothesis of equivalence between host genome and viral genome times burst size:

$$B = hg/vg \tag{3}$$

where hg=host genome, vg=viral genome, both expressed in nucleotides.

Substituting this relationship into the rearranged Mann (2003) equation:

$$P = D/[(hg/vg)k] \tag{4}$$

leads to the prediction that for the host to escape population trimming or bloom collapse by viral proliferation, either:

$$\begin{aligned} &P \leqslant D/[(hg/vg) \cdot k] \quad \text{or} \\ &hg \leqslant D \cdot vg/(P \cdot k) \end{aligned} \tag{5}$$

In other words, to reduce viral success and increase host success, the host density must be low enough to restrict viral contacts, or the host genome small enough to limit the viral burst size to an ineffective number. Conversely, for the virus to proliferate:

$$vg \leqslant (hg \cdot P \cdot k)/D. \tag{6}$$

Meaning, for viral success and therefore population trimming to occur, the viral genome must be small enough to result in a large burst size. Alternatively, for a given host genome size, viruses with larger genomes will require a higher host population for success, when compared to viruses with smaller genomes.

Cavalier-Smith (2005) cites metabolic and spatial economy and replication speed as the primary forces driving genome reduction. Our analysis suggests that the demands of viruses for nucleic acids could also drive host genome reduction in response to persistent and ubiquitous viral attack. A compensatory evolutionary response could be genome reduction in those viruses attacking host cells with the smallest genomes.

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