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Adaptive evolution of viruses infecting marine microalgae (haptophytes), from acute infections to stable coexistence

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ABSTRACT

Collectively known as phytoplankton, photosynthetic microbes form the base of the marine food web, and account for up to half of the primary production on Earth. Haptophytes are key components of this phytoplankton community, playing important roles both as primary producers and as mixotrophs that graze on bacteria and protists. Viruses influence the ecology and diversity of phytoplankton in the ocean, with the majority of microalgae–virus interactions described as 'boom and bust' dynamics, which are characteristic of acute virus–host systems. Most haptophytes are, however, part of highly diverse communities and occur at low densities, decreasing their chance of being infected by viruses with high host specificity. Viruses infecting these microalgae have been isolated in the laboratory, and there are several characteristics that distinguish them from acute viruses infecting bloom-forming haptophytes. Herein we synthesise what is known of viruses infecting haptophyte hosts in the ocean, discuss the adaptive evolution of haptophyte-infecting viruses -from those that cause acute infections to those that stably coexist with their host - and identify traits of importance for successful survival in the ocean.

Key words: haptophytes, algal viruses, phytoplankton, viral evolution, *Phycodnaviridae*, *Mimiviridae*, viral–host relationship, marine viral ecology, marine viral diversity

CONTENTS

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I. INTRODUCTION

Haptophytes are a diverse group of microalgae consisting both of ubiquitous bloom-forming and non-blooming species (Eikrem *et al.*, 2016). Viruses infecting marine haptophytes display a continuum in infection strategies from acute infections, where the host is rapidly lysed, to more persistent infections resulting in lower host mortality rates (Jacobsen, Bratbak & Heldal, 1996; Sandaa *et al.*, 2001; Castberg *et al.*, 2002; Baudoux & Brussaard, 2005; Johannessen *et al.*, 2015; Wagstaff *et al.*, 2017). In this review we suggest that the range of infection strategies among marine haptophyte viruses is the result of mutual trade-off processes between the virus and the growth strategy of its algal host. We further discuss how the development of acute to persistent relationships has resulted in differences in fitness traits and biological trade-offs. Table 1 provides a glossary of key terms used herein. We discuss marine haptophyte virus–host interactions, in the context of both general viral evolution and the trade-off hypothesis, by using results from *in situ* observations and laboratory experiments. The trade-off hypothesis states that natural selection should result in an optimal balance between the costs and benefits of harming hosts, i.e. that there is a virulence-related trade-off between rate of transmission and duration of infection (Anderson & May, 1982; Alizon *et al.*, 2009).

Hallmarks of new virus–host interactions are infections with short durations and high mortality rates and are often referred to as acute infection systems (Fig. 1). Viruses switching from one host species to another have led to some of the most devastating disease epidemics including the HIV pandemic (Sharp & Hahn, 2010), the 'Spanish flu' (Webby & Webster, 2001), Ebola (Leroy *et al.*, 2005), and recently the COVID-19 pandemic (Cui, Li & Shi, 2019). Other important human pathogenic viruses, such as measles and smallpox may also have had their origin in wildlife or domesticated animals in prehistoric times (Wolfe, Dunavan & Diamond, 2007).

New virus–host interactions start with a virus switching to a novel host strain or species, requiring that the virus already possesses the biochemical components for successful infection and propagation (Woolhouse, Haydon & Antia, 2005; Longdon *et al.*, 2011, 2014). A virus's ability to switch hosts and thereby increase the abundance of available hosts, likely comes with life-history trade-offs for the virus (Table 2; Record, Talmy & Våge, 2016; Weitz, 2015, Alizon *et al.*, 2009). Examples of trade-offs for broad host ranges include reduced reproductive fitness in the original host (Duffy, Turner & Burch, 2006), and decreased efficiency of infection (Jover, Cortez & Weitz, 2013). Once a virus successfully infects a new host, the host and virus will co-evolve, whereby the host evolves towards resisting the infection and the virus towards maintaining its parasitic relationship with the host (Longdon *et al.*, 2015) (Fig. 1). One of the best studied examples of co-evolution developed when wild European rabbits (*Oryctolagus cuniculus*) in Australia and Europe were first exposed to the myxoma virus, which originally infected South American tapeti (*Sylvilagus brasiliensis* and *Sylvilagus bachmani*) where it only resulted in mild disease. Upon introduction to rabbits of European origin the initial mortality rate was as high as 99.8%, leading to a dramatic reduction in the number of viable infected rabbits able to transmit the virus to new hosts *via* mosquito vectors (reviewed by Alves *et al.*, 2019). However, within a two-year period a more attenuated form of the virus was established that still killed 90–99% of the infected rabbits, but allowed infected rabbits to survive for longer periods, thus increasing the chance of transmission of the virus. For the next 30 years the virulence of the myxoma virus was further reduced (70–95%), and the rabbits developed resistance towards it, resulting in a more persistent relationship. As resistance was not complete, virulence then increased again in response to the host's resistance

Table 1. Glossary of terms and their definitions as used in this review

Terms	Definition
Co-evolution	The process of reciprocal, adaptive genetic changes between interacting populations (host and virus).
Virulence	The degree of host mortality within a population (host mortality rate). Virulence will be affected by traits such as infectivity, latent period, transmission mode and burst size.
Acute relationship	A relationship with highly susceptible hosts and highly virulent viruses resulting in rapid lysis of the culture/population.
Persistent relationship	A relationship where both hosts and virus stably co-exist.
Latent time	The time interval between when a virus particle enters the host cell and when the progeny viral particles are released from the host cell.
Infectivity	Percentage of infectious particles of total viral particles produced during an infection cycle.
Decay	Loss of infectivity and degradation of biochemical elements in the environment.
Clade	A group of virus or host strains within a cluster of a phylogenetic tree with a common ancestor. The ancestor can be known or unknown. A clade might be defined both at deep or shallow nodes in the tree.

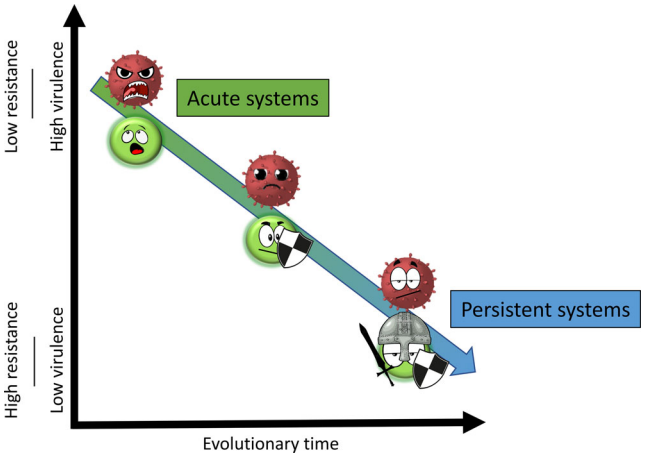


Fig 1. Development of a new virus–host relationship (virus–host arms race). The virulence of viruses will be shaped by different biological trade-offs. See Table 2 and references within Cressler *et al.* (2016) and Alizon *et al.* (2009).

(Gandon & Michalakis, 2000; Kerr *et al.*, 2017; Alves *et al.*, 2019). This well-studied example demonstrates how virus–host relationships evolve as each of the two players struggle for survival, and may lead to an oscillation between acute and persistent infections (Fig. 2B).

Here we review theoretical and empirical studies of the co-evolution of virus–host systems, with a particular focus on the virus–host co-evolution of large double-stranded DNA (dsDNA) viruses and haptophytes. We argue that every new relationship starts as an acute infection, developing into persistent infections with inherent trade-offs (Fig. 1, Table 2). As the two players adjust to the new symbiosis, they may oscillate between acute and persistent infections (Fig. 2B). Further, the virus' infection strategy will be set by its trade-off with the host growth strategy (Fig. 2A, B). As a consequence, frequent events of virus host switching maintain a high diversity of virus–host relationships in terms of the balance between infection acuteness and persistence.

II. MARINE HAPTOPHYTES AND THEIR dsDNA VIRUSES

Haptophytes are increasingly recognised as major primary producers of the global marine phytoplankton communities found in the epipelagic layer of tropical, temperate and polar oceans (Liu *et al.*, 2009; Not *et al.*, 2012). They have been shown to represent up to 30–50% of the photosynthetic standing stock (biomass) in the photic layer of the world's oceans. Haptophytes are highly diverse with important roles in the microbial food web both as primary producers (autotrophs) and as mixotrophic bacterial grazers (Frias-Lopez *et al.*, 2009; Unrein *et al.*, 2014). Morphological and molecular evidence support the division/separation of haptophytes into two classes: the Pavlovophyceae and the Prymnesiophyceae (Edvardsen *et al.*, 2000). Additional lineages, probably representing novel classes, have been discovered based on molecular data from environmental samples (Egge *et al.*, 2015; Shi *et al.*, 2009; Edvardsen, Egge & Vaulot, 2016). The greatest diversity is currently found within the class Prymnesiophyceae, which includes the non-calcifying Phaeocystales and Prymnesiales together with the calcified coccolithophores (Edvardsen *et al.*, 2000; Not *et al.*, 2012). Cultured viruses are only described to infect members of Prymnesiophyceae, whereas no viruses have been described infecting members of Pavlovophyceae, which includes only 13 formally described species (Edvardsen *et al.*, 2016).

Most haptophyte species are thought to reach relatively low abundances in the ocean (up to *ca.* 10^5 cells l^{-1}), co-occurring with several other haptophyte species (Leadbeater, 1972; Estep & MacIntyre, 1989; Thomsen,

Table 2. Key traits in an algal virus–host relationship that affect viral fitness. A fitness trait will involve a biological trade-off (Record *et al.*, 2016). Traits in bold are discussed in this review

	Trait type			
	Morphology	Physiology	Infection mechanism	Infection strategy
Viral traits	Outer lipid membrane *versus* naked viral capsid	**Latent period**	Entry (absorption)	**Host range**
	Size of capsid	Burst size	Release	**Virulence**
		Genome size		**AMGs**
		Decay		**Infectivity**
				Mode of transmission
Host traits	Size of cells	Mobility		
		Growth strategy (gleaners or opportunists)		
		Resistance		

AMG, auxiliary metabolic gene.

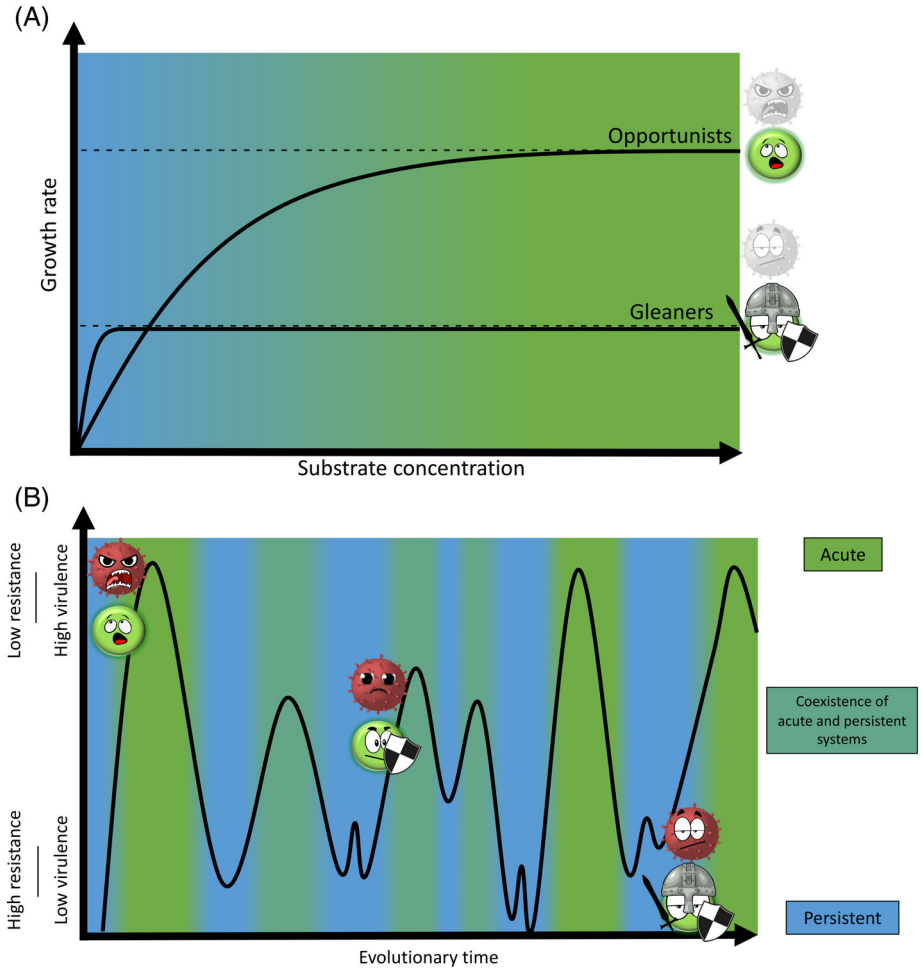


Fig 2. (A) Difference between opportunists and gleaners. At low substrate concentrations gleaners will dominate (blue) while at higher substrate concentrations opportunists will be dominating (green). Dashed lines represent maximum achievable growth rate for either opportunists or gleaners. (B). Virus–host relationships evolve as the two players adjust to a new symbiosis and may oscillate between acute (green) and persistent infections (blue). The oscillation may happen at the clonal, strain or species level. For viruses infecting haptophytes, the range of infection strategies will be the result of mutual trade-off processes between the virus and the growth strategy of its algal host. Haptophyte growth strategies range from opportunists with high growth rates that dominate the plankton during ephemeral blooms (e.g. *Emiliania huxleyi*, *Phaeocystis pouchetii* and *Ph. globosa*) when substrate concentrations are high, to gleaners that co-occur year-round at low abundances (e.g. *Prymnesium kappa* and *Haptolina ericina*) with other haptophyte species, when substrate concentrations are limited. Infection strategies of haptophyte viruses are also on a continuum, from acute infections that rapidly lyse fast-growing hosts, to more persistent infections that are marked by longer latent periods and that infect slower growing hosts.

Buck & Chavez, 1994). However, some haptophytes form extensive, recurrent blooms with large ecological and economic impacts. As major primary producers they produce oxygen and food for the marine food web and assimilate CO_2, but some, such as members of *Prymnesium*, also produces toxins harmful to marine biota (Granéli *et al.*, 2012). Bloom-formers include colony-forming haptophytes of the genus *Phaeocystis*, and the coccolithophores such as the well-studied species *Emiliania huxleyi* (Eikrem *et al.*, 2016). Haptophyte diversity, abundance and dynamics are largely regulated by physico-chemical factors, but also by grazers and parasites, including viruses. Several studies have shown that viruses are instrumental in the regulation of haptophyte blooms (Jacobsen *et al.*, 1996; Castberg *et al.*, 2002; Wilson, Tarran & Zubkov, 2002*a*; Baudoux & Brussaard, 2005).

To date, nine viruses infecting marine haptophyte species have been isolated and thoroughly characterised (see Table 3 and references within). In addition, sparse information exists of a tenth dsDNA virus infecting the haptophytes *Chrysochromulina brevifilium* and *Chrysochromulina strobilus* (CbV-PW1) (Suttle & Chan, 1995; Table 3). Based on a partially sequenced *DNA pol B* gene CbV-PW1 was, as for all other dsDNA algal viruses isolated at that time, suggested to belong to the *Phycodnaviridae* family. Since then, the taxonomy of these algal viruses has been rearranged (Monier *et al.*, 2008)

Table 3. Characteristics of viruses in culture infecting marine unicellular eukaryotic algae belonging to the order Haptophyta

Virus		Host			Characteristics of virus							
Strains	Family/ subfamily	Strain	Class	Growth strategy	Size (nm)	Genome size (kbp)	Latent period (h)	Host specificity	Burst size	Infectivity (%)	Origin of isolation	References
EhV99B1	*Phycodnaviridae*	*Emiliania huxleyi*	Coccolithophyceae	O	160–180	415	12–14	Three of 3 *E. huxleyi* strains tested	400–1000	0.32–1.20	West Coast, Norway	Castberg *et al.* (2002); Saltvedt (2019)
PgV group II	*Phycodnaviridae*	*Phaeocystis globosa*	Prymnesiophyceae	O	100	177	12–16	Five of 12 *Ph. globosa* strains tested	345–381	60–100	Southern North Sea	Baudoux & Brussaard (2005); Brussaard *et al.* (2007)
CeV 01B	*Mimiviridae/ Mesomimivirinae*	*Haptolina ericina*[a]	Prymnesiophyceae	G	160	474	14–19	Two of 4 *H. ericina* strains tested	1800–4100	3	West Coast, Norway	Sandaa *et al.* (2001); R.-A. Sandaa (unpublished)
HeV RF02	*Mimiviridae/ Mesomimivirinae*	*H. ericina*	Prymnesiophyceae	G	190 × 160	581	14–18	Four of 4 *H. ericina* and 1 of 3 *Prymnesium kappa* strains tested	683–933	13	West Coast, Norway	Johannessen *et al.* (2015); Blanc-Mathieu *et al.* (2021)
PgV group I	*Mimiviridae/ Mesomimivirinae*	*P. globosa*	Prymnesiophyceae	O	150	466	10	Four of 12 *Ph. globosa* strains tested	127–356	60–100	Southern North Sea	Baudoux & Brussaard (2005)
PkV RF01	unclassified algae-infecting *Mimiviridae*	*P. kappa*	Prymnesiophyceae	G	400	1420	24–32	Four of 4 *H. ericina* and 1 of 3 *Pr. kappa* strains tested	34–253	2	West Coast, Norway	Johannessen *et al.* (2015); Blanc-Mathieu *et al.* (2021)
PkV RF02	*Mimiviridae/ Mesomimivirinae*	*P. kappa*	Prymnesiophyceae	G	160	580	12–16	Two of 3 *Pr. kappa* strains tested	305–471	44	West Coast, Norway	Johannessen *et al.* (2015); Blanc-Mathieu *et al.* (2021)
PpV 01	*Mimiviridae/ Mesomimivirinae*	*Phaeocystis pouchetii*	Prymnesiophyceae	O	130–160	~485[b]	12–18	Two of 2 *Ph. pouchetii* strains tested	350–600	60–100	West Coast, Norway	Jacobsen *et al.* (1996); Bratbak *et al.* (1998)
PpDNAV	*Mimiviridae/ Mesomimivirinae*	*Prymnesium parvum*	Prymnesiophyceae	O	221	~ 500	ND[c]	Two of 4 *Pr. parvum* and 2 of 3 *Pr. patelliferum* strains tested	ND	ND	East Coast, England	Wagstaff *et al.* (2017)
CbV-PW1	*Phycodnaviridae*[d]	*Chrysocromulina brevifilum*	Prymnesiophyceae	G	145–170	ND	ND	*Chrysocromulina strobilus*	Approx 320	ND	Gulf of Mexico	Suttle & Chan (1995)

ND, not determined; O, opportunists; G, gleaners.
[a]Host taxonomy reassigned from *Chrysochromulina ericina* to *Haptolina ericina*.
[b]Determined by pulsed field gel electrophoresis (R.-A. Sandaa, unpublished data).
[c]Eclipse time reported as 24–48 h. No measurements were preformed between these two timepoints post-infection. Virus particles were detected by transmission electron microscopy (TEM).
[d]Taxonomy based on a partially sequenced *DNA polB* gene.

and divided into two families: *Phycodnaviridae* and *Mimiviridae*. Our phylogenetic analysis confirms the placement of CbV-PW1 in the *Phycodnaviridae* (data not shown) but since restricted genetic information for CbV-PW1 is available, its placement within the *Phycodnaviridae* remains uncertain, and CbV-PW1 is not included in our phylogenetic tree (Fig. 3).

The haptophyte viruses isolated to date all have dsDNA genomes and belong to the nucleocytoplasmic large DNA virus (NCLDV) assemblage (Koonin, Senkevich & Dolja, 2006; Sandaa *et al.*, 2021). The evolutionary relationships among giant algal viruses have been inferred by comparing a set of conserved core genes common to all NCLDVs (Iyer, Aravind & Koonin, 2001; Yutin *et al.*, 2009). Eight of 47 suggested core genes of NCLDVs (DNApolB, D5-like primase/helicase, VLFTF3-like transcription factor, TFIIS, pATPase, MCP, RNAP-a and b) are the most conserved and are present in more than 92% of the sequenced genomes (Yutin *et al.*, 2009; Guglielmini *et al.*, 2019). Based on these genes, viruses infecting phytoplankton fall within two related families, *Phycodnaviridae* and *Mimiviridae* (Fig. 3). Another striking feature of algal viruses within the NCLDV is the array of host-derived auxiliary metabolic genes (AMGs), which encode a diverse range of putative functions (Moniruzzaman *et al.*, 2020; Schulz *et al.*, 2020). These genes make the viruses more independent from their hosts by allowing the virus to manipulate the host during infection. The functions of AMGs have been linked to central roles in photosynthesis in cyanobacteria (Lindell *et al.*, 2004), sphingolipid biosynthesis of *E. huxleyi* (Moniruzzaman *et al.*, 2020; Schulz *et al.*, 2020), nitrogen uptake in *Ostreococcus* (Monier *et al.*, 2017) and even central roles in the tricarboxylic acid (TCA) cycle/oxidative phosphorylation chain, potentially controlling energy production in the host cells during infections (Blanc-Mathieu *et al.*, 2021).

The haptophyte-infecting phycodnaviruses fully described to date infect the bloom-forming *E. huxleyii* and *Phaeocystis globosa* (Table 3). The haptophyte-infecting *Phycodnaviridae* tend to have smaller capsids and genomes compared to haptophyte-infecting *Mimiviridae* (Table 3). The EhV viruses, which infect *E. huxleyi*, belong to the genus *Coccolithoviruses*, and form a distinct clade within the *Phycodnaviridae* family (Wilson, Van Etten & Allen, 2009) (Fig. 3). This is the most studied haptophyte–virus system where several examples of both chemical and molecular arms races between viruses and hosts have been described (Vardi *et al.*, 2012; Rosenwasser *et al.*, 2014; Schatz *et al.*, 2017). It is also suggested that EhV may affect the life cycle of its host (Frada *et al.*, 2008; von Dassow *et al.*, 2015). Viruses infecting *Ph. globosa* are divided into two groups that differ in genome and particle size, where those of the smallest size (group II), are assigned to *Phycodnaviridae* family, whilst group I is assigned to the *Mimiviridae* family (Baudoux & Brussaard, 2005; Santini *et al.*, 2013).

Most cultured haptophyte viruses group within the *Mimiviridae* family (7 out of 10 characterised species; Table 3). The members of this family include extremely large viruses infecting heterotrophic protists (Megavirinae), and viruses infecting photosynthetic protists that fall in, or close to, the Mesomimivirinae group (Claverie & Abergel, 2018) (Fig. 3). The Mesomimivirinae group includes viruses infecting bloom-forming hosts like *Phaeocystis pouchetii*, *Ph. globosa* and *Prymnesium parvum* (PpV, PgV Group II, and PpDVAV, respectively (Jacobsen *et al.*, 1996; Santini *et al.*, 2013; Wagstaff *et al.*, 2017). In addition, the group also consists of several viruses infecting hosts such as *Haptolina ericina* (previously named *Chrysochromulina ericina*) and *Prymnesium kappa* (previously named *Chrysochromulina kappa*), that normally do not form massive blooms, but rather are present at low densities all year round (Sandaa *et al.*, 2001; Johannessen *et al.*, 2015; Johannessen *et al.*, 2017). These viruses are Prymnesium kappa virus RF02 (PkV RF02), Haptolina ericina virus RF02 (HeV RF02) and Chrysochromulina ericina virus 01B (CeV 01B) (Table 3). The name CeV 01B reflects the original name of its host, which was changed from *C. ericina* to *H. ericina* after the naming of the virus (Edvardsen *et al.*, 2011). PkV RF02 and CeV 01B each infect two strains within their host species, while HeV RF02 has a broader host specificity, infecting four strains of *H. ericina* and one strain of *Pr. kappa* (Table 3).

PkV RF01, a virus infecting *Pr. kappa* in addition to four strains of *H. ericina*, belongs to an unclassified group that makes a separate branch in the *Mimiviridae* family, relatively close to the Mesomimivirinae group (Fig. 3). This virus is the largest of the haptophyte viruses (1.42 Mbp genome and 400 nm particle size; Table 3) with a structure that also differs from other characterised NCLDVs (Blanc-Mathieu *et al.*, 2021). An internal rod-shaped core filled with dense material is found in the centre of the virion and convoluted internal membranes cover up to 60% of the interior of the particle. The biological function of such internal membranes has been linked to the release of the viral nucleoprotein core or genome by fusion with the host plasma membrane, and also to the assembly processes of the particle (see references within Huiskonen & Butcher, 2007).

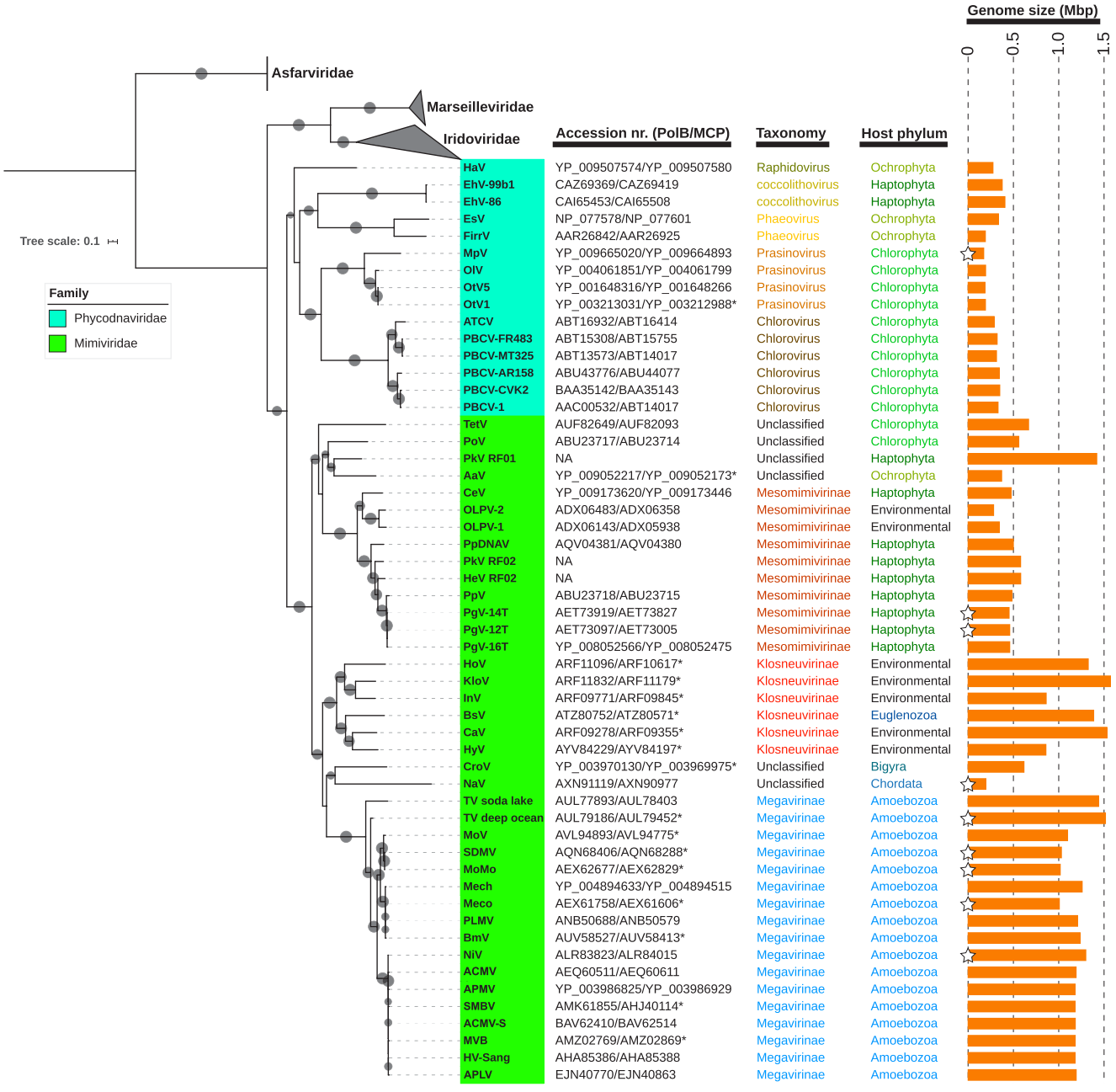
III. CO-EVOLUTION OF ALGAL VIRUSES AND THEIR HAPTOPHYTE HOSTS

(1) Characterisation of haptophyte–virus infection strategies

Phytoplankton balance biochemical resource acquisition with growth rates, and are often categorised as opportunists, which are adapted to feeding in nutrient-rich environments and with high growth rates (Fig. 2A), or gleaners, which have a higher substrate affinity but lower growth rates (Fig. 2A) (Lévy *et al.*, 2015; Vallina *et al.*, 2019; Kiørboe & Thomas, 2020). Gleaners will outcompete opportunists at low nutrient levels, while opportunists will out-grow gleaners under nutrient-replete conditions (Vallina *et al.*, 2019). Shifts in biochemical resource availability occur seasonally, creating environments that alternately favour opportunists or gleaners. In the period from late spring to early summer, vertical mixing leads to high nutrient levels at the surface, which favour opportunists with high growth rates, as demonstrated

by ephemeral algal blooms. Stratification of the water column, as often seen during late autumn and in the winter period, leads to lower nutrient levels and favours gleaners with high substrate affinity and low maximum growth rates. Haptophytes can be divided into these two different growth strategies, with opportunists dominating the plankton during ephemeral blooms when nutrient supply is high, and gleaners co-occurring year-round at low abundances when nutrient supply is limited (Thomsen *et al.*, 1994; Egge *et al.*, 2015).

Phytoplankton diversity will also be affected by nutrient input due to the trade-off between rapid growth and competition for limited resources (Lévy *et al.*, 2015). Studies on haptophyte richness in two fjords in Norway document lowest richness during late spring (April–May) followed by the winter period (Egge *et al.*, 2015; Johannessen *et al.*, 2017). Highest richness was detected between August and November, which would be the period between perturbation and stratification, with fluctuating conditions where both opportunists and gleaners might co-exist due to the trade-off between rapid growth and competitive ability (Litchman *et al.*, 2007; Lévy *et al.*, 2015).



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Infection strategies of haptophyte viruses are also on a continuum, from acute infections that rapidly lyse the host, to more persistent infections that are marked by longer latent periods and lower virulence (Table 3, Figs 2B and 4). This range of infection – and growth – strategies used by haptophyte viruses and their hosts provides us with a unique opportunity to examine trade-offs between virulence and transmission, how infection strategies evolve, and how a diversity of infection strategies is maintained. While the number of virus–host pairs currently available for such examination is limited, an interesting framework emerges when they are compared that is presented here to stimulate further exploration.

Viruses that infect bloom-forming haptophytes, such as EhV (Castberg *et al.*, 2002), PpV (Jacobsen *et al.*, 1996) and PgV (Baudoux & Brussaard, 2005), which infect certain strains of *E. huxleyi*, *Ph. pouchetii* and *Ph. globosa* respectively, have short latent periods of 10–18 h (mean 13 h) and end with host lysis (Table 3). This acute infection strategy results in the rapid lysis of annual *E. huxleyi* blooms in nature by specific EhV strains with reported mortality rates between 40 and 100% (Jacquet *et al.*, 2002; Wilson *et al.*, 2002*b*; Schroeder *et al.*, 2003). Surprisingly, the proportion of infectious particles determined by most probable number (MPN) for EhV was very low (0.3–1.2%, Table 3) when tested on viruses and hosts that had been kept in culture for decades. Fresh lysates of a newly isolated EhV produced plaque and MPN assays of infectious particle number that were similar to total virus counts derived from SYBR Green I staining (Vaughn *et al.*, 2010), indicating that a high proportion of the virus particles produced by the new isolate were infectious. This suggests that some virus–host systems lose their infectivity in culture and can evolve towards more stable coexistence with their hosts during cultivation. Interestingly, no resistance occurred in the freshwater alga *Chrysocromulina parva* after infection with its virus CpV-BQ1 (Mirza *et al.*, 2015). Even after 6-month incubations no regrowth was observed. This shows that the arms race between viruses and hosts is complex and probably multifactorial even in cultures.

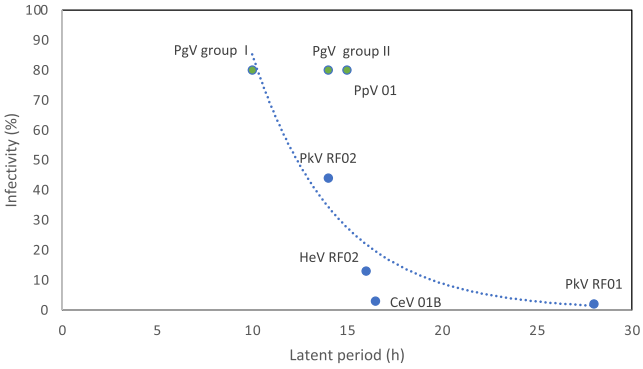

Fig 4. Correlation between infectivity, e.g. percentage of infectious particles of total viral particles produced during an infection cycle and latent period for the characterised haptophyte viruses ($R^2 = 0.464$). Green dots are viruses infecting opportunists (acute systems), blue dots are viruses infecting gleaners (more persistent systems). CeV 01B, Chrysochromulina ericina virus 01B; HeV RF02, Haptolina ericina virus; PgV group I, Phaeocystis globosa virus group I; PgV group II, Phaeocystis globosa virus group II; PkV RF01, Prymnesium kappa virus RF01; PkV RF02, Prymnesium kappa virus RF02; PpV 01, Phaeocystis pouchetii virus 01.

High proportions of infectious particles (60–100%) are observed for both PgV groups (I and II) and PpV (Table 3), which contributes to rapid transmission rates and population lysis. This presents what appears to be a paradox; highly virulent viruses risk extinction due to their potential to exterminate their obligate hosts. Models indicate that high virulence is supported by large, dense host populations because high host densities ensure successful horizontal transmission of

(Figure legend continued from previous page.)
Fig 3. Bayesian phylogenetic tree of nucleocytoplasmic large DNA viruses (NCLDVs) reconstructed from a concatenated alignment of two core nucleocytoplasmic virus orthologous genes: major capsid protein (*MCP*) and DNA polymerase B (*PolB*). Grey circles indicate branches with bootstrap values above 50. The tree was rooted to midpoint. The scale bar indicates substitutions per site. The taxonomy lists the genus of viruses in *Phycodnaviridae* and the sub-families of viruses in *Mimiviridae*. The star symbol indicates partially sequenced genomes. The tree was edited using ITOL (Letunic & Bork, 2019). AaV, Aureococcus anophagefferens virus BtV-01; ACMV-H, Acanthamoeba castellanii mamavirus Hal-V; ACMV-S, Acanthamoeba castellanii mimivirus shirakomae; APLV, Acanthamoeba polyphaga lentillevirus; APMV, Acanthamoeba polyphaga mimivirus; ATCV, Acanthocystis turfacea Chlorella virus 1; BmV, Bandra megavirus; BsV, Bodo saltans virus NG1; CaV, Catovirus CTV1; CeV, Chrysochromulina ericina virus; CroV, Cafeteria roenbergensis virus BV-PW1; EhV-99b1/86, Emiliania huxleyi virus; EsV, Ectocarpus siliculosus virus 1; FirrV, Feldmannia irregularis virus 1; HaV, Heterosigma akashiwo virus 01 HaV53; HeV RF02, Haptolina ericina virus; HoV, Hokovirus HKV1; HV-Sang, Hirudovirus Sangsue; HyV, Hyperionvirus; InV, Indivirus ILV1; KloV, Klosneuvirus KNV1; Mech, Megavirus chiliensis; Meco, Megavirus courdo7 Mv13-c7; MoMo, Moumouvirus Monve Mv13-mv; MoV, Moumouvirus australiensis 10A; MpV, Micromonas pusilla virus SP1; MVB, Mimivirus Bombay; NaV, Namao virus; NiV, Niemeyer virus; OLPV-1, Organic Lake phycodnavirus 1; OLPV-2, Organic Lake phycodnavirus 2; OlV, Ostreococcus lucimarinus virus 1; OtV1/OTV5, Ostreococcus tauri virus; PBCV-1/FR483/MT325/AR158/CVK2, Paramecium bursaria Chlorella virus; PgV-12T/14T/16T, Phaeocystis globosa virus; PkV RF01, Prymnesium kappa virus; PkV RF02, Prymnesium kappa virus; PLMV, Powai lake megavirus 1; PoV, Pyramimonas orientalis virus 01; PpDNAV, Prymnesium parvum DNA virus BW1; PpV, Phaeocystis pouchetii virus 01; SDMV, Saudi moumouvirus; SMBV, Samba virus; TetV, Tetraselmis virus 1; TV deep ocean, Tupanvirus deep ocean; TV soda lake, Tupanvirus soda lake. NA: not available in public databases. [Correction added on 24 September 2021, after first online publication: Figure 3 has been updated in this version.]

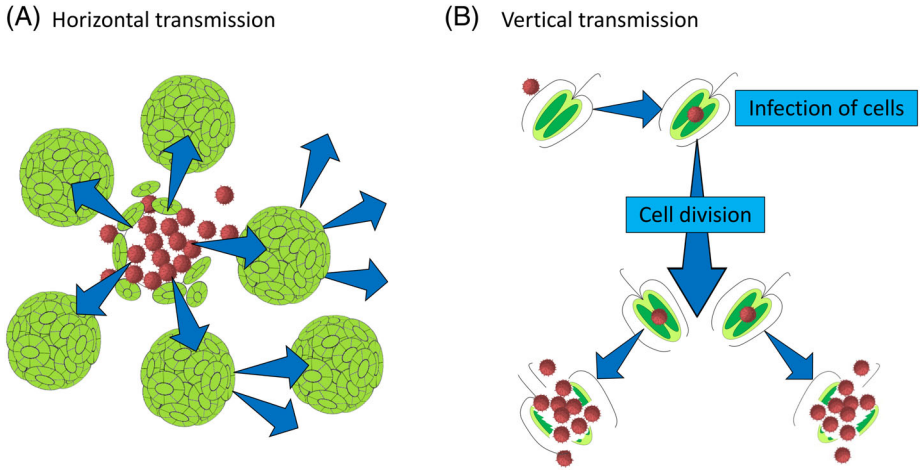

Fig 5. Abundant hosts increase the chance of horizontal transmission (A) while viruses of low-abundance host cells should favour long decay, vertical transmission and/or long latency to ensure survival (B). Vertical transmission should select for reduced virulence, but mixed-mode transmission will also select for evolutionary reduction in virulence, regardless of which transmission (horizontal or vertical) mode is more common (see references within Cressler *et al.*, 2016).

viral progeny to new hosts (King *et al.*, 2009; Fig. 5). As such, haptophyte blooms may create the conditions that favour and sustain acutely infecting viruses.

Less is known about the role of viruses infecting haptophytes occurring at lower abundances in the sea. Host populations presumably have to exceed a certain threshold density to sustain a virus population (Wiggins & Alexander, 1985; Murray & Jackson, 1992; Suttle & Chan, 1994; Wommack & Colwell, 2000; Johannessen *et al.*, 2015), a condition that is met given that viruses such as HeV RF02, CeV 01B, PkV RF01 and PkV RF02 infect non-blooming strains of *H. ericina* and *Pr. kappa* (Table 3). These viruses have slightly longer latent periods (mean 18.6 h) and produce a lower proportion of infectious particles (mean 15.5% infectious particles compared to those infecting the bloom-former *Phaeocystis* group [PgV group I and II, PpV, mean 80% infectious particles (Fig. 4)]. This trend towards longer-lasting infections as hosts become scarce increases the chances of vertical transmission rather than horizontal transmission (Fig. 5), and is predicted to have an effect on virus fitness (Table 2) (Weitz *et al.*, 2019; reviewed in Cressler *et al.*, 2016).

In addition to differences in latent periods and mortality rates, we also see differences in the host ranges described to date for haptophyte-infecting viruses. However, defining the complete host range for phytoplankton viruses is impossible as all potential hosts will never be available in culture collections. In addition, the phylogenetic relationships of all haptophyte, and possibly other hosts, would need to be firmly established. Regardless, we can compare the relative ranges of haptophyte viruses to one another, and make some interesting observations. The highly acute viruses within the group PgV-I are more host-specific and have a shorter latent period (10 h) compared to the less-acute group II PgVs (mean 14 h), which are able to infect more diverse strains of *Ph. globosa* (Baudoux & Brussaard, 2005). Further, PpV 01, PkV RF02, EhV99B1, and CeV 01B all infect multiple strains of their host species and have longer latent periods (mean 14.6 h) compared to PgV-I. By contrast, several haptophyte viruses, e.g. PkV RF01, HeV RF02 and PpDNAV, have broad host ranges relative to their close counterparts (Table 3); their ability to infect different species of haptophytes increases the availability of these non-blooming hosts. This generalist strategy is common among pathogens (discussed in Woolhouse, Taylor & Haydon, 2001; Leggett *et al.*, 2013), and is associated with trade-offs in the form of 'paying' a higher infectivity cost and decreasing transmission with longer replication times, higher decay rates and decreased infectivity. Consistent with this, the two multi-species-infecting haptophyte viruses, HeV RF02 and PkV RF01, produce lower proportions of infectious particles (13 and 2%, respectively) and have slightly longer replication times (16 and 28 h, respectively) relative to other haptophyte viruses with more restricted host ranges (PgV, PkV RF02, PpV; mean 71% infectious particles, and mean 13.9 h replication time; Fig. 4). CeV, on the other hand, has a restricted host range of only two strains of *H. ericina*, but shows infectivity values more similar to those of multi-species-infecting viruses (Table 3).

Based on these findings, the infection strategy used by a virus seems to reflect the growth strategy of its host(s) (Fig. 2) (Thingstad, 2000; Våge, Storesund & Thingstad, 2013; Thingstad *et al.*, 2014). Hence, we suggest that the diversity of infection strategies used by different haptophyte viruses results from mutual trade-off processes between the virus and the diversity of host growth strategies, changing from acute systems with opportunistic hosts to more persistent systems with gleaners as hosts (Figs 2B and 6).

(2) Co-evolution between haptophytes and their viruses

An inevitable outcome of virus–host interactions is co-evolution, whereby two organisms influence the evolutionary path

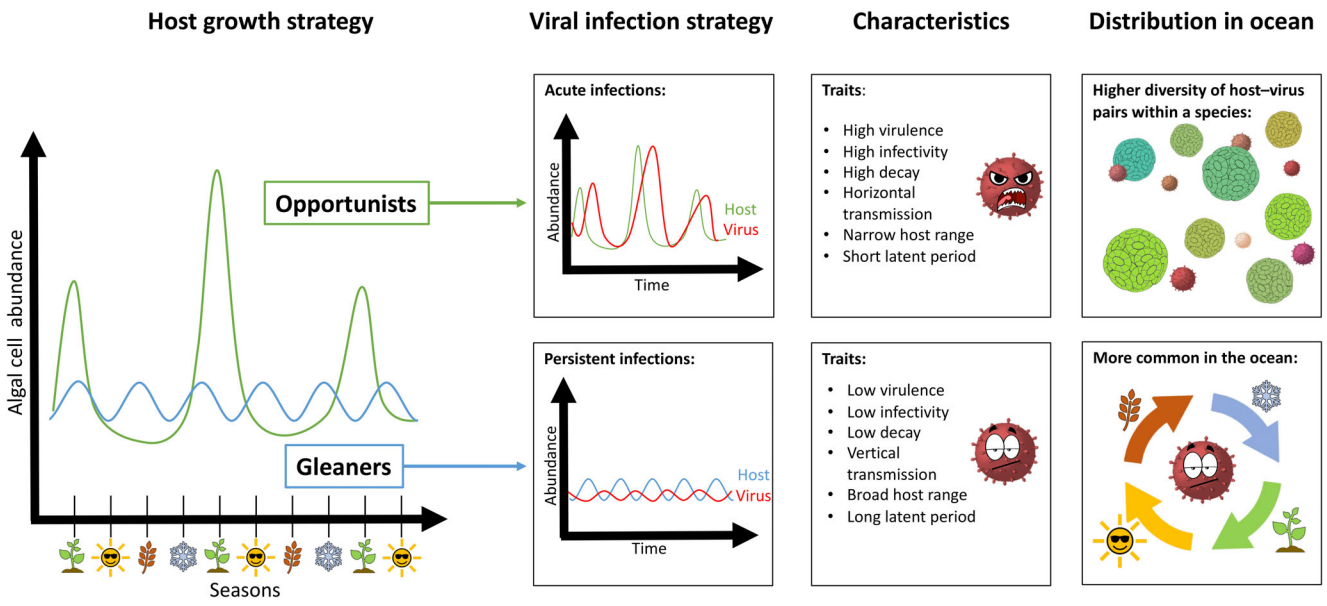

Fig 6. Differences in phytoplankton host growth strategies might have a major effect on the development of different viral infection strategies (Thingstad, 2000). We suggest that opportunistic microalgae, which form recurrent blooms in the ocean, are associated with viruses with an acute infection strategy. Acute viruses are characterised by a short latent period, high virulence, high infectivity, high decay, a narrow host range and are transmitted horizontally to their hosts. By lysing the most rapidly growing hosts, acute viruses enable the co-existence between slow and fast-growing host populations, contributing to the maintenance of diversity on the strain/clone (within a clade) level (Thingstad *et al.*, 2014). Thus, strong viral control contributes to the large diversity within certain virus–host systems, as seen for example for *Emiliania huxleyi*–EhV (Rowe *et al.*, 2011). Further, we suggest that microalgae that co-occur year round at low abundances (gleaners) with other microalgae species are associated with viruses of a more persistent nature, characterised by a longer latent period, lower virulence, low infectivity and low decay compared to the acute systems. These systems have a broader host range and are transmitted to their host vertically or by a mixed mode (Fig. 5). We suggest that persistent systems are more common in the ocean, although they often are neglected due to their low abundances and less eye-catching symptoms compared to their acute relatives. Within each system there will always be a continuum of acuteness and persistence as each trait involves a life history trade-off.

of one another. All known viruses infecting haptophytes have been described as lytic viruses. Nevertheless, there is a continuum in infection strategies from rapidly lysing the host to more persistent infections resulting in reduced host mortality. Little is known, however, about how persistency is developed within these virus–host systems.

Laboratory experiments with infected *E. huxleyi*, *H. ericina* and *Ph. pouchetii* demonstrated the recovery of host populations after virus-induced lysis, leading to the stable coexistence of surviving hosts and their viruses for up to 1 year (Thyrhaug *et al.*, 2003). The recovery effect was most pronounced in cultures with high virus:host ratios (100, 10) relative to low virus:host ratios (1, 0.25). The ecological significance of differences in virus:host ratios in nature has, however, been debated (Parikka *et al.*, 2017). It could also not be determined if stable coexistence emerged from a shift in the type of infection (i.e. lytic to latent), or as a consequence of host resistance. In related viruses in the *Phycodnaviridae* family it has recently been shown that viruses can reach stable coexistence with their host (persistence), i.e. population maintenance of host and virus instead of sudden culture lysis. The mechanism behind the resistance involves a large deletion on one chromosome generating susceptible cells that maintain viral production (Yau *et al.*, 2020). Coexistence of virus and host has also been demonstrated for PkV RF01 and its haptophyte host, *Haptolina ericina*. In a recent study, *H. ericina* rapidly developed resistance (10 days post-infection) when infected with PkV RF01. The culture was maintained and PkV RF01 was detected more than a year later, being present but without lysing the culture, suggesting a persistent or latent relationship between the virus and its host (M.R. Saltvedt, unpublished results).

Virus–host interactions may even extend beyond the cell, as seen for some bacteriophages where certain phages may modify the state of the host cells by a quorum sensing-like mechanism, shifting the outcome of the infection from lysis to lysogeny or *vice versa* (Erez *et al.*, 2017; Stokar-Avihail *et al.*, 2019), or by using host-encoded signalling molecules (Silpe & Bassler, 2019). A similar communication system may also be involved in haptophyte–virus systems as virus-free filtrate from lysed cultures confers protection to the host, or at least a shift away from lytic infection towards a more persistent infection (Thyrhaug *et al.*, 2003). Recent modelling efforts on bacteriophage–host systems have revealed conditions where chronic viruses require lytic viruses for survival, invasion and persistence (Gulbudak & Weitz, 2019). All of these examples illustrate the existence of several dimensions to virus–host relationships beyond the simple lytic–lysogenic

continuum. The diversity in these relationships may be important for virus–host coexistence in nature.

As viruses and hosts interact, hosts respond to new threats by developing resistance. If resistance is complete, a virus must find a new host or risk extinction. If resistance is not complete, the virus will evolve to counter host resistance and *vice versa*, resulting in a continuous arms race (Fig. 2). Embedded in this arms race, each benefit (fitness trait) comes with a cost in the form of a trade-off (Record *et al.*, 2016). Examples of host trade-offs for viral resistance include reduced competitiveness for nutrient sequestration (Martiny *et al.*, 2014; Bidle, 2016) and the sacrifice of a host subpopulation by programmed cell death to prevent disease transmission to kin (Bidle, 2016), while virus fitness traits are linked to successful production of progeny and transmission of disease and include among others, viral persistence, latent period, host range, adsorption, beneficial auxiliary metabolic genes, burst size, and proportion of infectious progeny (Table 2; Record *et al.*, 2016; Weitz, 2015).

(3) How does host switching develop?

To establish a sustainable relationship with a new host, a virus must evade an array of host defence mechanisms, and also satisfy its biochemical needs by using a host's metabolic intermediates. The virus also needs to proliferate within the host before efficient transmission to another host. While some host spillovers are successful, most are unsuccessful, resulting in dead-end infections (Brown & Bidle, 2014; Longdon *et al.*, 2014; Wood *et al.*, 2012; reviewed in Parrish *et al.*, 2008) where the virus can infect the host but not transmit to new hosts due to small/non-existent bursts or a low proportion of progeny being infectious. The low maximum growth rates of gleaners could also lead to an evolutionary dead end for viruses, but may be evaded by a reduction in virulence that permits vertical transmission (Fig. 5). Such spillover infections may either die out or result in local transmissions in the new host population, which in turn may either perish or eventually serve as a stepping stone for new infections. The latter scenario could lead to survival of the virus through extended periods in sub-optimal hosts, eventually colonising distantly related hosts (Parrish *et al.*, 2008). Additionally, the reversible attachment of viruses to host receptors that do not result in infections might serve as a refugium for the viruses until more susceptible hosts become available.

Host range expansion to closely related hosts may be more successful and less costly for the virus than expanding to infect distantly related hosts, as closely related hosts will present an intracellular environment to which the virus is already adapted (Longdon *et al.*, 2011, 2014). Furthermore, switches to close relatives may benefit from an increased chance of exposure due to the shared ecological niches of closely related hosts, as would occur among the non-blooming haptophytes that coexist in the environment (Endo, Ogata & Suzuki, 2018). This means that switching to hosts belonging to the same phylogenetic clade is more probable than switching to a clade with increased phylogenetic distance (Engelstädter & Fortuna, 2019).

Many of the acute prasinoviruses (which infect green algae of the Mamiellophyceae) and EhVs can infect several different strains within a species (Rowe *et al.*, 2011; Bellec *et al.*, 2014), but rarely other species within the same genus (Castberg *et al.*, 2002; Derelle *et al.*, 2008). This high degree of host specificity is common among the algal viruses characterised to date (Nagasaki & Bratbak, 2010; Clerissi, Desdevises & Grimsley, 2012; Bellec *et al.*, 2014). Certain host clades (strain or clone level) may be more prone to infection than others, and the number of members within the host clade, rather than the characteristics of the clade members, may be an important factor for the overall infection level of viruses (Engelstädter & Fortuna, 2019). An alternative explanation might be that viral infection creates high diversity within certain host clades, as seen in other systems (Duxbury *et al.*, 2019). By lysing the most competitive, fast-growing hosts, viruses enable the co-existence of slow and fast-growing host populations, contributing to the maintenance of diversity on the strain/clone (within a clade) level (Thingstad *et al.*, 2014). As such, strong viral control might contribute to the high levels of diversity observed within some acutely infected hosts such as *E. huxleyi*, *Ostreococcus tauri*, and *Micromonas pusilla* (Rowe *et al.*, 2011; Bellec *et al.*, 2014).

Viruses are also able to shift to host clades distantly related to the original host, as evidenced by the number of human pathogens that have originated through host switches, including HIV (Sharp & Hahn, 2010), Ebolaviruses (Leroy *et al.*, 2005), SARS-CoV-2 (Cui *et al.*, 2019), Influenza viruses (Webby & Webster, 2001) but also NCLDVs and their eukaryotic hosts (see Section III.4). The ability to jump between distantly related species may be linked to genetic factors such as the use of conserved host receptors to enter the cell (Baranowski, Ruiz-Jarabo & Domingo, 2001; Woolhouse *et al.*, 2005) or jumping to hosts that do not possess broad resistance mechanisms to that type of virus (Streicker *et al.*, 2010). There are several factors that would, in theory, decide the outcome of such switches, like the number of mutations required for receptor binding, recombination or reassortments of viral genomes that allow the acquisition of multiple genetic changes in a single step. The mutation/recombination/reassortment rate of the virus genome will determine the rate of variation and will thus also decide the outcome of switches. Further, trade-offs linked to host switching, such as mutations that optimise the ability of a virus to infect a new host, will likely reduce its fitness in the original hosts. Mutation rates normally vary dramatically between DNA and RNA viruses (Parrish *et al.*, 2008; Longdon *et al.*, 2014).

The number of mutations required for a host switch might be less within closely related species, such as *Pr. kappa* and *H. ericina* as hosts for HeV RF02 and PkV RF01, which belong to two sister clades within the order Prymnesiales (Edvardsen *et al.*, 2011), than for a switch between more distant relatives. Even so, viruses have been able to switch to hosts distantly related to their original host, showing that

factors other than genetics are important. Among environmental factors, close physical contact has been shown to facilitate host jumps, such as from birds or bats to humans (Parrish *et al.*, 2008), and infection strategy does not limit the potential for jumps, as both specialist and generalist viruses are able to switch to new hosts (Parrish *et al.*, 2008). Host-range expansions beyond the species level, however, would theoretically be more common among generalist viruses due to their increased potential for encountering new hosts, but would also come at the expense of a virus's reproductive fitness (Duffy *et al.*, 2006). This may explain why the haptophyte viruses with the widest host ranges are the least virulent (HeV RF02, PkV RF01; Table 3).

(4) How can we detect host switching?

Different phylogenetic methods have been used to describe virus–host co-evolution (Longdon *et al.*, 2011; Bellec *et al.*, 2014; Martínez-Aquino, 2016). Evidence for co-evolution typically comes from a match between the phylogenetic trees of viruses and their hosts. For prasinoviruses and their hosts belonging to the order Mamiellales, such analyses have shown that these viruses are mainly host specific as they are restricted to infecting strains within the same species (Bellec *et al.*, 2014). If there is an incongruence between the host and virus phylogenetic analysis, e.g. if the topology of the viral phylogenetic tree is different from the host it infects, this indicates a host switch by the virus. Similarly, a mismatch in the topology of phylogenetic trees of viruses and their hosts provides evidence for several events of host switching among NCLDVs. For example, although the relatively distantly related viruses EhV (*Phycodnaviridae*) and PkV (*Mimiviridae*) both infect haptophytes, there are phylogenetically closer relatives of PkV within *Mimiviridae* including viruses infecting a wide range of hosts, such as amoebae, heterotrophic protists, fish, haptophytes and green algae (Fig. 3).

Evolutionary relationships between algal viruses and hosts may also be investigated using the phylogenetic information available in viral AMGs (vAMGs). Viral AMGs may often be derived from cellular life and, as such, might give insight into historical hosts. Close evolutionary relationships of viral and host AMGs might indicate recent acquisition of the vAMGs from their present hosts by horizontal gene transfer. In Ostreococcus tauri virus (OtV) the viral gene for ammonium transporter (vAmt) branches together with the *Ostreococcus tauri* version of the gene, indicating a recent transfer of the gene to the virus genome (Monier *et al.*, 2017). A similar case is seen in the genomes of EhVs, where sphingolipid-synthesising enzyme genes resemble those of their host, *E. huxleyi* (Wilson *et al.*, 2009). By contrast, for PkV RF01 the phylogeny of two genes involved in energy production (*vSdhA*, *vSdhB*) branch deeply within eukaryotic lineages, distant from the *Sdh*s of the few sequenced haptophytes *Chrysochromulina* sp. and *E. huxleyi* (Blanc-Mathieu *et al.*, 2021). This suggests that the *Sdh* genes in PkV RF01 were acquired at an early stage in the radiation of eukaryotic lineages.

IV. ARE INFECTION STRATEGIES AND *IN SITU* DIVERSITY RELATED?

Haptophytes and the viruses that infect them are ubiquitous, being found in the epipelagic layer of tropical, temperate and polar oceans (Liu *et al.*, 2009; Endo *et al.*, 2018; Mihara *et al.*, 2018). The abundance of NCLDVs reaches over 10^4–10^5 genomes ml^{-1} in the photic zone (Hingamp *et al.*, 2013) and their taxonomic richness exceeds what has been found for prokaryotes (Mihara *et al.*, 2018). Of the NCLDV core gene sequences found in microbial metagenomes 88% are from the families *Phycodnaviridae* and *Mimiviridae* (referred to as Megaviridae herein). Within the family *Phycodnaviridae*, 86% are prasinoviruses, whereas 14% are assigned as other *Phycodnaviridae*, some with phylogenetic similarity to EhV. Most members of *Mimiviridae* cluster with viruses infecting autotrophic protists (CeV, PoV, PpV, OLPVs) and CroV, while only a few cluster with the amoeba-infecting viruses mimi- and megaviruses. Mihara *et al.* (2018) also confirm the high abundance of mimiviruses infecting autotrophic protists, as most reads (95.1%) were assigned to the *Mesomimivirinae* subfamily, and only 4.6% of the reads were similar to the *Megamimivirinae* subfamily. Recent metabarcoding studies targeting *Mimiviridae* revealed several hundreds to thousands of operational taxonomic units (OTUs) (at 97% identity) in a few litres of seawater samples (Prodinger *et al.*, 2020). These studies highlight the potential high diversity and abundance of viruses infecting haptophytes in the ocean, suggesting an important ecological role. For example, viruses have been suggested to increase the efficiency of the biological carbon pump – the downward vertical transport of particulate carbon in the ocean (Suttle, 2007). Eukaryotic viruses were recently shown to be strongly associated with variation in carbon export efficiency (Kaneko *et al.*, 2020). Of these eukaryotic viral linages, viruses infecting putative haptophytes, together with prasinoviruses, were the most strongly associated with this variation.

Seasonal studies of haptophytes and their viruses have been performed on samples from different fjords in Norway using a metabarcoding approach (Egge *et al.*, 2015;Johannessen *et al.*, 2017; Gran-Stadniczeñko *et al.*, 2019). These results show uncoordinated variation in the virus and host community composition and diversity throughout the year (Johannessen *et al.*, 2017; Gran-Stadniczeñko *et al.*, 2019). A minority of the viral OTUs are highly abundant at specific time points, indicating a boom–bust relationship with their host, whereas most of the viral OTUs are very persistent. This pattern has also been reported from other marine viral–host systems (Waterbury & Valois, 1993; Zingone, Sarno & Forlani, 1999) and in freshwater viruses infecting haptophytes (Short & Suttle, 2003; Short, Rusanova & Short, 2011). An explanation for this persistence in nature might be that the viruses are able to coexist with their hosts through chronic infections, and/or are able to exploit several host species. The latter might also be linked to vertical transmission and low virulence as several taxa within the haptophytes can be characterised as gleaners (Thomsen

et al., 1994). The haptophyte taxa in the above study belong to *Phaeocystis*, *Chrysocromulina*, *Haptolina*, *Prymnesium* and *Emiliania* – genera that are well known to include species susceptible to viral infection. Diversity was highest for the order Prymnesiales, with 35 and 21 unique OTUs assigned to Chrysochromulinaceae and Prymnesiaceae, respectively (Bittner *et al.*, 2013; Egge *et al.*, 2015; Johannessen *et al.*, 2017) – gleaners that are infected by persistent viruses (e.g. PkV RF01, Cev 01B, and HeV RF02). Although these data support our hypothesis about persistent relationships being common in nature, we cannot rule out that the available molecular methods are not sensitive enough to capture strain- and clonal-level variation in viruses and their hosts.

V. CONCLUSIONS

(1) Different viral infection strategies result from mutual trade-off processes between the virus and the growth strategy of its algal host. The different infection strategies come with differences in fitness traits (Fig. 6) and biological trade-offs. We suggest that acute viruses are characterised by a short latent period, high virulence, high infectivity, high decay, a narrow host range and are transmitted horizontally to their hosts. By lysing the most rapidly growing hosts, acute viruses enable the co-existence between slow and fast-growing host populations, contributing to the maintenance of diversity on the strain/clone (within a clade) level. Diversity within acute virus–host systems might develop faster compared to persistent systems due to the growth strategy of the host.

(2) Considering the abundance of slow-growing gleaners in the ocean, persistent and chronic infections are likely much more common than currently known (Weitz *et al.*, 2019). These low-virulence viruses employ a variety of strategies to co-exist with their gleaning hosts (Fig. 6). These systems are characterised by viruses with a longer latent period, lower virulence, low infectivity and low decay compared to acute systems. Further they have a broader host range and are transmitted to their hosts vertically or by mixed modes. We highlight their potential role and importance in shaping haptophyte populations and communities, hoping to stimulate future research into these understudied systems.

(3) Within each of these two types of viral host systems (acute and persistent) there will always be a continuum of acuteness and persistence as each trait involves a life history trade-off.

(4) There is a critical need for culturing different types of microalgae virus–host systems, including the rare ones, using unconventional culturing techniques. Only cultured virus–host systems will provide basic knowledge of the important biological factors that control the evolution of virus–host relationships and how their evolutionary trajectories affect the diversity of primary producers in the ocean. This information is crucial for gaining a better understanding of viral ecology in a constantly changing ocean, and also for basic evolutionary understanding of virus–host relationships in general, including pathogenic viruses of humans, animals and plants.

VI. ACKNOWLEDGEMENTS AND AUTHOR CONTRIBUTIONS

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Author contributions: R.-A.S. and J.L. developed the ideas and wrote the initial draft. M.R.S. created the illustrations. All authors contributed ideas and provided assistance and substantial revisions.

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