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Adding a cost of resistance description extends the ability of virus–host model to explain observed patterns in structure and function of pelagic microbial communities

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Summary

By adding a generic description of cost of resistance (COR) to the existing 'killing-the-winner' model, we show how this expands the model's explanatory power to include rank-abundance relationships in the host population. The model can predict a counter-intuitive relationship previously suggested in the literature, where abundant viruses are associated with rare hosts and *vice versa*. The model explains the observed dominance of slow-growing prokaryotes as the result of successful defence strategies, rather than as dormancy of hosts lacking essential substrates. In addition to these important conceptual aspects, the model is able to reproduce realistic values for virus : host ratios and partitioning of bacterial production between predatory loss and viral lysis. A high COR is also shown to increase the community's richness and Shannon diversity index. This model thus not only couples life strategies at the cellular level with system properties, but it also links the two system level properties of biogeochemical flows and diversity to each other. The model operates with host groups, and consequences for biodiversity when interpreting these groups in terms of species and strains are discussed.

Introduction

Understanding the driving forces and control of biodiversity and its relation to ecosystem functioning is a central issue in microbial ecology. Analogous to micro- and macroeconomic theory (Schelling, 2006), these are system level properties that emerge from the life strategies of individuals. In the pelagic, where microorganisms may have a life expectancy of hours to days before they are either consumed by a predator or have been lysed by a virus, selection pressure for efficient life strategies involving competition for nutrients and defence against predation or parasitism is likely to be high. While competition has been a central theme for much of the classical research, in particular in phytoplankton ecology (Tilman *et al*., 1982), top-down control by predation has received increasing attention both in algal (Irigoien *et al*., 2005) and prokaryotic (Pernthaler *et al*., 1996; Matz and Jurgens, 2003) assemblages. The role of an additional top-down control from viruses, and the interactions between viral lysis and grazing has been subject to both experimental (Simek *et al*., 2001; 2010) and theoretical (Thingstad, 2000) analysis. The theoretical analysis by Thingstad (2000) is based on the general idea that a 'defense strategist' can stably coexist with a 'competition strategist', both competing for the same resource. Heuristically, such coexistence can be explained as a result of the abundance of competition strategists being kept low by predation (or parasitism), thereby leaving resources for the competitively inferior defence strategist. While solid experimental support for the role in natural virus systems of this 'killing-the-winner' (KtW) mechanism has been somewhat elusive (Winter *et al*., 2010), simple laboratory model systems have been shown to follow the theoretical predictions (Bohannan and Lenski, 2000). More recently, circumstantial evidence for a strong selective pressure towards viral defence in natural prokaryotic communities has come from sequencing data. Strains of the same prokaryote species (as defined by 16S rRNA genes) have a common 'core genome' (Charlebois and Doolittle, 2004), while there are 'genomic islands', which vary between strains (Langille *et al*., 2010). The high content of genes related to surface properties in these genomic islands has been taken as an indication of their role in viral defence (Rodriguez-Valera *et al*., 2009). Some resistance-rendering mutations in genomic island regions of the cyanobacterium *Prochlorococcus* conferred fitness costs for the host, manifested in slower growth rates or increased infection by other viruses (Avrani *et al*., 2011).

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However, none of the approaches above have given any direct clues to what a successful host or viral strategy would be in the pelagic environment. In a review of viral ecology, Suttle (2007) suggested that dominating hosts may be slow growing defence strategists. One could hold the idea that dominant viral populations belong to dominant host populations. Interestingly, however, the rank-abundance curves for hosts and viruses suggested by Suttle (2007) indicate the opposite, with the virus population being dominated by viruses infecting the less dominant, but fast-growing, competition strategist hosts. Indirect experimental support for such inverse rank-abundance curves may be found in the observation that reducing top-down pressure from viruses leads to a dominance of previously rare species (Bouvier and del Giorgio, 2007). This effect can be explained if viruses exert a strong abundance control on fast-growing competition strategists. In agreement with this, higher 16S rRNA to 16S rDNA ratios were found for rare bacteria compared with abundant ones in the Delaware coastal ocean, suggesting that rare bacteria combine fast growth with strong top-down viral control of abundance (Campbell *et al.*, 2011).

The net result of these host–virus interactions is that virus-to-host ratios (abundance) in natural samples from the upper ocean are usually found to be in the order of 10:1 (Wommack and Colwell, 2000), and that there is an approximately even partitioning of heterotrophic prokaryote production between viral lysis and protozoan grazing (Fuhrman and Noble, 1995; Fuhrman, 1999). Thus, host–virus interactions are intriguing since the mechanisms and their consequences span from the molecular level of organization, via the evolution of organism strategies, to food web properties. Such food web properties include the different aspects of diversity and biogeochemical cycling (Brussaard *et al.*, 2008). The relationships between diversity and ecosystem functioning are likely to be complex and have been the subject of empirical studies (Woolhouse *et al.*, 2002). Without a sufficiently developed theoretical framework, the connection between diversity and ecosystem functioning is, however, likely to remain obscure (DeLong, 2009).

Here we present for the first time a mechanistic explanation for the observed inverse rank-abundance curves of hosts and their associate viruses. By adding an idealized representation of cost of resistance (COR) to the model previously discussed by Thingstad (2000), host groups with defensive abilities experience reduced fitness in terms of nutrient competition. At high COR, inverse rank-abundance curves for hosts and viruses as discussed by Suttle (2007) are found. With reasonable parameter values, the model also reproduces realistic virus-to-host ratios and flux partitioning.

Model

The model is based on Lotka–Volterra type equations for a system consisting of prokaryotic host groups (H_i), which are all grazed by a non-selective protozoan grazer (P), and host-group-specific viruses (V_i) (Fig. 1). The analysis is based on the steady-state assumption. The steady state solutions for the model as well as the parameter functions with the incorporated trade-off are shown in Table 1. Symbols and parameter values are summarized in Table 2. Matlab version R2011a was used for the computations and plotting of the results.

The total abundance of prokaryotic hosts in the system is set to the typical abundance of pelagic bacteria of 10^9 individuals l^{-1} (Li, 1998). The underlying mechanism for this is assumed to be non-selective control by protozoan grazers (Thingstad and Lignell, 1997), represented by a specific grazing loss rate (δ_P), which is uniform to all n host groups. In addition, the abundance in each host group H_i is top-down controlled by a host-group-specific virus V_i (for $i < n$). Growth rates vary between host groups, depending upon their competitive abilities. Growth rates exceeding the loss rate due to protozoan grazing are balanced by viral lysis (Eq. 1, Fig. 1). The slowest growing host group (H_n) has a growth rate equal to the loss rate through protozoan grazing, such that no virus can establish for this group (Eq. 3).

The production of free viruses of a particular viral group equals the cumulative loss through decay and infection (Eq. 2). From this the abundance of host groups H_i ($1 \leq i \leq n-1$) with established viruses is calculated (Eq. 4). The abundance of the slowest growing host group H_n is given by the condition that all host groups add up to

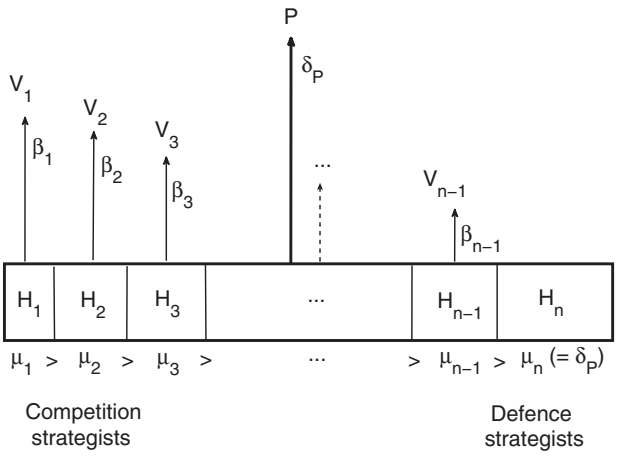

Fig. 1. Structure of the model system used in this study. All host groups (H_i) get top-down controlled by protozoan grazers (P). In addition, viruses (V_i) are established for all host groups that have growth rates μ_i exceeding the grazing loss rate δ_P. The host growth rates μ_i decrease from competition strategists (low S_i, left) to defence strategists (high S_i, right).

Table 1. Model equations and parameter functions with incorporated trade-off.

Equation at steady state	Nr.	Description
$\mu_i H_i^* = \beta_i H_i^* V_i^* + \delta_P H_i^*$	(1)	Mass balance for host groups i with established viruses (i < n)
$m_i \beta_i V_i^* H_i^* = \delta_i V_i^* + \beta_i V_i^* H_i^*$	(2)	Mass balance for host group i-specific viruses (i < n)
$\mu_n H_n^* = \delta_P H_n^*$	(3)	Mass balance for slowest growing host group n without established virus
$H_i^* = \frac{\delta_i}{(m_i - 1)\beta_i}$	(4)	Host group i at steady state (i < n)
$H_n^* = H_T - \sum_{i=1}^{n-1} H_i$	(5)	Host group n at steady state
$V_i^* = \frac{\mu_i - \delta_P}{\beta_i}$	(6)	Host group i-specific viruses at steady state (i < n)
$V_n^* = 0$	(7)	Non-established viruses for host group n
$\mu_i = (1 - S_i)^\tau \mu_{max}$	(8)	Growth rate function with incorporated strategy trade-off (h^{-1})
$\beta_i = (1 - S_i^\tau)\beta_{max}$	(9)	Effective adsorption coefficient function with incorporated strategy trade-off (l h^{-1})
$\mu_n = (1 - S_{max})^\tau \mu_{max} = \delta_p$	(10)	Growth rate function for slowest growing host group n
$\Rightarrow S_{max} = 1 - \sqrt[\tau]{\frac{\delta_P}{\mu_{max}}}$	(11)	Maximum strategy index for given trade-off

For a description of the symbols and the parameter values used, see Table 2.

the total abundance of 10^9 individuals l^{-1} (Eq. 5). The amount of free viruses V_i of a particular host group (Eq. 6) follows from the equilibrium condition (growth equals sum of losses) of their hosts H_i (Eq. 1).

Our model describes the dimension in life strategies from a pure competition strategist (i = 1) with a high growth rate ($\mu_1 = \mu_{max}$), where all viral encounters lead to successful infection (effective adsorption coefficient $\beta_1 = \beta_{max}$), to host groups (increasing i) that increase their defence ($\beta_i < \beta_{max}$) at the expense of reduced growth rates ($\mu_i < \mu_{max}$). Technically, this is represented by a host-group-specific life strategy trait S_i, which in combination with a trade-off parameter τ describes the competitive and defensive abilities of the members of each host group. Our trade-off parameter τ thus modulates the COR in viral defence. The pure competition strategy of H_1 is represented by the strategy trait $S_1 = 0$, which implies that the members of H_1 cannot defend themselves against viruses ($\beta_1 = \beta_{max}$). A pure defence strategy is represented by $S = 1$, implying that the members of this hypothetical group are completely immune against viruses ($\beta = 0$). The price of complete defence in our model is a growth rate equal to zero. This strategy is not sustainable in our model due to the grazing loss. The maximum defence strategy S_n sustained in our model is the one allowing a growth rate equal to the grazing loss. The set of strategies S_1–S_n found in the host groups, ranging from pure competition specialists to defence strategists, is referred to as strategy spectrum below.

The equations used to express the relationships described above are given in Table 1. Specifically, the growth rate of the host group H_i is expressed as $\mu_i = (1 - S_i)^\tau \mu_{max}$ (Eq. 8), and the effective adsorption coefficient by $\beta_i = (1 - S_i^\tau)\beta_{max}$ (Eq. 9). With these relationships, both μ_i and β_i decrease with an increase in defence strategy S_i. Importantly, this is modulated by the trade-off τ so that, at low trade-off values, only a small initial loss in μ_i is required to have a large reduction in β_i.

Table 2. Symbols and parameter values used.

Name	Value	Units	Description
S_i	$0 \leq S_i \leq 1$		Strategy index of host group i (0 corresponds to pure competition specialist, 1 to pure defence specialist)
τ	$0 \leq \tau$		Trade-off
H_i^*		ind. l^{-1}	Host group i at steady state
V_i^*		ind. l^{-1}	Virus i at steady state
μ_i		h^{-1}	Growth rate of host group i
β_i		l h^{-1} ind. $^{-1}$	Effective adsorption coefficient of virus i
n		host groups l^{-1}	Number of host groups in the system (Richness)
H_T	10^9	ind. l^{-1}	Total number of host cells
δ_P	ln(2)/48	h^{-1}	Grazing loss
δ_i	ln(2)/24	h^{-1}	Viral decay rate (constant)
m_i	50		Viral burst size (constant)
β_{max}	2.5×10^{-9}	l h^{-1} ind.$^{-1}$	Maximum effective viral adsorption coefficient
μ_{max}	ln(2)/10	h^{-1}	Maximum host growth rate

Note that in Fig. 5, μ_{max} varies between ln(2)/3 h^{-1} and ln(2)/15 h^{-1}.

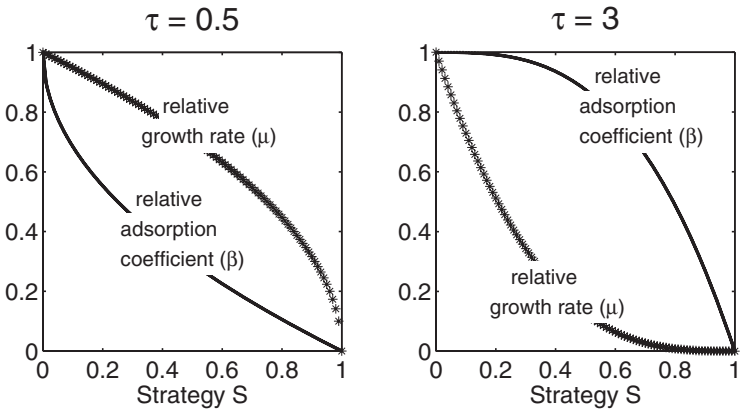

Fig. 2. Relative growth rate and effective adsorption coefficient as functions of the life strategy index S as described in Table 1 for trade-off $\tau = 0.5$ (left) and $\tau = 3$ (right). Strategy indices close to zero represent competition strategists, while defence strategists have strategy indices close to one. Note that growth rates for pure defence specialists (S = 1) are zero, implying that pure defence strategies cannot establish in our model.

For a high trade-off, this is reversed, so that a large initial loss in μ_i is required to get a small reduction in β_l (Fig. 2).

The uniform grazing loss, δ_P, is set to ln(2)/48 h^{-1}, denoting a generation time of the slowest growing host group H_n of 2 days. The maximum host growth rate, μ_{max}, for the host group with pure competition strategists (H_1, S = 0) is set to ln(2)/10 h^{-1}, implying a generation time of 10 h for the fastest growing host group (Table 2). Note that μ_{max} is not the maximum growth rate physiologically obtainable, but the maximum growth rate obtainable for the given environmental conditions when there is no reduction due to viral resistance. The maximum defence strategy S_{max} of host group H_n that gets established in the system (Eq. 11) is derived from the steady state condition that the growth rate μ_n of the slowest growing host group H_n equals the loss rate through protozoan grazing (Eq. 10). [Correction added on 24 April 2013 after first online publication: In the last sentence of the paragraph, citations of Eqs. 12 and 13 were changed to Eqs. 10 and 11.]

The strategy values for the host groups with intermediate defensive abilities (i.e. host groups H_2 to H_{n-1}) are determined as follows. The interval between 0 and S_{max} is divided into n equally spaced intervals, where the number n is chosen such that the sum of the individuals of all established host groups ($\sum_{i=1}^{n} H_i^*$) adds up to the total host abundance of 10^9 individuals l^{-1} (where the number of individuals in each host group is given by Eq. 4).

The number of host groups established in the system (*n*) corresponds to the richness. Note that the richness is a variable depending on the trade-off, giving the peculiar situation in which the number of variables (and equations) in the system also is a variable.

The Shannon index of the system is computed as $\sum_{i=1}^{n} -p_i \ln(p_i)$, where $p_i = H_i/H_T$ is the relative abundance of host group H_i (Shannon, 2001).

The maximum effective adsorption coefficient (2.5×10^9 l h^{-1}) for the viruses in our model is taken from Stent (1963), and the viral burst size (50) corresponds to values from Raunefjorden, Norway (Heldal and Bratbak, 1991). The chosen value for the viral decay rate (0.029 h^{-1}) is similar to the value found by Suttle and Chen (1992) in the Gulf of Mexico (0.028 h^{-1}). The minimum and maximum host growth rates (ln(2)/48 h^{-1} and ln(2)/10 h^{-1} respectively) fall within ranges determined for marine bacterial communities, while it remains difficult to measure growth rates of individual taxa (Franco-Vidal and Moran, 2011). We demonstrate the effect of maximum host growth rates in our model by varying μ_{max} between ln(2)/15 h^{-1} and ln(2)/3 h^{-1} (Kemp *et al.*, 1993).

Results

The model produces the distribution of viral and host abundances as function of host growth rates and trade-off (Fig. 3). For trade-off values $\tau > 1$, inverse rank-abundance curves of hosts and their associated viruses emerge, where slow growing defence strategists are more abundant than fast growing competition strategists, while the viruses with high effective adsorption coefficients infecting the rare competition strategists are more abundant than the less virulent viruses infecting the numerically dominant defence strategists (Fig. 3 top middle and top right). The abundance of the defence strategists (i.e. slow growing hosts) increases with decreasing trade-off. For trade-off values $\tau < 1$, the virus distribution reaches a maximum at intermediate competitive and defensive abilities of the hosts (Fig. 3, top left) due to a steep increase of β for high growth rates (Fig. 3, middle left), which leads to decreasing virus populations (Eq. 6). The trends shown in Fig. 3 are also valid for an increased maximum host growth rate of ln(2)/3 h^{-1} (not shown).

In addition to the inverse rank-abundance curves for trade-offs $\tau > 1$, our model reproduces higher-level properties of the pelagic microbial ecosystem. This includes virus abundances that are on the order of 10–100 times larger than bacterial abundances (Fig. 4, middle left), and an approximately even partitioning of the bacterial pro-

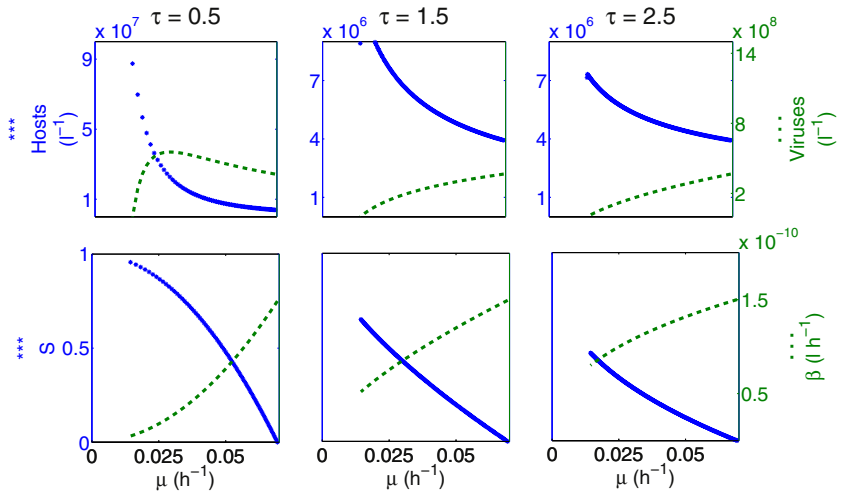

Fig. 3. Virus-host rank-abundance curves (top) as well as host strategy S_i and effective viral adsorption coefficients β_i (bottom) as functions of the host growth rate μ_i. Defence strategists are to the left in the subfigures (slow growing), and competition strategists to the right (fast growing). Trade-offs are set to $\tau = 0.5$ (left), 1.5 (middle), and 2.5 (right). Note the different host abundance *y*-axis for $\tau = 0.5$.

duction between viral lysis and protozoan grazing (Fig. 4, middle right). Although these trends are maintained on the same order of magnitude for different trade-off values, the trade-off strength affects the structure and diversity in the system. Both the community richness (number of host groups) as well as the Shannon index increase with increasing trade-offs and reach maxima around 250 (richness) and 5.5 (Shannon index) for sufficiently large trade-offs (Fig. 4, top). Similarly, viruses are most abundant when trade-offs are high (Fig. 4, middle left). An inconspicuous virus maximum of about 2.4×10^{10} l^{-1} occurs at $\tau = 2$, while the total viral abundance decreases only slightly for trade-offs exceeding 2. Accordingly, the fraction of bacterial production being passed down into the viral shunt through lysis is slightly larger for high trade-offs (Fig. 4, middle right). The maximum strategy index S_{max} decreases with high trade-offs, such that only relatively fast growing competition strategists with low strategy indices get established when defence becomes expensive in terms of reduced growth rates (Fig. 4, bottom right).

Besides the trade-off, the width of the strategy spectrum (adjusted by varying the maximum host growth rate μ_{max}) strongly affects the system structure and in particular the total virus abundance (Fig. 5). Increasing μ_{max} from $\ln(2)/15$ h^{-1} to $\ln(2)/3$ h^{-1} roughly quadruples the total viral abundance to over 100 times higher abundances than hosts (Fig. 5, middle left), while the partitioning of the bacterial production increases accordingly from a near 50:50% partitioning between viral lysis and grazing to over 80:20% for the highest μ_{max} (Fig. 5, middle right). The richness and the Shannon index decrease slightly with increasing μ_{max} (Fig. 5, top).

Discussion

It is recognized that viruses are important for structuring microbial communities and for enhancing microbial diversity (Wilhelm and Suttle, 1999; Weinbauer and Rassoulzadegan, 2004; Brussaard *et al.*, 2008). Suggested processes include arms-race driven coevolution of hosts and their viruses (Gomez and Buckling, 2001; Weitz *et al.*,

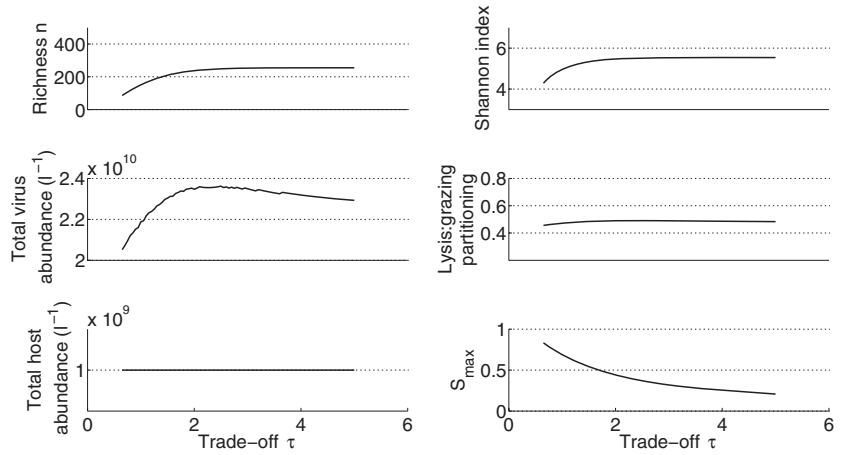

Fig. 4. Richness, Shannon index, total virus abundance, lysis to grazing partitioning of bacterial production, total host abundance, and maximum strategy index S_{max} as functions of the trade-off τ.

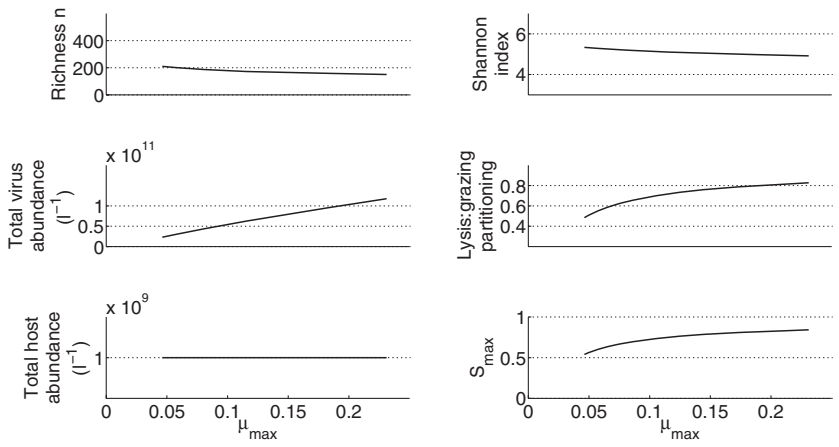

Fig. 5. System properties as in Fig. 4, here as functions of the maximum host growth rate μ_{max} for a trade-off of $\tau = 1.5$. The same trends are also true for smaller trade-offs ($\tau < 1$) and trade-offs exceeding 1.5 (not shown).

2005), top-down control of the most competitive hosts by viruses (Thingstad, 2000), and COR allowing for the coexistence of both susceptible and resistant hosts (Lenski, 1988; Buckling and Rainey, 2002; Lennon *et al*., 2007). The incorporated trade-off functions in our study, which describe the competitive and defensive abilities of the hosts based on a strategy index S, is a new way of incorporating COR in mathematical models of microbial ecology. This allowed us to evaluate the significance of COR in the structuring of microbial communities. We intentionally keep the COR in our model general since different competition trade-offs may occur for different defence mechanisms. Generally, Eqs 8 and 9 imply that strong defence specialists (with S close to 1) pay with reduced competitive abilities in terms of growth rates, which is well known from macroecology in plants (von der Meijden *et al*., 1988).

This extended 'killing-the-winner' model manages to reproduce major trends in the pelagic ecosystem and is, to the best of our knowledge, the first model to generate inverse rank-abundance curves for hosts and their associated viruses as discussed in Suttle (2007). Based on a generic trade-off between competitive and defensive abilities of the host, the model thus suggests a mechanistic explanation for the recent findings of dominant slow growing bacteria and low abundances of fast growing hosts. Hence the study represents an important advancement of our conceptual understanding of how viruses and trade-offs associated with viral defence may structure marine pelagic food webs.

Influence of COR and growth rate spectrum on food web structure and biogeochemistry

For high COR (high trade-off τ), inverse rank-abundance curves of prokaryotic hosts and their associated viruses are generated. If host groups are interpreted as species, this is in qualitative agreement with the trends suggested in the marine virology review by Suttle (2007). Field data from the North Atlantic Ocean (Malmstrom *et al*., 2004), coastal Mediterranean waters (Ferrera *et al*., 2011) and lakes of Michigan (Jones and Lennon, 2010) match with Suttle's predictions of many low and few highly active prokaryotic clades, fitting well with the rank-abundance curves in our model. Support for the idea that viruses exert a strong abundance control on fast-growing competition strategists is also found in Bouvier and del Giorgio (2007), where reducing top-down pressure from viruses lead to a dominance of previously rare species.

The original KtW-model suggests that the main control of lysis to grazing partitioning of prokaryote production lies in the width of the growth rate spectrum (Thingstad, 2000). The presented model shows that the trade-off also affects this partitioning. The increased proportion of bacterial production being passed down into the viral shunt when trade-offs are high means that more organic matter remains in the microbial loop instead of being transferred to higher trophic levels. This agrees with a model analysis where viral lysis increased bacterial production and reduced secondary eukaryotic production (Fuhrman, 1999). Hence, an important consequence of trade-off between competition and defence strategies seems to be its effect on the marine biogeochemistry by indirectly controlling the importance of different pathways in the system.

The effect of COR is further illustrated by the increased richness and Shannon index for high trade-offs (Fig. 4). Intuitively, this makes sense. If there was no COR in terms of reduced growth rates, the resistant hosts would quickly outcompete the susceptible ones due to lysis pressure, leaving only one resistant winner in the system. COR is also recognized to be important for differentiation of ecological strategies in phytoplankton communities (Litchman *et al*., 2007).

The change of the richness and Shannon index was most pronounced for increasing trade-off (Fig. 4), while the total viral abundance increased most strongly for

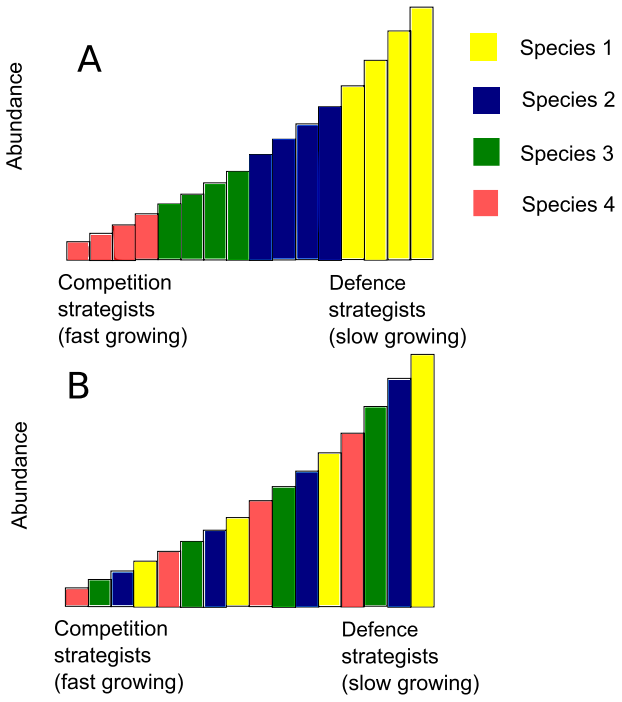

Fig. 6. Distribution of host strains (rectangles) of different species (colours) along the growth rate spectrum, depending on two scenarios that our model can describe.
A. Strains of a species are clustered in a narrow window along the growth rate spectrum. This is possible if strains of the same species have similar maximum growth rates, and if the COR decreases for species with lower maximum growth rates.
B. Strains of species are spread along the entire growth rate spectrum, which is possible if the maximum growth rates and the COR is similar for all species.

increasing maximum host growth rates (Fig. 5). Hence, the flux from the microbial loop to either the viral shunt or to higher trophic levels seems predominantly controlled by the width of the host growth rate spectrum. Reversing this idea, we propose that the partitioning of bacterial production between viral lysis and protozoan grazing can be used as a proxy to estimate the width of the strategy spectrum and the differences between the host group growth rates in a natural bacterial community. Chemostat experiments where the rate of cell lysis and viral production was positively correlated with the host growth rate support the idea (Middelboe, 2000), but further experiments are required to establish these relationships.

Diversity within or between host groups?

An interesting question is how the different strategies (from fast to slow growing) are distributed between or within species. In this study, we considered 'host groups', without specifying whether they should represent functional groups, species, or strains.

In experimental systems with one, or a few prokaryote host species, resistant strains seem to rapidly become dominant, accompanied by a small virus community (Middelboe *et al.*, 2001; 2009). The contrast to natural aquatic systems, where virus : host ratios often exceed 10, has been considered as a paradox in this field (Weinbauer, 2004). The proposed model describes the qualitative aspects of the single-species situation quite well: In a system with only one sensitive strain and its virus, the sensitive host strain would be reduced to a small host group. An immune mutant would then have the possibility to become dominant on the remaining unused resources. In a chemostat system, this would give a new steady state situation where the immune mutant would have to grow at the dilution rate, while the virus population would have to be large enough to give the sensitive strain an additional loss equal to the difference in growth rate between the two strains. Interestingly, viral abundance would thus reflect the COR associated with the defence system of the host. A continuing red queen dynamics (Little, 2002) presumably would split these two strains further until the system approaches an equilibrium of the type modelled here, where host groups represent strains, all belonging to a single species.

The natural situation with many host species together is open to several theoretical possibilities. As one extreme (Fig. 6A), strains belonging to a species may be clustered in narrow windows of the growth rate spectrum, so that species are arranged along the growth rate axis with a characteristic growth rate for each species. This pattern would be expected if there are large between-species differences in maximum growth rate (at the given substrate concentration), combined with species-specific CORs that decreases with decreasing maximum growth rate. If, alternatively, the different species have comparable maximum growth rates and CORs, strains from different species would be interspersed along the growth rate axis (Fig. 6B). Interestingly, microautoradiography-based activity spectra seem to suggest a spectrum for SAR11 covering approximately the same range as that of the rest of the prokaryote community (Malmstrom *et al.*, 2004). This is consistent with the last alternative, but more difficult to reconcile with the first, clustered alternative, where the notion of SAR11 as a defence strategist (e.g. Suttle, 2007) would imply a lack of SAR11 members in the high-activity end of the spectrum.

If strains with different strategies represent one species, a shift in environmental conditions favouring only a small subset of strategies would not necessarily harm the entire species. The system would hence be more resilient if species strains were spread across the strategy spectrum. To shed more light on this question, further experimental and modelling work and development of techniques to measure bacterial growth rates *in situ* is necessary.

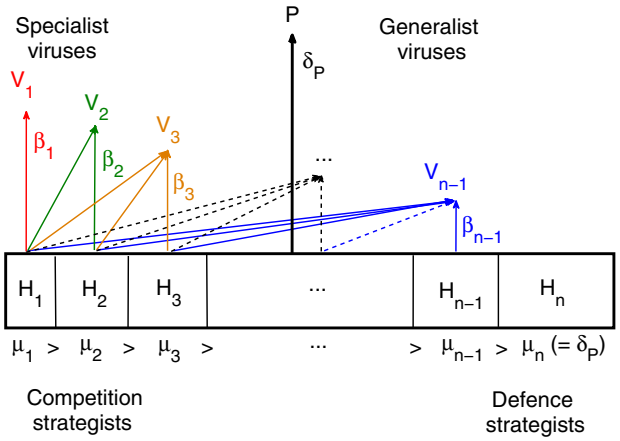

Fig. 7. Model with nested infection as discussed in the *Supporting information*: Same as basic model (Fig. 1), but in addition to the primary viruses V_i that infect host group H_i, viral groups with higher indices than i also infect host group H_i. This leads to the nested structure, where the fastest growing host (H_1) is infected by all viruses present in the system, while increasingly slower growing hosts have decreasing numbers of infectious virus groups. Viruses with low adsorption coefficients (high indices) are thus generalists, while viruses with high adsorption coefficients (low indices) are specialists.

Model assumptions

Our model is based on the assumption that fast growing hosts (competition specialists) are associated with highly virulent viruses with large adsorption coefficients. This assumption follows suggestions by Suttle (2007) and makes intuitively sense because fast growing hosts may provide more resources for viruses than slow growing ones (Parada *et al.*, 2006).

In general, the structure of infection and resistance between viruses and bacteria remains poorly understood (Holmfeldt *et al.*, 2007; Flores *et al.*, 2011). Infection patters in our model are assumed to consist of one-to-one interactions between the host and virus groups. Many marine viruses indeed appear to have a high degree of species or strain specificity (Wichels *et al.*, 1998; Wommack and Colwell, 2000), and Flores and colleagues (2011) hypothesize that when looking at an entire community across different host groups, one-to-one interactions between host groups and host group specific viruses should occur. As our model is an attempt to explain the structuring of the entire microbial community in the pelagic ocean including many different host groups and their corresponding viruses, the model with one-to-one interactions seems a valid first approximation. It is furthermore the simplest possible infection model for a virus–host community, which we therefore argue is a necessary step towards future understanding of more complex models. We are aware, however, that many experimental infection studies show nested infection patterns (Flores *et al.*, 2011), where some generalist phages manage to infect many different hosts, including the more resistant ones, while some phages are more specific. This infection pattern seems most likely observed when experiments are conducted within host groups (Flores *et al.*, 2011). In certain situations, a KtW-model with nested infection may thus be more adequate. We have analysed this situation by extending the model to include nested infection (Fig. 7). The mathematical description and a detailed discussion of its results can be found in the *Supporting information*. Similarly to the one-to-one infection model, nested infection reproduces a dominance of slow growing defence specialists, while the viruses with high adsorption coefficients dominate the viral community (*Supporting information* Fig. SI). A direct comparison to Suttle's (2007) inverse rank-abundance curves of hosts and their associated viruses is, however, no longer possible, as most viruses are associated with several host groups.

Selective grazing could readily be incorporated in our model by introducing a grazing resistant host community, whose host groups are only susceptible to viral. The KtW-model can thus not only be applied to different trophic levels, but it can also combine KtW-mechanisms acting on different trophic levels (Winter *et al.*, 2010). Here, we intentionally keep the focus on the effects of virus–host interactions in the structuring of the microbial community, while keeping other interactions as simple as possible.

Our analysis relies on the steady-state assumption. We argue that understanding the equilibria of conceptual systems like the one presented here is a prerequisite to eventually understand the dynamics of more complex and more realistic models and ultimately natural systems (Thingstad *et al.*, 1996).

Comparison to previous modelling studies

Previous theoretical studies of simple systems have incorporated trade-offs between growth-rate and susceptibility as well as cross-infection. A two-host system with one limiting resource allowed for coexistence of two hosts with differing growth rates and sensitivities to viral infection (Levin *et al.*, 1977). Also, infection and spreading of strains with different levels of immunity to a range of phages were simulated using a CRISPR model, where hosts with intermediate growth rates could not persist in a well-mixed environment (Haerter and Sneppen, 2012). In contrast, the models presented here give coexistence of intermediate hosts at steady state in a well-mixed environment, also indicated by simulations (not shown).

Our model differs from previous analyses by including a range of different host groups and viruses, where also the viral community is structured in terms of viral fitness. Besides, our model is, to the best of our knowledge, the first to treat nested infection. For natural communities, nested infection appears to be more realistic than an

infection network where all viruses in a system potentially infect all hosts, as modelled by Haerter and Sneppen (2012) (Flores *et al*., 2011).

Model predictions and testing

We predict that higher maximum host growth rates support higher total viral abundances in a given environment. Techniques to measure *in situ* growth rates of marine prokaryotes are currently improving and will be an important tool to experimentally test the skill of the presented model. Our model also predicts that higher CORs will increase the richness and Shannon index of the community. To test this, we first need to learn how trade-offs of different defence systems differ qualitatively. Presumably, there is a lower COR for adding an additional recognition sequence to a CRISPR array (Barrangou *et al*., 2007) than for porin alterations (Middelboe, 2000; Labrie *et al*., 2010). Choice of defence mechanism would therefore be expected to influence how species and strains in a mixed population are distributed along the growth rate axis.

Conclusions

Models indicate the presence of COR (Middelboe, 2000) and observational evidence for it exists (Lennon *et al*., 2007), but COR remains difficult to measure and is not always confirmed experimentally (Avrani *et al*., 2011). In this study, we used a new representation of COR in trade-off functions describing competitive and defensive abilities of hosts. The extended 'killing-the-winner' model reproduces major trends found in marine microbial communities, including inverse rank-abundance distribution for hosts and their associated viruses, a nearly equal partitioning of bacterial production by lysis and grazing as well as virus–host ratios on the order of 10:1. In its idealized form, the 'killing-the-winner' model with incorporated COR may be a powerful framework to explain much of the higher-level structure and functioning of the pelagic microbial ecosystem based on trade-offs between defence and competition strategies at the cellular level. This provides an alternative explanation for the dominance of slow growing prokaryotes in the pelagic environment, as opposed to the idea that slow growing hosts are waiting for optimal environmental conditions in terms of resource availability (Jones and Lennon, 2010). While serving as an interpretation tool for experimental results, predictions from the model such as the partitioning of bacterial production between viral lysis and protozoan grazing may be used for new experimental designs to estimate ranges of host-group-specific growth rate spectra.

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Conflict of interest

The authors declare no conflict of interest.

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Supporting information

Additional Supporting Information may be found in the online version of this article:

Supporting information.

Fig SI. Virus–host rank-abundance curves as functions of the host growth rate μ and effective viral adsorption coefficient β in the nested infection model. Defence strategists are to the left (slow growing), and competition strategists to the right (fast growing). Viruses with low effective adsorption coefficients are generalists, while viruses with high effective adsorption coefficients are specialists. Trade-offs are set to $\tau = 0.5$ (left), 2 (middle), and 3.5 (right). Note the different scales on the y-axes for the virus distributions. The logarithmic *y*-axes for the host distribution was used to include the fastest growing host group H_1.