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Changing elemental cycles, stoichiometric mismatches, and consequences for pathogens of primary producers

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Human-induced changes in biogeochemical cycles alter the availability of carbon (C), nitrogen (N) and phosphorus (P) in the environment, leading to changes in the elemental stoichiometry of primary producers. These changes in elemental ratios may, in turn, alter the degree of stoichiometric mismatch between primary producer hosts and their pathogens. Here, we outline how ecological stoichiometry could be used as a framework to predict the effects of changing nutrient supply on stoichiometric mismatches in autotroph–pathogen interactions. We discuss empirical evidence linking pathogen performance to stoichiometric mismatches arising from shifts in elemental availability. Our synthesis indicates that fungi may be particularly sensitive to changes in N supply and viruses generally respond strongly to changes in the supply of either of these elements, but it also highlighted the need for additional data, especially for bacteria. Consequently, fungal pathogens may respond more strongly to changes in host C:N stoichiometry, whereas viruses may be highly sensitive to both changes in C:N and C:P of hosts. Additionally, our synthesis suggests that viruses may be more homeostatic than fungi, and therefore respond more strongly to changing elemental supplies. Revealing stoichiometric mismatches may greatly support our understanding

> We use the framework of ecological stoichiometry to generate hypotheses and assess empirical evidence about how changes in nutrient supply may modify interactions between primary producers and their pathogens. General trends of pathogen–host stoichiometric interactions depend on the type of pathogen (fungi, bacteria or virus) and nutrient (nitrogen or phosphorus). We show how changes in elemental supply can modify host–pathogen interactions, deepening our understanding of ecological differences among pathogen types, and providing expectations for different responses to future environments. Thus, ecological stoichiometry provides a predictive framework for future disease incidence under scenarios of changes in biogeochemical cycles.

of how host–pathogen interactions in primary producers will respond to changes in global biogeochemical cycles, controlling disease incidence in primary producers under scenarios of global change.

A framework to study impacts of changing elemental cycles on primary producer–pathogen interactions

Since the industrial revolution, human activities have massively changed global cycles of carbon (C), nitrogen (N) and phosphorus (P). The availability of these three elements is, however, not changing at uniform rates (Elser et al. 2007, Vitousek et al. 2010, Yuan et al. 2018). On a global scale, C flux to the atmosphere has increased over 10-fold, reactive N has increased 2.5-fold and availability of P has increased up to 5-fold (Galloway et al. 2014, Yuan et al. 2018, Friedlingstein et al. 2019). This differential human imprint on elemental cycles is also causing spatially heterogeneous changes in reactive C, N and P, and on the C:N:P ratios of the biosphere (Smith et al. 1999, Peñuelas et al. 2013, Yuan and Chen 2015).

The availability of elements such as C, N and P is essential to all organisms and can strongly affect the interactions between primary producers and their pathogens (Huber and Haneklaus 2007, Dordas 2009, Budria 2017, Borer et al. 2021). More specifically, the supply of N and P can induce positive or negative effects on pathogen prevalence and disease severity in primary producers (Bruning and Ringelberg 1987, Lacroix et al. 2014, Borer et al. 2016). For example, N addition can increase the severity of foliar fungal disease in terrestrial plants by releasing pathogens from growth-limitation by N (Veresoglou et al. 2013), but can also decrease disease severity by enhancing plant host resistance (Mur et al. 2016). N limitation likewise can reduce the prevalence of fungal infections in phytoplankton, whereas P limitation (and N excess) can increase infection rates (Frenken et al. 2017).

The overall consequences of nutrient availability on infectious disease dynamics depend on the combined responses of hosts and pathogens. This net response may also depend on the type of pathogen involved (e.g. fungus, bacterium or virus) and the identity of the growth-limiting nutrient. However, these variable effects of nutrients on primary producer disease outcomes have not been placed into a general framework to aid understanding and prediction. Here, we use ecological stoichiometry to generate hypotheses for host and pathogen interactions under changing nutrient supplies. Although these relationships may extend to the host–vector interactions critical for transmitting some pathogens, we focus on directly-transmitted pathogens. We furthermore confine our synthesis to obligate pathogens that entirely rely on their hosts for carbon and nutrient acquisition, and cannot take up these elements directly from their environment.

Ecological stoichiometry describes how the ratios of multiple elements in nature can alter biological rates and processes and has been widely applied to study organismal physiology, growth, population dynamics and ecological interactions (Sterner and Elser 2002, Hessen et al. 2013, van de Waal et al. 2018). A core concept from stoichiometric theory is that primary producers are generally characterized by relatively high stoichiometric plasticity, in which their elemental content shifts in response to changes in nutrient availability in the environment (Sterner and Elser 2002, Van de Waal et al. 2010). However, consumers differ in their relative elemental composition from primary producers and generally exhibit higher demands for elemental nutrients than their autotroph hosts (Sterner et al. 1992, Sterner and Elser 2002). This stoichiometric mismatch between primary producers and consumers may limit consumer performance through reductions in physiological efficiency (Hessen et al. 2013). Furthermore, consumers often have less capacity for stoichiometric plasticity than primary producers, for instance, because consumers contain a relatively large amount of structural compounds or have a limited ability to store nutrients (Sterner and Hessen 1994, Hessen and Anderson 2008). This may cause more significant mismatches between primary producers and consumers in very high or low carbon:nutrient environments (i.e. if food is too rich in carbon or nutrients), and subsequently may reduce consumer performance because it is energetically costly to get rid of excess nutrients, to respire carbon or to engage in compensatory feeding behaviors (Anderson et al. 2005, Boersma and Elser 2006, Hessen and Anderson 2008).

Here we hypothesize that analogous to other consumers, pathogens (i.e. pathogenic fungi, bacteria and viruses) also exhibit relatively high demands for elemental nutrients (e.g. N and P), and thus may become more growth limited with increased host carbon:nutrient ratios (and vice versa, see section 'Do pathogen groups vary in stoichiometric plasticity?'). Stoichiometric plasticity of pathogens infecting primary producers is virtually unstudied, but like other organisms, pathogens are likely to vary along the stoichiometric continuum from relatively homeostatic to relatively plastic (Sterner and Elser 2002, Meunier et al. 2014, 2017). Along this continuum, some pathogens may continue to replicate, potentially reaching epidemic rates of infection despite changes in the stoichiometry of their hosts, whereas others will not be able to replicate or transmit under altered stoichiometric conditions.

A few reviews have explored the potential of a stoichiometric framework for host–pathogen interactions (Aalto et al. 2015, Bernot and Poulin 2018, Sanders and Taylor 2018). However, previous work has not yet explicitly used a collection of empirical evidence to synthesize the role of changing elemental availability and ratios, nor has it examined the effects of changes in resource supply on host–pathogen stoichiometric mismatches.

Using ecological stoichiometry to link changing elemental cycles to pathogen performance

Applying core concepts from stoichiometric theory to primary producer–pathogen interactions, we hypothesize that:

1. Primary producers have higher carbon:nutrient (C:N and C:P) ratios than their pathogens, which will lead to stoichiometric mismatches.
2. Changes in the carbon:nutrient stoichiometry of primary producers will increase or decrease stoichiometric mismatches with their pathogens, consequently reducing or increasing pathogen performance.
3. Different types of pathogens (i.e. fungi, bacteria or viruses) will differ in their degree of stoichiometric plasticity; stoichiometrically plastic pathogen types should be better able to cope with shifts in host stoichiometry compared to stoichiometrically-constrained pathogens.

We illustrate these hypotheses and their implications for pathogen performance in response to changes in elemental cycles with a hypothetical scenario involving a primary producer host and two different pathogens (Fig. 1). In this scenario, as noted in hypothesis 1, the pathogens differ from their host and from one another in their carbon:nutrient (e.g. C:N or C:P) ratios (Fig. 1A). The stoichiometric mismatch between each pathogen 'consumer' and its host 'resource' may be quantified as the maximum mismatch in carbon:nutrient content for each consumer–resource pair (as in Hillebrand et al. 2009). The variation in carbon:nutrient ratios of the two pathogens in this scenario leads to a difference in the magnitude of the stoichiometric mismatch that both experience when compared to their host resource. By the simplest approximation, we expect that a pathogen with a carbon:nutrient ratio strongly deviating from its host has a large stoichiometric mismatch, and will thus replicate at a lower rate than a pathogen more closely matching its host's elemental ratio. Consequently, the pathogen with a larger mismatch may transmit less, whereas the pathogen with a closer stoichiometric match may experience greater transmission. We note that this simplified scenario does not account for the effects of nutrient supply on host immunity that may arise (see section 'Other factors masking stoichiometrically driven trends').

The carbon:nutrient content of hosts may considerably increase (Fig. 1B) or decrease (Fig. 1C) due to environmental changes, including shifts in temperature, CO_2 availability or nutrient supply (Finkel et al. 2010, Van de Waal et al. 2010, Yang et al. 2011, Sardans et al. 2012). By analogy to other consumers such as herbivores or predators, a change in carbon:nutrient content of primary producers may induce an energetic cost, resulting in reduced organismal performance (Persson et al. 2010, Hessen et al. 2013). It remains under debate whether (and when) stoichiometric homeostasis benefits or constrains herbivores and predators (Hood and Sterner 2010, Meunier et al. 2014, Sperfeld et al. 2017). However,
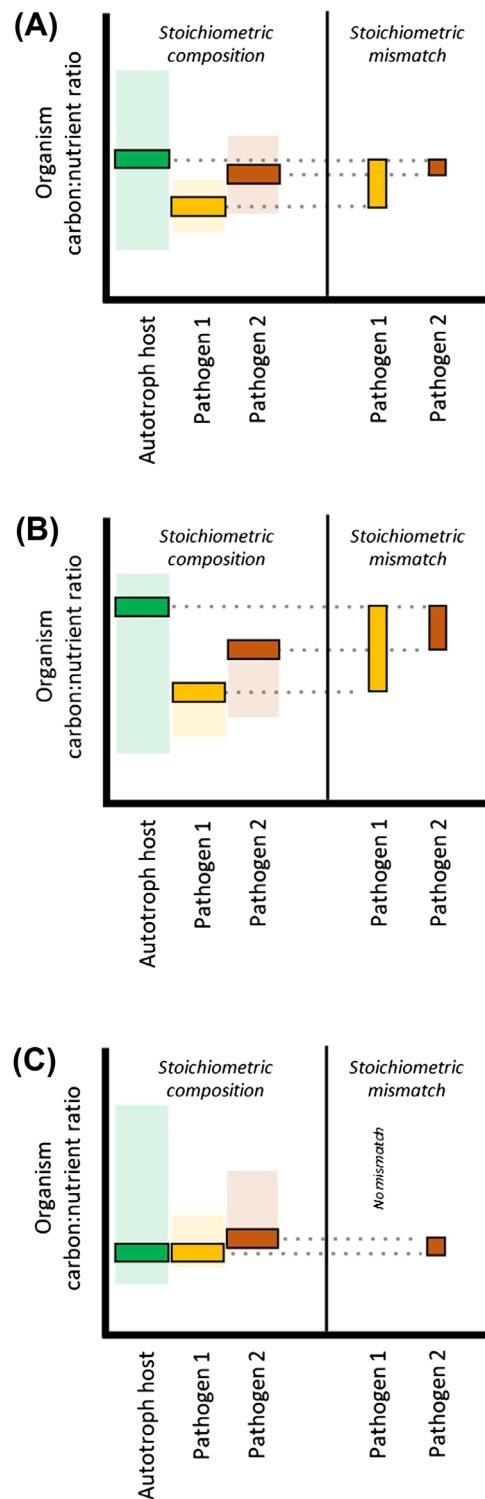

Figure 1. A conceptual overview of stoichiometric mismatches between primary-producer hosts and two pathogens with a different carbon:nutrient ratio (dark bordered rectangles) and stoichiometric plasticity (shaded areas behind). Primary producers and pathogens differ in stoichiometric composition, which may lead to stoichiometric mismatches (A). Changing elemental supply may increase (B) or decrease (C) host stoichiometry, and as such increase or decrease stoichiometric mismatch.

this analogy to pathogens is incomplete because herbivores and predators typically consume many resource items over their lifetimes, and as such can potentially compensate for a stoichiometric mismatch by foraging more on a particular primary producer (i.e. compensatory feeding) or eating more of a particular prey (Hillebrand et al. 2009). Therefore, hypothesis 2 arises from the expectation that the stoichiometric mismatch will be more potent for pathogens than for other consumers because a single, infectious unit of pathogen extracts its lifetime nutrition from a single host.

If we further consider our analogy to free-living consumers, the degree of stoichiometric plasticity can differ among consumer species (Persson et al. 2010, Meunier et al. 2014). While this variation is important in predictions of consumer–resource dynamics from stoichiometric theory (Loladze et al. 2004), the concept of stoichiometric plasticity has not been explored for pathogens. Thus, while it may have important implications for infection, the degree to which various pathogenic taxa can shift their carbon:nutrient contents in response to changing resource stoichiometry is unknown. However, existing data on the stoichiometric plasticity of the taxonomic groups to which the different pathogen types belong does indicate potential differences among pathogen types, giving rise to hypothesis 3. We depict two hypothetical pathogens that vary in the relative degree of stoichiometric plasticity (Fig. 1). We consider pathogens that maintain a relatively constant carbon:nutrient ratio to be relatively homeostatic (pathogen 1 in Fig. 1), while pathogens with a carbon:nutrient ratio that can better track that of their host to be more plastic (pathogen 2 in Fig. 1).

Linking changing elemental supply to host–pathogen stoichiometry and performance

To test our hypotheses, we collected examples of empirical studies that assessed the effects of carbon or nutrient amendments on primary producer host or pathogen (fungi, bacteria or viruses) stoichiometry and performance (Table 1). We did not find examples of studies investigating the effects of shifting nutrient supplies on host stoichiometry combined with pathogenic bacteria responses, pointing to an important gap in our current knowledge. Moreover, studies that explicitly analyze the organismal stoichiometry of primary producer pathogens under different nutrient supplies are currently very rare. We are aware of only one study that describes the stoichiometry of both host and pathogen under different

Table 1. Empirical studies that assessed the effects of carbon or nutrient amendments on primary producer host stoichiometry (C:N and C:P) and subsequent response in parasite performance (virulence, infectivity, reproduction rate, etc.). Green shading indicates when change in host stoichiometry and response of parasite are consistent with hypotheses, while blue shading indicates the lack of support to our hypotheses. (Empty cells indicate that the elemental ratio or response was not measured or reported., increase ↑ or decrease ↓, not consistent or no change was observed −.)

Habitat	Host class	Parasite group	Change in elemental cycle	Host C:N	Host C:P	Response parasite performance	Reference
Freshwater	Phytoplankton	Fungus	−N	↑	−	↓	Frenken et al. 2017
	Phytoplankton	Fungus	−P	−	↑	↑	Frenken et al. 2017
	Plant	Fungus	+N	↓		↑	Limpens et al. 2003
	Plant	Fungus	+P	↑		↓	Limpens et al. 2003
	Phytoplankton	Virus	−P		↕	↓	Cheng et al. 2019
	Phytoplankton	Virus	−P	−	↑	↓	Clasen and Elser 2007
	Phytoplankton	Virus	+CO$_2$		↑	↑	Cheng et al. 2019
	Phytoplankton	Virus	−P, +CO$_2$		↑	↓	Cheng et al. 2019
Marine	Phytoplankton	Virus	−N	↑		↓	Maat and Brussaard 2016
	Phytoplankton	Virus	−N	↑		↓	Maat and Brussaard 2016
	Phytoplankton	Virus	−P	↑	↑	↓	Maat et al. 2014
	Phytoplankton	Virus	−P		↑	↓	Maat and Brussaard 2016
	Phytoplankton	Virus	−P		↑	↓	Maat and Brussaard 2016
	Phytoplankton	Virus	+CO$_2$	↑	↑	↓	Maat et al. 2014
	Phytoplankton	Virus	−P,+CO$_2$	↑	↑	↓	Maat et al. 2014
Terrestrial	Plant	Fungus	+N	↓		↑	Thompson et al. 1993
	Plant	Fungus	+NPK	↓	↓	↑	Paul and Ayres 1990
	Plant	Fungus	+CO$_2$	−		↑	Kobayashi et al. 2006
	Plant	Fungus	+CO$_2$	↑		↓	Mcelrone et al. 2005
	Plant	Fungus	+CO$_2$	↑		↓	Thompson et al. 1993
	Plant	Fungus	+CO$_2$	↓		↓	Thompson and Drake 1994
	Plant	Fungus	+CO$_2$	−		↑	Thompson and Drake 1994
	Plant	Virus	+N	↓		−	Lacroix et al. 2017
	Plant	Virus	+N	↓		−	Lacroix et al. 2017
	Plant	Virus	+P		↓	−	Lacroix et al. 2017
	Plant	Virus	+P		↓	↕	Rúa et al. 2013
	Plant	Virus	+CO$_2$	−		↕	Rúa et al. 2013

nutrient supplies (Frenken et al. 2017). This study shows that with an increasing stoichiometric mismatch between the host and its pathogen, the pathogen's performance declined (under N-limited conditions), consistent with our predictions (Fig. 2). This lack of studies points to an important knowledge gap, limiting our ability to directly quantify the role of stoichiometric mismatches between a pathogen and its host on pathogen performance. Nonetheless, we use existing studies to evaluate whether observations of host stoichiometry and pathogen performance under changes in CO_2, N and P, are consistent with our hypotheses. While additional direct evidence is currently lacking, indirect evidence from a variety of other study systems is also consistent with our hypotheses (Table 1).

In aquatic systems, nutrient limitation often causes an increase in carbon:nutrient ratios of phytoplankton, which results in reduced virus performance, expressed as a decline in the number of virus particles produced per lysed host cell or per unit of time (Clasen and Elser 2007, Maat et al. 2014, Maat and Brussaard 2016, Cheng et al. 2019). Shifts in nutrient availability in aquatic systems cause a wide array of responses in parasitic fungi, which seem to depend on the identity of the elemental nutrient that is limiting (Table 1). For example, fungi infecting phytoplankton and aquatic
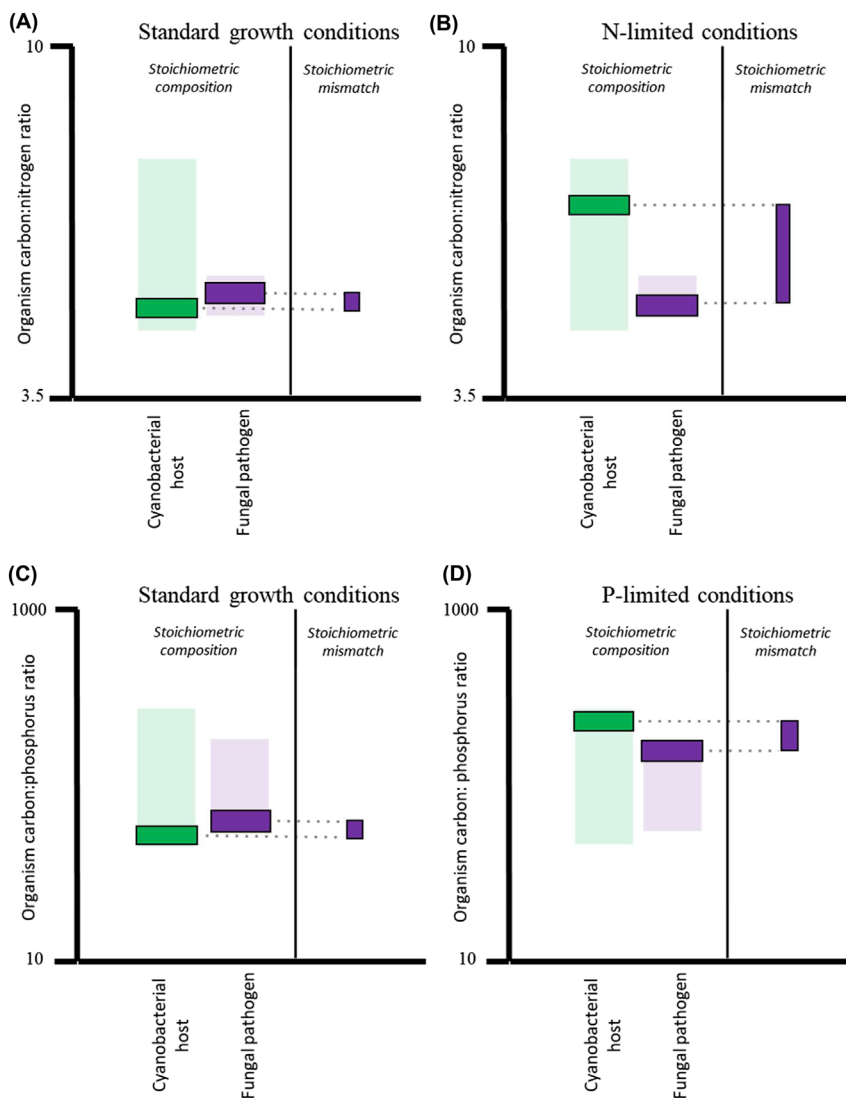

Figure 2. Case study of a cyanobacterium infected by a fungal parasite exemplifying how host and pathogen carbon:nutrient stoichiometry (dark bordered rectangles), and their differences in stoichiometric plasticity (shaded areas behind), can differ under certain conditions, thereby leading to a stoichiometric mismatch. During standard growth conditions, the stoichiometric composition of a cyanobacterium (*Planktothrix rubescens*) and that of one of their fungal parasites (the chytrid *Rhizophydium megarrhizum*) does not differ much (C:N in (A), C:P in (C), y-axes on log scale). During nitrogen-limited (B) or phosphorus-limited (D) conditions, C:N and C:P of the cyanobacterial host increased. Pathogen stoichiometry did not increase during nitrogen-limited conditions but increased during phosphorus-limited conditions. As a result, the stoichiometric mismatch was large during nitrogen-limited and remained small during phosphorus-limited conditions – figures based on data published in Frenken et al. (2017).

primary producers respond strongly to an increased host C:N ratio, with reduced infection efficiency, prevalence and necrosis, whereas the performance of these pathogens increased at higher C:P and N:P ratios when hosts were P limited (Limpens et al. 2003, Frenken et al. 2017).

Nutrient amendments and subsequent effects on plant stoichiometry and pathogen performance in terrestrial systems are generally consistent with aquatic systems. During conditions resulting in a higher carbon:nutrient ratio of plants, pathogen performance often decreased, such as reduced virus titer, compared to conditions with lower plant carbon:nutrient ratio (Table 1; Paul and Ayres 1990, Thompson et al. 1993, Lacroix et al. 2017). Studies that tested the effect of elevated CO_2 on terrestrial plants show much more variation in the response of plant carbon:nutrient stoichiometry (Thompson and Drake 1994, Kobayashi et al. 2006, Rúa et al. 2013). However, in most of these experiments, fungal pathogen performance decreased with increasing carbon:nutrient ratios, as indicated by proxies such as severity and prevalence of infection.

This pairing of the ecological stoichiometric framework with direct and indirect empirical support shows that a stoichiometric lens can provide unique insights into host–pathogen interactions. Existing evidence is largely consistent with our hypotheses (Table 1, Fig. 3). Overall, we found that 21 of the 31 experiments are in line with our hypothesis (Fig. 3). More specifically, an increase in C:N or C:P of primary producer hosts was associated with a decrease in pathogen performance (16 out of 18 cases), and when C:N or C:P of primary producer hosts decreased, the response of the parasite was less consistent (4 out of 9 cases). Interestingly, these studies were dominated by nutrient addition experiments on terrestrial plants, suggesting that a fuller understanding of the generality of these effects would benefit from studies in other ecosystem types. Our overview also shows that pathogen responses to altered primary producer host C:P ratios are dominated by viruses, with only a single example of a pathogenic fungus (Fig. 3).

Do pathogen groups vary in stoichiometric plasticity?

Different groups of pathogens may differ in their responses to altered nutrient environments within a host because of differing elemental content and degree of stoichiometric plasticity. A limited number of studies suggest that fungi as a group (i.e. inter- and intra-specifically, including pathogenic and non-pathogenic species) can be relatively plastic in elemental composition (Danger and Chauvet 2013, Danger et al. 2016). Fungi generally have a high N demand, which is necessary for the production of the N-rich compounds (e.g. enzymes) involved in the colonization and digestion of host cells (Tudzynski 2014, Jabiol et al. 2018). Therefore, the stoichiometric plasticity of fungi should be more constrained by N than P. This is supported by the one available example of a fungal parasite infecting a freshwater cyanobacterium, showing that fungal C:N ratios are more constrained than C:P (Fig. 2; Frenken et al. 2017). Although these fungal parasites infecting phytoplankton may be more sensitive to N, enhanced P limitation was also shown to reduce parasite reproduction (Bruning and Ringelberg 1987, Bruning 1991). Comparably, non-pathogenic fungi associated with aquatic litter showed different stoichiometric and growth responses toward N and P additions (Gulis et al. 2017). Specifically, N addition had no effect on fungal stoichiometry but significantly impacted fungal growth rate, whereas P addition caused a decrease in C:N and N:P ratios, while not affecting growth rate.

While we currently lack evidence for the responses of pathogenic bacteria to shifts in nutrient supply, recent studies have shown that bacteria can be stoichiometrically plastic, and the degree of plasticity can vary widely among bacterial taxa (Makino et al. 2003, Cotner et al. 2010, Scott et al. 2012). Like fungi, bacterial biomass is relatively homeostatic in terms of C:N in response to the availability of nutrients in the environment, but bacterial C:P can be highly variable (Cotner et al. 2010, Phillips et al. 2017). Bacterial strains
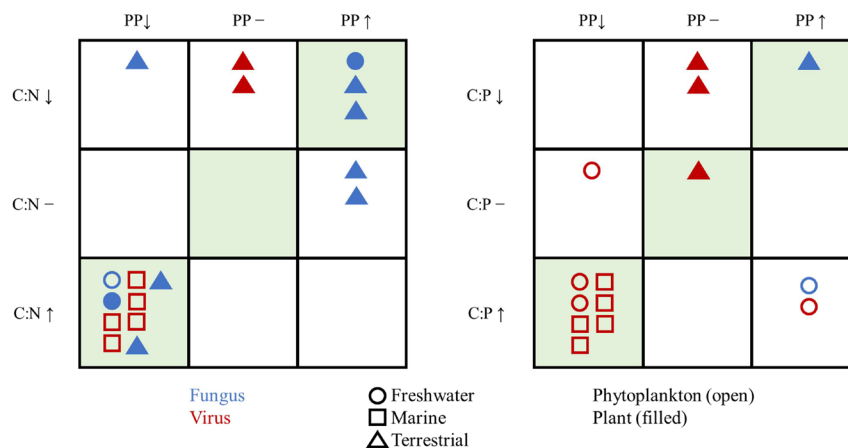

Figure 3. A visual summary of the experiments reviewed and reported in Table 1. Studies were categorized based on the change in host stoichiometry (C:N in the left panel, C:P in the right), and the response of pathogen performance (PP, increase ↑ or decrease ↓ or − when the response was not consistent or no change was observed). Experiments in the green-shaded quadrants are consistent with our hypotheses.

and consortia showed high variation in C:P and N:P ratios, suggesting a highly dynamic and essential role of bacteria in coupling multiple elemental cycles (Godwin and Cotner 2015). We speculate that if pathogenic bacteria have a high stoichiometric plasticity, they can successfully infect hosts with a wide range of C:P ratios, and will only experience a mismatch with their host under extreme P limitation.

Viruses consist of a distinct set of N and P enriched biochemicals, i.e. proteins and nucleic acids, translating into low C:N and C:P ratios (Jover et al. 2014). Viruses, themselves, cannot be stoichiometrically plastic since they have no cells to hold non-nucleic elements. If the chemistry of their structure serves as the largest stoichiometric constraint, this may make them particularly sensitive to increases in host carbon:nutrient ratios, like this, will enhance the stoichiometric mismatch with their host (Fig. 1). However, since viruses depend on the machinery of their host for replication, we hypothesize that they may still experience a fitness boost during conditions that favor host growth, for example, during increased nutrient availability. Observations that within-host (i.e. phytoplankton) virus replication can be limited under both low-N and low-P conditions are consistent with this hypothesis of both N and P limitation of viruses (Clasen and Elser 2007, Maat et al. 2014, Maat and Brussaard 2016, Cheng et al. 2019).

Other factors masking stoichiometrically driven trends

Net disease outcomes in response to shifts in environmental resource availability will not only depend on the response of the pathogen itself but also on that of its host and their interaction. Obligate pathogens, by definition, depend on their hosts, and the virulence of infectious diseases is a product of many factors, including pathogen traits and host immune response. Host resistance to infections may, for instance, respond to changes in CO_2 or nutrient availability, thereby shifting the outcome of infection. For example, P limitation can reduce plant immune responses to infections by fungi, oomycetes or pathogenic bacteria (Hacquard et al. 2016, Castrillo et al. 2017). In contrast, N limitation may lead to enhanced plant host resistance to infections by fungi or bacteria, but this also seems to depend on the form in which N is provided (Mur et al. 2016, Schwachtje et al. 2018).

Pathogens may directly or indirectly affect host nutrient content. For instance, the source of N for cyanophage protein synthesis has been shown to shift over the course of infection from mostly host derived in the early stages to more environmentally derived later on (Waldbauer et al. 2019), which suggests that the nutrient content of phytoplankton hosts at the start of an infection may not always suit the pathogen to reproduce optimally. Some viruses infecting phytoplankton have strategies to cope with nutrient limitation within their host, for example, by minimizing interference with N-fixation (Kuznecova et al. 2020) or manipulation of host metabolism to boost N or P uptake (Monier et al. 2012, 2017). These strategies can result in a reduced carbon:nutrient content

of infected versus healthy host tissue (Ankrah et al. 2014), stimulating viral reproduction, but also enriching the quality of the cell material released in the water after cell lysis (Ankrah et al. 2014, Zheng et al. 2020). Pathogens may indirectly alter plant chemistry by inducing plants to reallocate nutrients as a defense mechanism. For example, N-rich proteins are often reallocated away from pathogen-infected tissues, while the same infection sites may draw C-rich carbohydrates to them (Schultz et al. 2013). The local enrichment or impoverishment of elemental nutrients and proteins may also affect pathogen growth and reproduction, while the overall host tissue stoichiometry may remain unaltered.

Returning to our analogy of consumers, the stoichiometric plasticity of grazers is relatively constrained compared to primary producers, which may result in reduced herbivore performance if stoichiometric mismatches occur (Hessen 1997, Elser et al. 2000, Anderson et al. 2004, 2005, Frost et al. 2005). Although viruses show comparable patterns in response to stoichiometric mismatches with their hosts, we note that the actual mechanisms underlying these responses may fundamentally differ. For example, a grazer ingests the biomass of a whole plant, leaf or cell (and all its different internal components) at the provided elemental ratio and thus acquires some elements in excess of others relative to its needs, which may be energetically costly to expel (Anderson et al. 2005, Hessen and Anderson 2008, Peace and Wang 2019). However, previous examples in this review have shown that viruses can direct host cellular machinery to synthesize biochemicals more suited to their own needs. Thus, when host growth and the synthesis of certain cellular biochemicals are nutrient-limited, so is virus reproduction, which could explain the observed general decline in burst size – the number of viruses produced from each infected host cell – in response to nutrient limitation (studies in Table 1). On the other hand, parasitic fungi may be more similar in their response to mismatches with host stoichiometry compared to grazers and predators. For example, when parasitic fungi infect single-celled phytoplankton, they digest the host's entire interior, thus potentially experiencing a stoichiometric mismatch. However, it is unclear if parasitic fungi can use their enzymes to selectively digest or take up biochemicals from their digested host (Frenken et al. 2017, 2020). Such selective digestion may reduce a potential stoichiometric mismatch, in analogy to extraoral digestion of prey by spiders using enzymes, which can effectively separate (and thus select) edible nutrients from inedible parts of prey to maximize nutrient intake and to minimize ingestion of less edible parts (Wilder 2011).

Changes in the availability of nutrients may also change competition between species of both hosts and pathogens. By analogy, consumers can only adjust their stoichiometry in response to changes in resource quality to a limited extent (Teurlincx et al. 2017). However, during more extreme conditions of nutrient supply, pathogen species that are poorer resource competitors will be replaced by superior competitors (Hall 2004). These changes in host and pathogen identity or diversity may also affect pathogen community assembly,

evolution and subsequently epidemic development (Mideo 2009, Susi et al. 2015, Sallinen et al. 2020). Nutrient availability may also shift the size structure and biomass of host populations, leading to, for instance, larger individuals and higher population densities (Irwin et al. 2006). Larger host species may support greater production of parasites, if they support the same parasite biomass per gram of host tissues as smaller host species (Poulin and George-Nascimento 2007). For diseases with density-dependent transmission, a population with a higher carrying capacity, and thus increased host biomass or density per unit of volume or area, may theoretically increase contact rates, shorten parasite searching time, and thus increase the probability of epidemic outbreak (Anderson and May 1979).

Concluding remarks

Existing empirical examples demonstrate that ecological stoichiometry provides a useful framework to understand the consequences of changing elemental cycles on primary producer host–pathogen interactions. This synthesis also revealed several knowledge gaps, notably the lack of data on pathogen elemental composition, responses of parasitic fungi to P limitation and responses of bacterial pathogens to shifts in nutrient supplies. A deeper understanding of the role of stoichiometry in mediating host–pathogen interactions will require quantifying the elemental content of pathogens, but could also be advanced by tracking changes in the phytoplankton and plant tissue carbon and nutrient contents before and after infection to indirectly estimate pathogen stoichiometry. Our synthesis points to a general trend of fungal pathogens responding more strongly to changes in the N content of hosts. Bacterial pathogens may be more sensitive to changes in host N as well and are expected to be more plastic in response to host P. Viral infection seems to respond strongly to any kind of change in carbon and nutrient supply, likely due to the tight reliance of this pathogen group on both the structure and biochemical composition of host cells.

Although knowledge about the stoichiometric plasticity of pathogen species remains very limited, our review supports the hypothesis that relatively homeostatic pathogens are particularly sensitive to stoichiometric changes of their hosts compared to species with greater stoichiometric plasticity, with dynamic implications for both virulence and transmission. This synthesis suggests the exciting and testable prediction that viruses will respond more strongly than fungi or bacteria to changes in nutrient availability and host cellular stoichiometry because increased carbon:nutrients may directly translate into an enhanced stoichiometric mismatch with their hosts.

Author contributions

Thijs Frenken: Conceptualization (equal); Investigation (lead); Methodology (lead); Writing – original draft (lead); Writing – review and editing (lead). **Rachel Paseka**: Conceptualization (equal); Investigation (equal); Methodology (equal); Writing – review and editing (equal). **Angelica L. Gonzalez**: Conceptualization (equal); Investigation (equal); Methodology (equal); Writing – review and editing (equal). **Lale Asik**: Conceptualization (equal); Investigation (equal); Methodology (equal); Writing – review and editing (equal). **Eric W. Seabloom**: Conceptualization (equal); Investigation (equal); Methodology (equal); Writing – review and editing (equal). **Lauren A. White**: Conceptualization (equal); Investigation (equal); Methodology (equal); Writing – review and editing (equal). **Elizabeth T. Borer**: Conceptualization (equal); Funding acquisition (lead); Investigation (equal); Methodology (equal); Writing – review and editing (equal). **Alexander T. Strauss**: Conceptualization (equal); Investigation (equal); Methodology (equal); Writing – review and editing (equal). **Angela Peace**: Conceptualization (equal); Investigation (equal); Methodology (equal); Writing – review and editing (equal). **Dedmer B. van de Waal**: Conceptualization (equal); Investigation (equal); Methodology (equal); Writing – review and editing (equal).

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