Received: 27 August 2021 | Revised: 22 November 2021 | Accepted: 30 November 2021

DOI: 10.1002/ecm.1510

CONCEPTS & SYNTHESIS

ECOLOGICAL MONOGRAPHS
ECOLOGICAL SOCIETY OF AMERICA

Disease-mediated nutrient dynamics: Coupling host–pathogen interactions with ecosystem elements and energy

Elizabeth T. Borer[1] | **Rachel E. Paseka**[1] | **Angela Peace**[2] | **Lale Asik**[3] | **Rebecca Everett**[4] | **Thijs Frenken**[5,6] | **Angélica L. González**[7] | **Alexander T. Strauss**[1,8] | **Dedmer B. Van de Waal**[5] | **Lauren A. White**[9] | **Eric W. Seabloom**[1]

[1]Department of Ecology, Evolution, and Behavior, University of Minnesota, St. Paul, Minnesota, USA

[2]Department of Mathematics and Statistics, Texas Tech University, Lubbock, Texas, USA

[3]Department of Mathematics and Statistics, University of the Incarnate Word, San Antonio, Texas, USA

[4]Department of Mathematics and Statistics, Haverford College, Haverford, Pennsylvania, USA

[5]Department of Aquatic Ecology, Netherlands Institute of Ecology, Wageningen, The Netherlands

[6]Great Lakes Institute for Environmental Research, University of Windsor, Windsor, Ontario, Canada

[7]Department of Biology and Center for Computational & Integrative Biology, Rutgers University, Camden, New Jersey, USA

[8]Odum School of Ecology, University of Georgia, Athens, Georgia, USA

[9]National Socio-Environmental Synthesis Center, University of Maryland, Annapolis, Maryland, USA

Correspondence
Elizabeth T. Borer
Email: borer@umn.edu

Funding information
National Science Foundation, Grant/Award Number: DBI-1639145

Handling Editor: Christine V. Hawkes

Abstract

Autotrophs play an essential role in the cycling of carbon and nutrients, yet disease-ecosystem relationships are often overlooked in these dynamics. Importantly, the availability of elemental nutrients like nitrogen and phosphorus impacts infectious disease in autotrophs, and disease can induce reciprocal effects on ecosystem nutrient dynamics. Relationships linking infectious disease with ecosystem nutrient dynamics are bidirectional, though the interdependence of these processes has received little attention. We introduce disease-mediated nutrient dynamics (DND) as a framework to describe the multiple, concurrent pathways linking elemental cycles with infectious disease. We illustrate the impact of disease–ecosystem feedback loops on both disease and ecosystem nutrient dynamics using a simple mathematical model, combining approaches from classical ecological (logistic and Droop growth) and epidemiological (susceptible and infected compartments) theory. Our model incorporates the effects of nutrient availability on the growth rates of susceptible and infected autotroph hosts and tracks the return of nutrients to the environment following host death. While focused on autotroph hosts here, the DND framework is generalizable to higher trophic levels. Our results illustrate the surprisingly complex dynamics of host populations, infection patterns, and ecosystem nutrient cycling that can arise from even a relatively simple feedback between disease and nutrients. Feedback loops in disease-mediated nutrient dynamics arise via effects of infection and nutrient supply on host stoichiometry and population size. Our model illustrates how host growth rate, defense, and tissue chemistry can impact the dynamics of disease–ecosystem relationships. We use the model to motivate a review of empirical examples from autotroph–pathogen systems in aquatic and terrestrial environments, demonstrating the key role of nutrient–disease and disease–nutrient relationships in real systems. By assessing existing evidence and uncovering data gaps and apparent mismatches between model predictions and the dynamics of empirical systems, we highlight priorities for future research intended to narrow

the persistent disciplinary gap between disease and ecosystem ecology. Future empirical and theoretical work explicitly examining the dynamic linkages between disease and ecosystem ecology will inform fundamental understanding for each discipline and will better position the field of ecology to predict the dynamics of disease and elemental cycles in the context of global change.

KEYWORDS
autotrophs, feedbacks, global change, infectious disease, nitrogen, nutrient recycling, pathogens, phosphorus, primary producers

INTRODUCTION

Host–pathogen interactions and elemental cycles are linked through a suite of direct and indirect connections that span levels of ecological organization. Elemental resources such as nitrogen (N) and phosphorus (P) can impact host chemistry as well as growth, birth, and death rates, scaling up to determine population attributes or community composition, and shaping infection patterns across scales (Aalto et al., 2015; Borer et al., 2016; Civitello et al., 2018; Dordas, 2008). In turn, pathogens are consumers, limited by both the energy and nutrients provided by their hosts (Smith, 2007) and can alter the physiology, defenses, and ecological function of individual hosts (Hatcher et al., 2012). Scaled up to host populations and communities, infection can impact ecosystem-level nutrient pools and fluxes (Eviner & Likens, 2008; Fischhoff et al., 2020; Preston et al., 2016; Ruardij et al., 2005; Suttle, 2007). These reciprocal processes occur simultaneously, creating the potential for feedback loops; yet most studies focus on individual, unidirectional relationships between elemental cycles and disease. However, the few studies that have specifically focused on these reciprocal effects demonstrate that failing to account for the feedbacks linking disease and nutrients may lead to fundamental shortfalls in ecological predictions (Borer et al., 2021; Narr & Frost, 2016).

Given the ubiquity of pathogens in nature, understanding the mechanistic links between disease and ecosystem nutrient dynamics has the potential to fundamentally enhance two vibrant subdisciplines of ecology: disease ecology and ecosystem ecology (Borer et al., 2021). Disease ecology is rooted in understanding the dynamics of host populations (Anderson & May, 1979), whereas ecosystem ecology, with its focus on elemental fluxes and pools, arose from geosciences, oceanography, and limnology (Chapin et al., 2011). The disparate origins of these lineages have exacerbated a persistent disciplinary divide between ecosystem ecology and disease ecology, hindering progress in understanding the role of the disease–ecosystem relationships that span these disciplines (Ostfeld et al., 2008; Preston et al., 2016). Furthermore, shifts in elemental cycles that range in scale from the local eutrophication of ecosystems to global changes in nutrient availability (Ackerman et al., 2019; Bhaduri et al., 2000; Fenn et al., 2003) are occurring simultaneously with shifts in the spatial extent and prevalence of infectious disease (Anderson et al., 2004; Fisher et al., 2012; Jones et al., 2008), yet we lack a general understanding of the interactions that dynamically link these changes.

Because autotrophs play an essential role in the cycling of Earth's carbon and nutrients, we examine disease-mediated nutrient dynamics in this context. We simultaneously consider the broad suite of processes linking elemental cycling with host–pathogen interactions and disease, the reciprocal effects of pathogens on elemental cycling, and the potential for dynamic feedback loops connecting infection with resource supply and recycling. To do this, we develop a new model of disease-mediated nutrient dynamics that combines approaches from ecological and epidemiological theory (*Disease-mediated nutrient dynamics*), synthesizing past unidirectional approaches into a unified framework. By focusing on the role of feedbacks, we examine how coupling disease with nutrients has the potential to alter both disease and ecosystem dynamics. We then use this model to guide a literature review examining the biology underpinning the links between disease in autotrophs and elemental cycles (*The cycle from nutrient supply to host–pathogen interactions and ecosystem nutrient dynamics*), from sub-cellular processes to host communities. We illustrate the role of nutrient supply in infection and infection in nutrient cycling using examples from a broad range of autotroph–pathogen systems in aquatic (freshwater, marine) and terrestrial (grassland, forest, agricultural) environments as well as a wide array of pathogen taxa (viruses, fungi, bacteria) and strategies (e.g., specialists and generalists, biotrophs and necrotrophs). Taken together, this synthesis provides a conceptual and mathematical framework and identifies gaps and future directions for advancing understanding at the intersection of disease and ecosystem ecology.

DISEASE-MEDIATED NUTRIENT DYNAMICS

The disease-mediated nutrient dynamics framework unites two sets of processes that have traditionally been studied separately (Figure 1): the bottom-up effects of environmental nutrient availability on disease (Aalto et al., 2015; Borer et al., 2016; Civitello et al., 2018; Dordas, 2008) and the reciprocal, top-down effects of disease on ecosystem nutrient dynamics (Eviner & Likens, 2008; Fischhoff et al., 2020; Preston et al., 2016). Studying these relationships as unidirectional processes is empirically convenient and a prerequisite to a broader perspective that encompasses many processes linking disease and ecosystem function. However, pathogens and nutrient availability can simultaneously impact host stoichiometry, growth rate, and mortality, scaling up to generate dynamic impacts on nutrients as well as host populations and communities (Borer et al., 2021; Vannatta & Minchella, 2018). Thus, these concurrent effects can interact to qualitatively alter the dynamics of hosts, pathogens, and nutrients.

Rethinking consumer-driven nutrient recycling for autotrophs and disease

Traditional models of ecosystem function emphasize the importance of autotrophs and environmental microbes as the major biotic drivers of productivity, decomposition, and elemental cycling (Rastetter & Shaver, 1992). The concept of consumer-driven nutrient dynamics (CND) has been built around the explicit recognition that consumer egestion and excretion influence ecosystem N

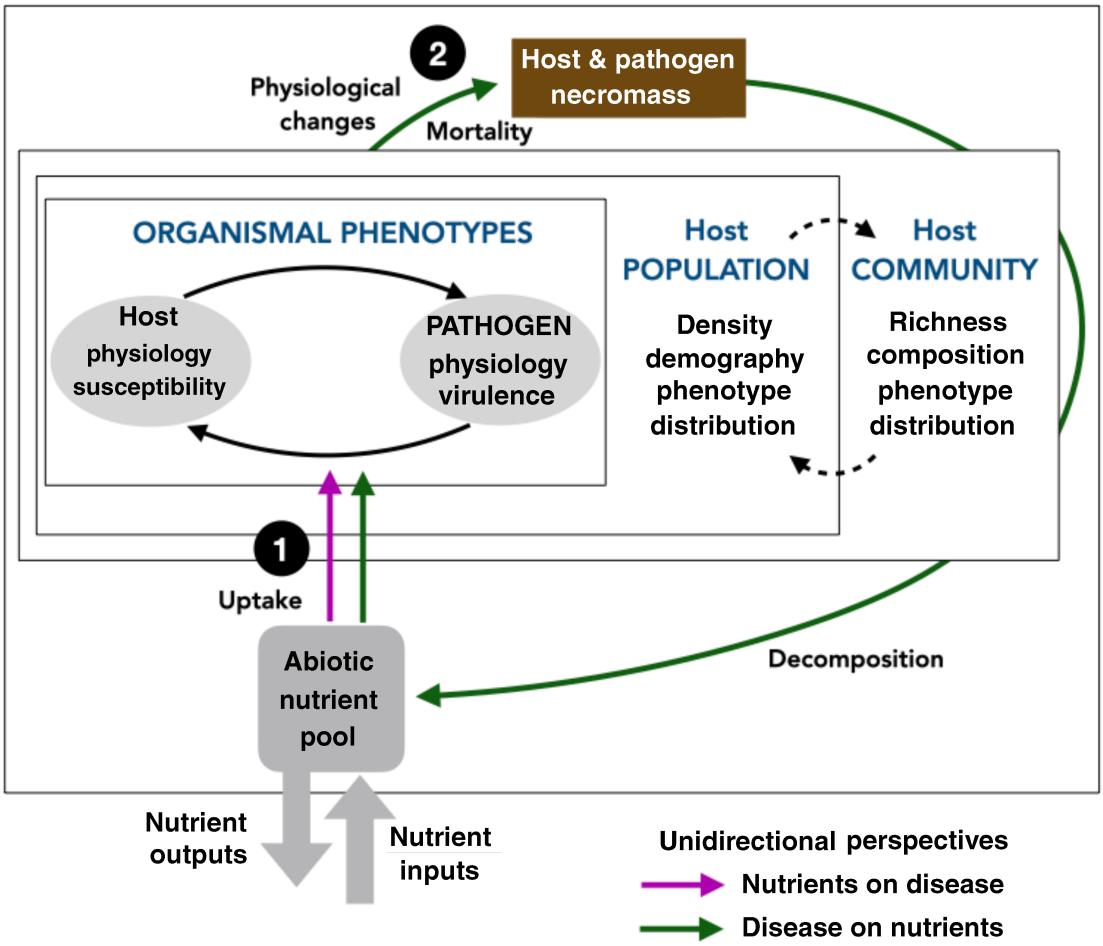

FIGURE 1 Disease-mediated nutrient dynamics place host–pathogen interactions into an ecosystem context. Environmental nutrients modify, and are modified by, infection. These processes include how uptake of environmental nutrients (purple arrow, 1) shapes pathogen prevalence and disease severity via individual host and pathogen phenotypes, population attributes, and community properties (inner boxes). Infection-induced changes to hosts at any of these scales can alter subsequent nutrient uptake (green arrow, 1). Infection also alters host physiology or mortality, modifying populations and communities, feeding back to change the quantity and nutrient content of necromass (dead host and pathogen biomass) that is recycled via decomposition (green arrow, 2). Jointly, these disease–nutrient relationships create the potential for both positive and negative feedbacks

and P dynamics via effects on nutrient uptake by autotrophs and via effects of nutrient availability on consumer performance (Atkinson et al., 2017; Elser & Urabe, 1999; Sterner, 1990). Importantly, the CND framework accounts for the mismatch between the elemental content of autotrophs and the dietary needs of herbivores. In response to a mismatch, the consumer will retain more of the element at lowest supply and will excrete more of the element in excess relative to its dietary needs, thereby altering the ecosystem-scale cycling rates of elements (Sterner & Elser, 2002). While the focus of the CND literature has been on free-living consumers, with the recent addition of parasites that infect herbivores (Vannatta & Minchella, 2018), pathogens of plants represent an important group of consumers for elemental cycling. In fact, the ubiquity of pathogens in nature and the degree to which infection can impact host physiology and survival points to the importance of pathogens for mediating ecosystem processes, including nutrient cycling, across Earth's environments (Sanders & Taylor, 2018; Suttle, 2007).

Disease-mediated nutrient dynamics (DND), the broad suite of pathways linking host–pathogen interactions with ecosystem-level storage and flux of nutrients like N and P, falls within the scope of CND. However, pathogens differ substantially from free-living consumers in terms of life history, movement patterns, physiology, nutrient acquisition strategy, and relationship to the environment (with a host often serving as a pathogen's immediate environment). Therefore, a shift to examine pathogens requires refocusing the CND framework. Some components of the CND framework can be reframed by analogy. For example, pathogens do not excrete elements in the same way as free-living consumers, although they typically have higher N:C and P:C than their autotrophic hosts. This discrepancy can lead to differential excretion of C relative to nutrients from infected hosts (Frenken et al., 2021). However, unique characteristics of pathogen biology require a novel model structure that differs from CND models. For example, infected hosts often continue to reproduce, a dynamic that differs from victims of predation. Spatial considerations also differ between CND and DND. Many free-living consumers move across space, potentially ingesting and egesting nutrients in different locations (Capps & Flecker, 2013). Plant pathogens typically only infect a single stationary host, but pathogen populations can reproduce and disperse to "consume" additional hosts on a much faster timescale (i.e., during an epidemic). Thus, focusing on pathogen–host interactions in a nutrient dynamic framework explicitly allows examination of rapid population-level responses of the pathogen, reproductive contributions by infected hosts, and a sharpened focus on the importance of pathogen biomass nutrients and C: nutrient excretions from infected hosts.

From an ecosystem perspective, pathogens of autotrophs are even more likely than consumers to impact nutrient cycling. In particular, most autotrophic biomass does not come in contact with free-living consumers (e.g., herbivores) (Chapin et al., 2011), whereas pathogens of autotrophs are ubiquitous (Burdon & Laine, 2019). The DND model developed in this section focuses on pathogens of autotrophs but is intentionally similar in structure to CND models (e.g., Atkinson et al., 2017; Elser & Urabe, 1999), with most parameter meanings redefined by analogy. For example, transmission in the DND model is analogous to ingestion (e.g., grazing) in a CND model, with nutrient dependence of transmission analogous to a shift in ingestion rate with food quality or stoichiometric mismatch. However, the relative parameter values for DND fall outside those describing free-living consumers, leading to new ranges of model dynamics and empirical predictions. Even the relatively simple DND model analyzed in this section produces surprisingly complex behavior. Taken together, the model and empirical review of DND highlight the many ways in which host-pathogen interactions differ from consumer-autotroph interactions, laying the groundwork for future empirical and theoretical exploration (*A case study of virus-mediated nutrient dynamics in marine phytoplankton*).

Dynamic model describing disease-nutrient feedback loops

Feedback loops in dynamic models linking disease with elemental cycles have received very little attention to date (but see Borer et al., 2021). Yet predicting the relationships between disease and ecosystem function, particularly in a changing nutrient environment, requires explicit attention to the interplay of these processes. To examine the dynamic effects that arise from coupling infection in primary producers with ecosystem nutrient recycling, we developed a simple dynamic model of disease-mediated nutrient dynamics (Figure 2a). Our framework merges ecological modeling of nutrient-dependent population dynamics (logistic and Droop growth) with epidemiological modeling (susceptible and infected compartments), building conceptually from consumer-driven nutrient dynamics theory (Atkinson et al., 2017; Elser & Urabe, 1999; Sterner, 1990). The resulting model links disease and nutrient dynamics via multiple pathways (Figure 2b).

In the disease-mediated nutrient dynamics (DND) model, host growth rate depends on environmental nutrients. This dependence, in turn, impacts host tissue chemistry, susceptible host population size, density-dependent pathogen transmission, and the resulting prevalence of infection (Figure 1, arrow 1). Pathogens reduce host

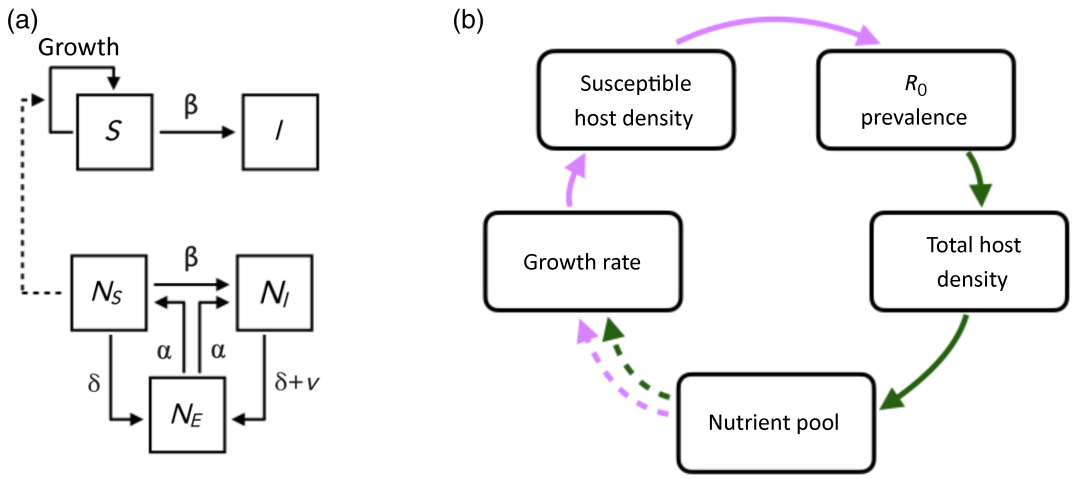

FIGURE 2 (a) The disease-mediated nutrient dynamics model includes nutrient-dependent growth rate (dashed arrow) for susceptible (S) and infected (I) autotroph hosts. The model tracks infection-dependent nutrient flux among susceptible hosts (N_S), infected hosts (N_I), and the abiotic environment (N_E). Removing the nutrient-dependent growth link breaks the feedback loop, producing a decoupled growth model, in which growth and infection are independent of environmental nutrients. (b) The DND model describes a disease-nutrient feedback loop. Abiotic nutrient availability impacts autotroph host growth rate and susceptible host density, with outcomes for pathogen spread and prevalence (purple arrows). Disease-induced changes in growth rate and mortality alter host density and the rate of nutrient return to the environmental nutrient pool (green arrows). Removing the nutrient dependence of growth (dashed arrows) breaks the feedback loop (decoupled growth model)

growth rate and increase host mortality rate, impacting the rate at which nutrients are returned to the environment (Figure 1, arrow 2). Host population dynamics are coupled with instantaneous environmental nutrient supply using a Droop-like formulation (Droop, 1973), in which the nutrient uptake rate increases asymptotically with environmental availability (Box 1). Hosts grow logistically, limited by low internal nutrient quotas at low environmental nutrients and by light availability at high environmental nutrients (see similar approach in Loladze et al., 2000). Nutrient uptake rate depends on whether or not a host is infected, reflecting empirical evidence for a wide range of autotrophs (Dordas, 2008; Fones & Gurr, 2017; Box 1).

We use this disease-mediated nutrient dynamics model (DND model) to examine the consequences of disease-nutrient feedback loops for host population density, host phenotype (as stoichiometric quota), disease dynamics, and environmental nutrient pools and fluxes. To examine the role of feedback loops, we compare the DND model to a simplified model in which host growth is independent of nutrient availability (decoupled growth model), thus allowing a direct comparison of dynamics with and without a disease-nutrient feedback loop (Figure 2, dashed lines). For illustration, we use parameter values describing a deciduous forest (Table 1; see Borer et al., 2021 for parameterization details). However, the relative simplicity of this model allows it to apply broadly to a wide array of autotroph–pathogen systems (Box 1).

Dynamics arising from disease–nutrient feedback loops

Model simulations comparing decoupled growth to the DND model with disease–nutrient feedbacks demonstrate the importance of this coupling for the dynamics of infection prevalence and the distribution of nutrients between autotrophs and the environment (Figure 3). Infection prevalence oscillates after pathogen introduction, with or without the model feedback (Figure 3a). In the decoupled growth model, these oscillations dampen, and prevalence quickly reaches a stable equilibrium. In contrast, cycles of infection prevalence and environmental nutrients persist in the DND model, although this feedback does not strongly impact the mean distribution of nutrients between the environment and host populations (Figure 3b). In the same nutrient environment, both per capita growth rates (Figure 3c) and organismal C:N stoichiometry (Figure 3d) settle to lower equilibria in the DND model than the decoupled growth model, with convergent oscillations persisting longer in the DND model. These examples clarify that the disease-nutrient feedback is destabilizing relative to the decoupled growth model, particularly under high nutrient conditions.

Environmental nutrient availability interacts with pathogen transmission rates to determine host and infection dynamics. In Figure 4a,b, with disease mediated nutrient recycling (DND model), R_0 increases with nutrients until host growth is no longer limited by nutrients;

BOX 1 Disease-mediated nutrient dynamics (DND) model equations and stoichiometric quota expressions. Modifications to the model include the decoupled growth model and a model of population growth with contributions from infected autotrophic hosts. Parameter definitions are presented in Table 1

DND model equations	Description
$\frac{dS}{dt} = r\left[1 - \frac{S+I}{\min\left\{\frac{Kr}{r-\delta}, \frac{N_S(S+I)}{qS}\right\}}\right]S - \beta SI - \delta S$	Susceptible host density (g C/m^2)
$\frac{dI}{dt} = \beta SI - [\delta + v]I$	Infected host density (g C/m^2)
$\frac{dN_S}{dt} = u(N_E)S - \frac{N_S}{S}\beta SI - \delta N_S$	Nutrients in Susceptible hosts (g N/m^2)
$\frac{dN_I}{dt} = u(N_E)I + \frac{N_S}{S}\beta SI - [\delta + v]N_I$	Nutrients in Infected hosts (g N/m^2)
$\frac{dN_E}{dt} = -u(N_E)S - u(N_E)I + \delta[N_S + N_I] + vN_I$	Nutrients in environment (g N/m^2)
Stoichiometric quota expressions	
$Q_s = \frac{N_S}{S}$	Susceptible host N:C ratio (g N/ g C)
$Q_I = \frac{N_I}{I}$	Infected host N:C ratio (g N/g C)
Decoupled growth model: replace S equation in DND model	
$\frac{dS}{dt} = r\left[1 - \frac{S+I}{\frac{Kr}{r-\delta}}\right]S - \beta SI - \delta S$	
DND model equations with infected growth: replace S equation in DND model	
$\frac{dS}{dt} = r\left[1 - \frac{S+I}{\min\left\{\frac{Kr}{r-\delta}, \frac{N_S(S+I)}{qS}\right\}}\right]S + \sigma r\left[1 - \frac{S+I}{\min\left\{\frac{Kr}{r-\delta}, \frac{N_I(S+I)}{qI}\right\}}\right]I - \beta SI - \delta S$	
Decoupled growth model with infected growth: replace S equation in DND model	
$\frac{dS}{dt} = r\left[1 - \frac{S+I}{\frac{Kr}{r-\delta}}\right]S + \sigma r\left[1 - \frac{S+I}{\frac{Kr}{r-\delta}}\right]I - \beta SI - \delta S$	

TABLE 1 Disease-mediated nutrient dynamics (DND) model parameter and function definitions with values used in Figures 3–6, based on a deciduous forest (see Borer et al., 2021 for details of parameter estimation)

Parameter/function	Meaning	Value
r	Maximum growth rate	0.0754/year
K	C-dependent carrying capacity	22 kg C/m^2
q	Minimum host N:C ratio	1/439 g N/g C
δ	C natural death rate	0.0412/year
ν	C disease-induced death rate	0.01/year
β	Transmission rate	1.2×10^{-5} m^2/g C/year
α	Maximum N:C uptake rate	3.8147×10^{-4} g N/g C/year
κ	N:C uptake half saturation constant	0.009 g N/m^2
$u(N_E)$	Nutrient uptake function	$\frac{\alpha N_E}{\kappa + N_E}$
σ	Reduction in growth rate for Infected	0–1

at this point, host growth and infection become light limited. However, with nutrient recycling in the DND model, ecosystems with very low nutrient availability (e.g., oligotrophic lakes) do not support a sufficient per capita host growth rate or reach sufficient host biomass to sustain density-dependent pathogen transmission. When recycled nutrients affect host growth rate (DND model), pathogens with low transmission rates require

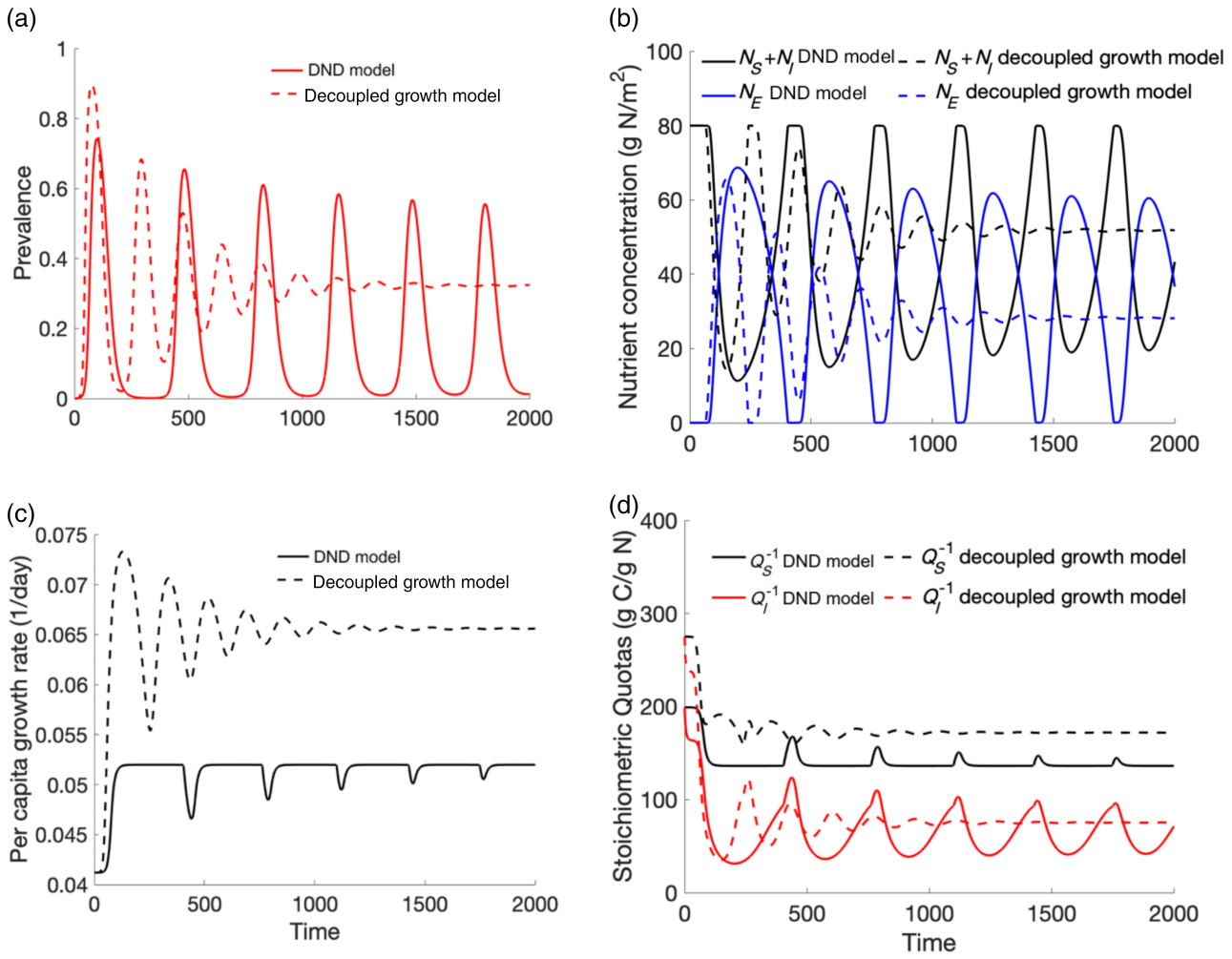

FIGURE 3 (a) Infection prevalence, (b) nutrient content, (c) growth rate, and (d) elemental stoichiometry dynamics resulting from the disease-mediated nutrient dynamics (DND) model (solid lines) and the decoupled growth model (dashed lines) under nutrient conditions with $N = 80$ g N/m^2. Time zero on these graphs is the moment of pathogen introduction; simulations began 1000 years prior to the pathogen introduction to allow for a steady state to be reached. Q_S is the susceptible host N:C ratio

substantially more nutrient-rich conditions to support the per capita host growth rate that sustains infection ($R_0 = 1$) compared to pathogens with higher transmission rates. In contrast, for these same parameter values in the decoupled growth model (Box 1, Table 1), the per capita growth rate is always high enough to sustain infection, even under low nutrient conditions.

With disease-mediated nutrient recycling (DND model), environmental nutrients also interact with transmission rates to control the cycling dynamics of infection prevalence (Figure 4c,d). In particular, the DND formulation with a high transmission rate leads to cycling at elevated nutrients, whereas the decoupled growth model does not cycle (Figure 4d). Like prevalence, nutrient availability impacts host dynamics differently at low and high transmission rates (Figure 4e,f). At high transmission and elevated nutrients, both susceptible and infected hosts in the DND model cycle, whereas neither transmission nor nutrients induce cycles in the decoupled growth model (Figure 4f).

From an empirical perspective, these results suggest that infection prevalence, even within the same host species or ecosystem type, could become destabilized, taking on an extremely wide range of values at high ecosystem nutrient supply, with long time periods of either high or low prevalence arising from small shifts in nutrient availability, as in the "paradox of enrichment" (Rosenzweig, 1971). Similarly, while the pathogen generally benefits from greater nutrient availability, these cycles also could lead to its stochastic extinction. Thus, this exploration suggests that in a system with disease-mediated nutrient dynamics, empirical data should reflect an increase in the basic reproductive number (R_0) and infection prevalence from low to intermediate nutrient availability. However, under high transmission

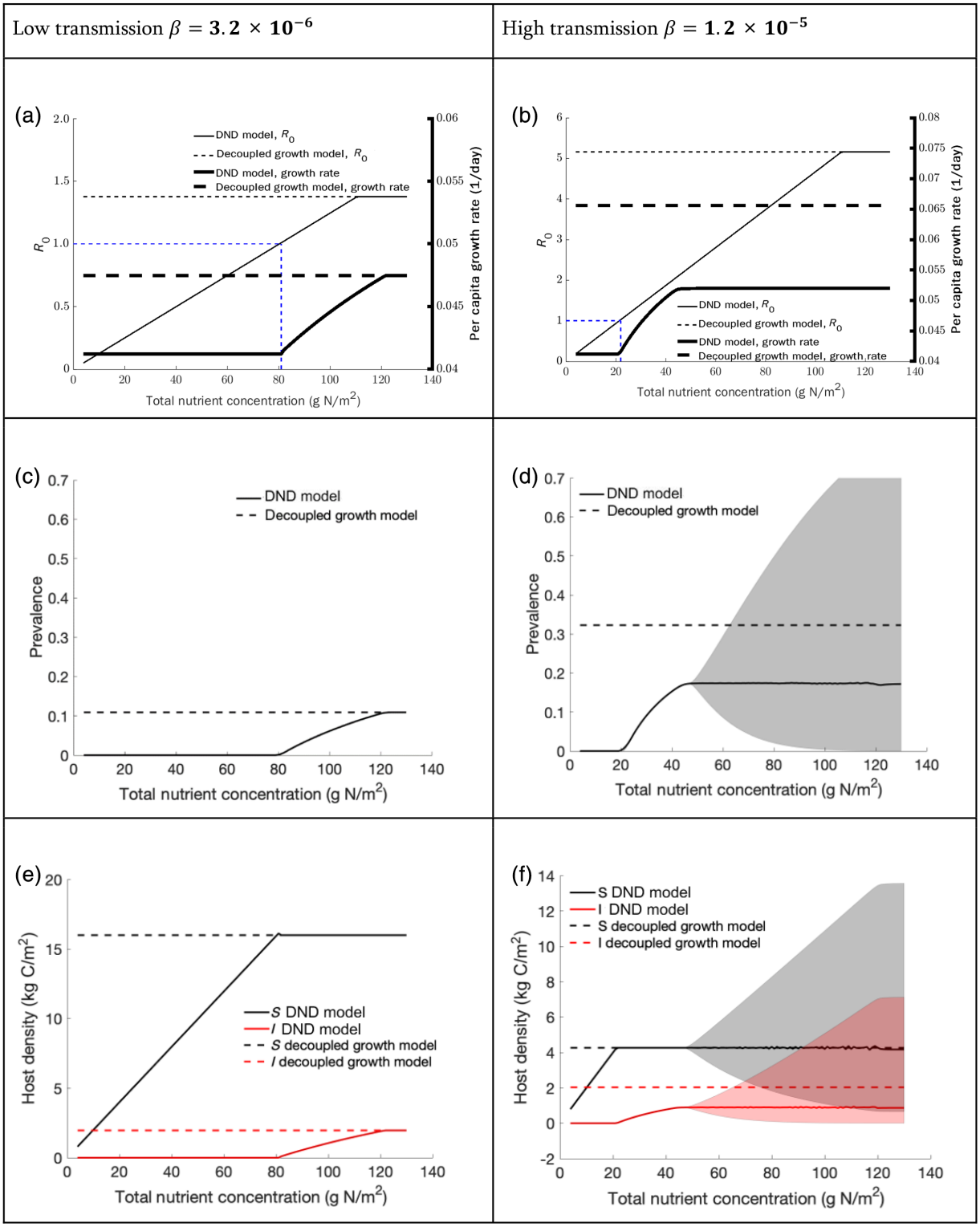

FIGURE 4 Ecosystem nutrients impact pathogen basic reproductive number (R_0, thin lines) and host per capita growth rate (heavy lines) at (a) low and (b) high transmission rates when autotroph growth depends on recycled nutrients (DND model) or not (decoupled growth model). Blue dashed lines indicate nutrient conditions below which infection is not sustained ($R_0 = 1$). Infection prevalence is impacted differently by nutrient availability at (c) low and (d) high transmission rates. Like prevalence, nutrients also impact host dynamics differently at (e) low and (f) high transmission rates. Shaded regions indicate magnitude of cycles. Based on numerically observed cycles, the DND model appeared to have sustained cycles after 1 million years using Matlab's Runga Kutta ode45 solver

rates and high nutrient availability, prevalence and R_0 may appear to become decoupled from environmental nutrient supply due to complex dynamics arising from the disease–ecosystem feedback. Highly transmissible pathogens also may shift between stable endemic infections and large amplitude epidemic cycles, depending on the environmental nutrient supply (Figure 4d,f).

This model comparison also demonstrates how disease-mediated nutrient recycling impacts mean host tissue chemistry, host growth rate and density, and infection prevalence. Host tissues in the DND model exhibit lower stoichiometric C : nutrient ratios (Figure 3d) and per capita growth is slower (Figure 3c) than for hosts in the decoupled growth model, even though the assumptions and parameterization of the nutrient uptake and release rates are the same in these models. These differences arise because of the nutrient limitation of growth in the DND model. Nutrient limitation reduces per capita growth rates in the DND model compared to the decoupled growth model, with convergence of per capita growth rates (Figure 4a,b) and host density (Figure 4e,f) only under high nutrient supply, when nutrients no longer limit growth. The models do not always converge, however. With high transmission rates in the DND model, as nutrients increase, host densities begin to oscillate and, on average, hosts remain limited by nutrients, even at high nutrient supply (Figure 4f). Because of this, host growth rates remain lower than those in the decoupled growth model, even at high environmental nutrient concentrations (Figure 4b). Thus, failing to account for dynamic feedbacks between disease and nutrients can lead to substantially different predictions for both disease and nutrient dynamics.

We also used the model to examine nutrient dynamics as a function of disease transmission (Figure 5). In particular, investment in defense modifies pathogen transmission, often trading off with growth investment in autotrophs (*Growth rate and size*), and this investment can covary with the stoichiometry of an organism (*Tissue chemistry*). However, our model allows us to decouple these effects to examine the independent influence of defense on pathogen dynamics and nutrient recycling along a gradient of transmission success (Figure 2, β). The DND model demonstrates that when transmission rates are very low, the pathogen cannot persist in the environment, and all hosts remain healthy. When the transmission rate crosses the threshold for the pathogen to persist ($R_0 = 1$) in the DND model, the C : nutrient content of individual host tissues (Q_s^{-1}, Q_I^{-1}) declines with increasing transmission rate until the transmission is high enough that the nutrient content no longer varies with further increases in transmission (Figure 5a). With increasing transmission, nutrient recycling in the DND

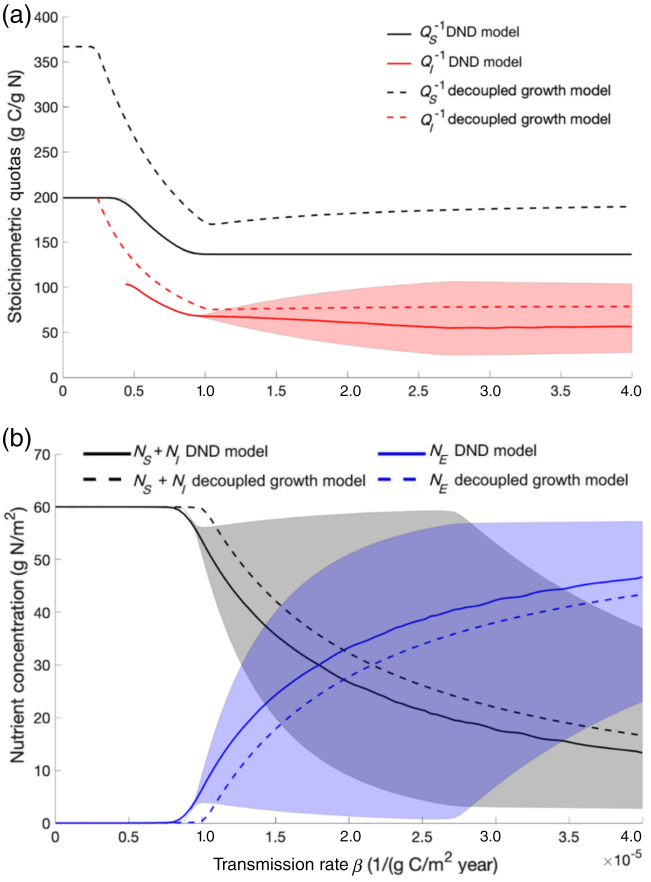

FIGURE 5 Pathogen transmission rate impacts (a) host stoichiometric quota and (b) nutrient pools in susceptible and infected autotrophs (N_S, N_I) and the abiotic environment (N_E). Feedbacks between disease and nutrients in the DND model cause cycling with increasing transmission; shaded regions show cycle minima and maxima, and solid lines indicate the mean. Without a feedback (decoupled growth model), equilibria are stable for all transmission rates. Nutrient conditions are set at 60 g N/m^2

model induces instability in infected hosts, but this oscillatory behavior does not occur in the decoupled growth model. Further, at low transmission rates, virtually all environmental nutrients are taken up by hosts (N_E). However, with increasing transmission in the DND model, host nutrient content experiences a bifurcation in which a small change in transmission leads to wide swings in environmental nutrients (Figure 5b). In short, transmission rate, and any host defenses that modify this rate, in the DND model controls host population density and stoichiometric phenotype, both of which contribute to the distribution of nutrients among infected hosts, susceptible hosts, and the abiotic environment.

While the simplest DND formulation leads to oscillatory dynamics associated with both transmission and nutrient supply, small, biologically motivated changes can alter these dynamics. For example, the addition of even a small amount of reproduction by infected hosts is

stabilizing in the DND model, causing the oscillation amplitudes to quickly dampen to stable equilibria (Figure 6). While this reflects the biology of a wide range of pathogens (with the obvious exception of complete infection by castrating pathogens; Clay & Schardl, 2002; Hartmann et al., 2019), the CND-DND analogy breaks down here, qualitatively changing the dynamics of hosts, infection, and nutrient recycling.

This model of disease-mediated nutrient dynamics is intentionally simple to clarify the importance of feedbacks linking the dynamics of a host, an environmentally transmitted pathogen, and elemental nutrients (Figure 2). Despite the model's structural simplicity, these results demonstrate that feedbacks between disease and nutrients can generate a surprisingly wide range of host elemental content and population dynamics, infection patterns, and environmental nutrients, and these results diverge from dynamics lacking this feedback (Figure 3). Even this simple coupling causes nutrients to influence disease prevalence, the pathogen's basic reproductive number, and host density (Figure 4). The rate of transmission (and host defenses that may reduce this) influences the distribution of nutrients among organisms and the abiotic environment (Figure 5), inducing instability where environmental nutrient supply (Figure 4) and transmission (Figure 5) are high.

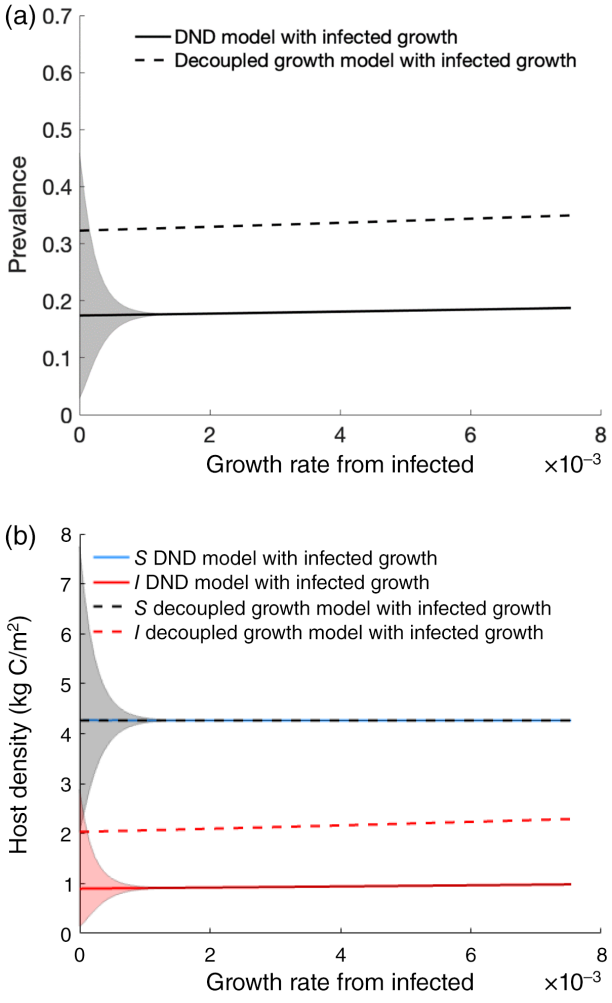

FIGURE 6 Incorporating infected population growth without vertical transmission (infected producing susceptible) influences (a) prevalence and (b) host density. Shaded regions show cycle minima and maxima, and solid lines indicate the mean. The basic DND model dynamics occur where the *x*-axis is zero. Predictions were obtained after running simulations for 100,000 years using Matlab's Runga Kutta solver ode45

In the following sections, we review a wide range of empirical autotroph–pathogen examples ranging from sub-cellular to host community scales. Many of the necessary data do not yet exist to fully link environmental nutrient supply with many of the dynamics uncovered in this modeling exercise. However, we use this review, spanning a wide range of real systems, to highlight key relationships between environmental nutrient supply and recycling, hosts, and pathogens that converge in the DND framework (Figure 1).

THE CYCLE FROM NUTRIENT SUPPLY TO HOST–PATHOGEN INTERACTIONS AND ECOSYSTEM NUTRIENT DYNAMICS

For pathogens infecting autotrophs, nutrient-induced changes to a host's phenotype may impact a pathogen's infection cycle through a range of pathways (Figure 1, arrow 1). The DND model simulations demonstrated that feedbacks and interactions among these changes can control the dynamics of nutrient cycling and disease. As documented in the following sections, plasticity in host growth rate, size, defense investment, and tissue elemental content may alter pathogen replication based on the quality of the host as a resource, and nutrient-induced shifts in host defense investment may alter host susceptibility, tolerance, or competence for a pathogen. Evidence from many host–pathogen systems demonstrates that individual-level shifts in characteristics such as growth rate, defense, or tissue elemental content, when examined across host populations and communities, play a key role in pathogen transmission and disease outcomes. Additional processes operating at the population and community scales alter infection dynamics as a function of environmental nutrient supply.

Shifts in infection within hosts can, in turn, lead to impacts on nutrient dynamics, particularly when the hosts are autotrophs, by altering individual host chemistry, physiology, and demographic rates (Borer et al., 2021, Figure 1, arrow 2). Although infection is often associated

with elevated mortality, pathogens can alter ecosystem function via both sublethal, trait-mediated effects or lethal, density-mediated effects (Fischhoff et al., 2020; Preston et al., 2016), including decoupling elemental flows into and out of infected hosts (Frenken et al., 2021). Because autotrophs sit at the nexus between the abiotic world of elements and energy and biotic food webs, disease-mediated variation in host traits such as growth rate, defense, tissue chemistry, and competitive ability, can control nutrient pools and fluxes through ecosystems when scaled up to the level of host populations or communities. Here, we synthesize a broad range of examples that, taken together with the DND model, point to the likelihood that nutrient supply and nutrient feedback loops play an important role in the nutrient and disease dynamics of natural systems.

Growth rate and size

All autotrophs share common biochemical machinery that requires N and P for growth, metabolic functions, and reproduction (Sterner & Elser, 2002). Because of this, we focus on nutrient impacts to host growth rate (Figure 2, Growth). By influencing organismal and species-level functioning, nutrient supply constrains species growth rates (Figure 2a, dashed arrow), ultimately shaping the diversity and composition of host communities (Harpole et al., 2016). Thus, nutrient supply and recycling through death and decomposition are critical processes fueling biological systems. The supply of growth-limiting nutrients can change host phenotype by increasing organism size for unicellular autotrophs or increasing total biomass or investment in specific tissues for multicellular autotrophs (Fay et al., 2015; Garcia et al., 2016). For pathogens, size differences among hosts can represent variation in space for colonization or replication (Holfeld, 2000; Kuris et al., 1980; Rasconi et al., 2012). Metabolic rates, generally declining with host body size (Makarieva et al., 2008), can set limits on rates of within-host pathogen replication (Banerjee et al., 2017; Cable et al., 2007). However, there is some evidence that cellular nucleotide content, which generally increases with host cell size (Machado et al., 2021), also may limit pathogen replication and the number of pathogen particles released into the environment (Machado et al., 2021).

Infection also can interact with nutrients to generate countervailing effects on host growth rate and size. In particular, infection can be energetically expensive for a host, feeding back to slow host growth and metabolic rate and diverting energy and nutrients to other functions (Berger et al., 2007), ultimately slowing population growth rate and reducing host density (Figure 4e,f). Reduced photosynthesis and increased respiration rate in response to infection leads to reduced primary productivity in autotrophic hosts (Kohli et al., 2021), ultimately reducing biomass. Following host death, this biomass becomes organic matter that eventually decomposes, recycling carbon and nutrients.

The biology of a pathogen also can interact with plant growth and development to determine impacts on nutrient recycling, and these impacts can vary with plant growth rate (Häffner et al., 2015). Necrotrophic pathogens that derive nutrients from dead host cells, for example, can manipulate hosts to speed development, inducing an earlier onset of senescence (Mengiste, 2012), which leads to more rapid nutrient recycling. Biotrophs, on the other hand, derive nutrients from living host tissues, and infection can slow host senescence (Häffner et al., 2015; Newton et al., 2010). Hosts and their pathogens have a wide range of strategies to control the signaling molecules that determine the host's metabolic rate and development, many of which alter nutrient mobilization within living hosts and recycling following senescence (Häffner et al., 2015).

Studies of pathogens and their autotrophic hosts provide evidence of host size and growth rate impacting pathogens with concurrent impacts of pathogens on host size and growth as a function of environmental nutrients. For example, experimentally elevated N supply to grasses generally increases individual growth rate, which is subsequently associated with altered viral titer, a measure of pathogen concentration within host tissues (Lacroix et al., 2017; Whitaker et al., 2015). For this group of grass hosts and their barley and cereal yellow dwarf viral pathogens, nutrients indirectly modify virus concentrations via effects on host size and growth rate, and virus infection interacts with nutrients to modify host traits associated with growth (e.g., leaf thickness; Lacroix et al., 2017). This influence of nutrients on host-pathogen interactions may be due to a general tradeoff between investment in growth and investment in defense. In particular, crops are often bred to maximize growth and nutrient responsiveness while minimizing investment in defense (Huot et al., 2014), which means that N supply to crops generally enhances growth rate and size (Luo et al., 2020). Because of this trade-off within and among species in the use of nutrients for growth or defense, faster-growing, larger individuals tend to experience more infection (Heckman et al., 2019; Huot et al., 2014). These relationships are similar for algae (Holfeld, 2000).

Defense

Although control of growth and senescence via signaling pathways is a key battleground for autotrophs and their

pathogens (Häffner et al., 2015), autotrophs also defend themselves from pathogens and other consumers using both chemical and structural defenses, the production of which depends on the nutrient environment (Chen & Ni, 2011; Lerdau et al., 1994). By reducing the transmission success of pathogens (Figure 2a, β), investment in defense can slow nutrient recycling by retaining nutrients in living tissue and reducing tissue or whole organism senescence.

Both structural and chemical defense can vary as a function of the nutrient environment, impacting transmission success. A host's cell wall serves as a first line of defense against invading pathogens, representing a less costly defense investment than host-induced cell or tissue death (Underwood, 2012). However, elevated environmental nutrient supply can reduce cell wall lignin and cellulose, reducing disease resistance (Ogden et al., 2018). While cell wall thickness can serve as a constitutive defense, cell walls also can be reinforced by papillae, an induced structural defense that is rapidly laid down on cell walls in response to the sensing of a wide range of fungal or bacterial pathogens (Ogden et al., 2018). While the general relationship with environmental nutrient supply is unclear, plant tissue C:N regulation is related to papillae formation (Maekawa et al., 2014). Thus, elevated nutrients likely cause reduced investment in structural defenses, leading to increased infection and more rapid nutrient recycling.

Although nutrients such as N generally reduce physical defenses, elevated N supply can increase defense-related enzymes, proteins, and gene expression in plants (Sun et al., 2020). For example, N-rich oligopeptides such as microcystins, produced by cyanobacteria, may defend against fungal pathogens (Rohrlack et al., 2013), and production of cyanobacterial toxins with similar molecular structure can increase with higher relative N availability (van de Waal et al., 2009). However, elevated N supply also has been shown to downregulate defensive chemical production in terrestrial plant species ranging from crops like soybeans, grapes, and rice to trees such as beech and Norway spruce (Sun et al., 2020). Importantly, investment in defense often trades off with growth investment in autotrophs (*Growth rate and size*) and can covary with organismal chemistry (*Tissue chemistry*).

Tissue chemistry

From the perspective of pathogens, plant elemental composition, including stoichiometric ratios among multiple elements, can represent host quality. In autotrophs, tissue chemistry can vary, often responding to elevated environmental nutrient supply with uptake that shifts the elemental composition of plant tissues (Figure 2, N_S). Ecological stoichiometry predicts that imbalanced ratios between consumers, such as pathogens, and their host resources will decrease consumer growth and fitness (Frenken et al., 2021; Sterner & Elser, 2002). This prediction has been tested extensively for herbivores, which are generally more homeostatic in elemental composition than autotrophs (Hillebrand et al., 2009). While the effects of elemental imbalance in pathogen–host interactions have not been studied as extensively (Frenken et al., 2021; Sanders & Taylor, 2018), these effects may be strong since most pathogens depend on their hosts for all chemical resources. Additionally, the high growth rates of many pathogens relative to their hosts correspond to high demands for elemental nutrients to support the synthesis of nucleic acids and proteins (Clasen & Elser, 2007; Sterner & Elser, 2002).

Increased host N or P content or reduced C:N or C:P may directly alleviate nutrient limitation of pathogen population growth via direct use of stored host nutrients (Fatima & Senthil-Kumar, 2015). Alternatively, host nutrient uptake may indirectly benefit pathogen reproduction via macromolecules produced by the host (Sun et al., 2020) or via increased host investment in growth, providing the cellular machinery also required for some pathogens (e.g., viruses) to replicate (Cuomo et al., 2012; Smith, 2007). In one example of P supply stimulating rapid pathogen growth, a Chlorella virus infecting green algal hosts (*Chlorella*) benefited from decreased host C:P (Clasen & Elser, 2007). In this case, P supply and host C:P limited virus replication and assembly. More recently, both N and P limitation of algal growth have been demonstrated to reduce viral replication within their phytoplankton hosts by up to 90% (Maat & Brussaard, 2016). N supply limits growth of fungal pathogens infecting autotrophic hosts as wide ranging as cyanobacteria (Frenken, Wierenga, et al., 2017) and grasses (Mitchell et al., 2003), clarifying that the impact of a change in the C:N:P nutrient environment on infection depends, at least in part, on the stoichiometric requirements of, and mismatch between, hosts and their pathogens (Frenken et al., 2021).

Although nutrients that increase host growth rate can increase pathogen reproduction (also see *Growth rate and size*), the nutrient environment limiting pathogen growth also can differ from that limiting host growth. For example, in the experiment with a virus and *Chlorella* algal hosts, even though the host growth rate and reproduction were independent of P supply, the increase in the P content of cells due to algal elemental plasticity alleviated the pathogen's nutrient limitation, leading to increased pathogen replication (Clasen & Elser, 2007). Similar effects occurred in a grassland field experiment, where N

addition increased grass-host biomass accumulation, but P addition increased the prevalence of a viral pathogen in these hosts (Borer et al., 2010).

Pathogens can stimulate host nutrient uptake (Figure 2a, N_I while simultaneously competing with their host for these resources These interactions between infection and nutrient supply can alter autotrophic host tissue chemistry and decomposition rates, ultimately regulating the storage and recycling of nutrients in ecosystems. When a host's growth-limiting resources are depleted by pathogen infection, this can lead to reduced host growth, lifespan, and lifetime reproduction (Smith, 2007; Smith & Holt, 1996). For example, infection by a phloem-limited virus of grasses reduces nutrient concentrations (N, Mg, Ca) of crop leaves (Riedell et al., 2007). For stoichiometrically driven host–pathogen interactions, elevated CO_2 can increase host C : nutrient ratios, potentially exacerbating the impact of infection on growth and reproduction (Mitchell et al., 2003). For example, mortality of European beech trees infected with an oomycete was substantially increased under elevated CO_2 and low N conditions, when C:N was very high (Fleischmann et al., 2010). However, at ambient CO_2, survival was high under all N conditions. Analogous to CND (Atkinson et al., 2017; Elser & Urabe, 1999; Sterner, 1990), higher requirements of N or P of the pathogen relative to host tissue may lead to greater retention of these nutrients in infected biomass (e.g., compare red and black lines in Figure 3d), thereby enhancing limitation of these nutrients and possibly increasing the recycling of non-limiting nutrients and C. Many empirical studies have found infection-induced increases in host tissue nutrients, ranging from increased N content in response to oomycete infection in bay laurel and European beech (Fleischmann et al., 2002; Wang et al., 2003) to increased N (Borer et al., 2015) and P content (Rúa et al., 2013) in response to viral infection in grasses. Importantly, these chemical signatures of infection can persist past death, influencing litter chemistry, decomposition (Cobb & Rizzo, 2016), and nutrient recycling (Hobbie, 2015).

Variation within and across host populations

The effects of nutrient supply can scale up, modifying the population size of an autotrophic host species (Figure 1, Host population) via changes in growth rate (*Growth rate and size*, Figure 2a, dashed arrow), tissue chemistry (*Tissue chemistry*, Figure 2a, N_s and N_I), and investment in defense (*Defense*, Figure 2a, β), all of which can interact with infection. Since transmission of many pathogens requires host density to exceed a minimum threshold (Anderson & May, 1981), population density, per se, can impact infection dynamics (Burdon & Chilvers, 1982). Importantly, small host populations that increase due to nutrient supply, crossing this threshold, become vulnerable to the spread of infections (Figure 4a,b, DND model). Within a host population, transmission heterogeneity, arising from variation in host characteristics, such as age, nutrition, defense, or genetics, can amplify (or slow) disease transmission within or among populations. While transmission heterogeneity has received far more attention in animal hosts (Lloyd-Smith et al., 2005; Paull et al., 2012), experimental work with the oomycete pathogen, *Phytophthora ramorum*, has uncovered evidence of substantial genetic variation in infection susceptibility among bay laurel host individuals (Anacker et al., 2008).

Infection can, of course, feed back to reduce host population size via reduced reproduction or increased mortality (Burdon, 1991), subsequently affecting rates of nutrient recycling. For multicellular autotrophs, the impacts of infection on reproduction can be both indirect and direct. Host population size can be reduced indirectly when infection reduces growth and investment in reproduction. For example, infection by viruses in the barley and cereal yellow dwarf virus group reduces biomass, the number of inflorescences, and seed production in a wide range of crops and wild grasses (Malmstrom, Hughes, et al., 2005, Riedell et al., 2007, also see *Growth rate and size*). However, some pathogen groups attack anthers (Falloon et al., 1988; Hartmann et al., 2019) or seed heads (Alderman et al., 1998; Clay & Schardl, 2002), directly reducing lifetime reproduction and survival of their hosts. Both direct and indirect impacts of infection on host population growth can interact with environmental nutrient supply to control host population size in a wide range of autotrophic hosts (Alexander, 2010).

Infection also can impact nutrient dynamics at the population scale through impacts on mortality. Perhaps the most well-known example of infection-induced nutrient recycling is that of viruses in marine systems, where estimates suggest that about 20% of all microbial biomass is killed by viruses daily, controlling biogeochemical cycling in oceans (Fuhrman, 1999; Suttle, 2005, 2007). In both freshwater and marine environments, infection by chytrid fungi also can cause mass mortality of phytoplankton, reducing or terminating algal blooms, and playing a major role in the recycling of carbon and nutrients (Frenken, Alacid, et al., 2017). In terrestrial systems, mass mortality in forest stands from fungal and oomycete infections also can alter nutrient dynamics. For example, in Hawaii, a ceratocystis fungal infection first reported in 2010 has already killed hundreds of thousands of *Metrosideros polymorpha* trees, the most abundant native tree species in the Hawaiian Islands (Barnes et al., 2018). Historically, chestnut blight (*Cryphonectria parasitica*)

led to an almost complete loss of the iconic American chestnut (*Castanea dentata*), declining from a cover of 36% across eastern North America to <1% (Elliott & Swank, 2008). As in aquatic systems, forest mortality from infection can have substantial consequences for nutrient and carbon recycling (Cobb et al., 2013; Hobara et al., 2001; Matson & Boone, 1984). For example, infection by the oomycete pathogen *Phytophthora ramorum* can increase forest litterfall mass by one to two orders of magnitude, and decomposing litterfall from infected hosts can increase soil N availability (Cobb et al., 2013; Cobb & Rizzo, 2016).

Variation among species in a community

By altering the competitive environment for autotrophs, nutrient supply can induce turnover in local species composition (Cleland & Harpole, 2010; Harpole et al., 2016; Huberty et al., 1998; Lehtinen et al., 2017), shifting the relative abundance of hosts and non-hosts (Figure 1, Host community). Autotroph diversity can amplify or reduce community-wide disease risk, depending on the characteristics of the community members (Keesing et al., 2006; Seabloom et al., 2018). Experiments simultaneously manipulating host richness and nutrient supply have demonstrated that the richness, composition, and relative abundance of species can be an even stronger predictor of fungal infection severity than nutrient supply or foliar nutrient content (Cappelli et al., 2020; Mitchell et al., 2003). Similarly, a study in a Tibetan grassland found that fertilization increased the community-wide pathogen load primarily via host compositional change; disease susceptible host species tended to be favored by fertilization whereas more resistant species were extirpated from the community (Liu et al., 2017). Pathogen life history (biotroph vs. necrotroph) and host specialization also are key predictors of host–pathogen interactions and responses to nutrients in multi-species communities (Keesing et al., 2006; Liu et al., 2020; Moury et al., 2017; Woolhouse et al., 2001, 2005). Thus, in addition to individual-level responses to nutrients (*Growth rate and size*, *Defense*, and *Tissue chemistry*), pathogen biology and the impact of nutrient supply on the richness, abundance, and identities of host and non-host species will jointly determine the impact of nutrients on disease dynamics in communities.

Pathogens also can control host community composition and nutrient recycling through differential impacts of infection among community members (Hennes et al., 1995; Mordecai, 2011; van Donk & Ringelberg, 1983). When these interactions alter the dominant traits of species in a community, they are most likely to impact ecosystem-scale processes, such as nutrient cycling (Litchman et al., 2015). For example, an infection-induced reversal in competitive ability has been implicated in the community trait shift in California grasslands from domination by perennial grasses to domination by lower biomass and C : nutrient annual grasses (Borer et al., 2007; Malmstrom, McCullogh, et al., 2005). This compositional shift dramatically reduced ecosystem-scale soil carbon storage (Koteen et al., 2011) and increased soil N availability (Parker & Schimel, 2010). Differential parasitism by chytrids in plankton communities can alter community composition, speeding nutrient recycling by causing higher mortality in large, inedible algal cells (Holfeld, 2000) and species (Rasconi et al., 2012). Similarly, species differences in pathogen-induced mortality in mixed forest stands increased nutrient recycling via changes in community composition (Metz et al., 2012), litterfall mass and chemistry, and soil N availability (Cobb et al., 2013).

A CASE STUDY OF VIRUS-MEDIATED NUTRIENT DYNAMICS IN MARINE PHYTOPLANKTON

While our model (*Disease-mediated nutrient dynamics*) and biological examples (*The cycle from nutrient supply to host–pathogen interactions and ecosystem nutrient dynamics*) suggest that the feedback loops integral to disease-mediated nutrient dynamics are likely general and dynamically important, systems for which we have the data to paint a more holistic view of these feedbacks remain rare. Here, we synthesize work on marine phytoplankton and viruses to illustrate disease-mediated nutrient dynamics and feedbacks in one system-focused example (Figure 7).

Marine phytoplankton, responsible for half of Earth's primary production (Field et al., 1998), play a key role in global biogeochemical cycles, and viral infections modify these cycles, from manipulation of individual algal host metabolism (Monier et al., 2017) to extensive mortality terminating massive algal blooms (Suttle, 2005). With increasing N and P supply (Figure 7, arrow 1), more virus particles are produced per host (increased burst size) and the time from infection to host cell lysis (latent period) is reduced (e.g., Maat & Brussaard, 2016). Infected hosts leak and excrete organic matter even before cell lysis, altering elemental cycling (Figure 7, arrow 2; Sheik et al., 2014). Viral infection also increases nutrient uptake rates (Figure 7, arrow 1), shifting the quantity and ratio of carbon and nutrients released from infected cells upon lysis (Figure 7, arrow 2, Monier et al., 2017).

These effects of infection on the physiology and mortality of marine phytoplankton cells can control population and community dynamics, scaling up to impact ecosystem nutrient recycling (Figure 7, feedback to arrow 1). For example, field studies of blooms of the dominant algal species, *E. huxleyi*, found up to 50% of the population

was infected by viruses (Brussaard et al., 1996), and 25%–100% of mortality could be attributed to infection (Bratbak et al., 1993). Because many of these viruses have narrow host ranges, viral-mediated mortality also can play an important role in the turnover of traits and species succession (Brussaard, 2004). At the community scale, infection-induced shifts in traits such as growth rate, size, and tissue chemistry impact the cycle rate and amplitude as well as the regional nutrient recycling feedback (Brussaard, 2004; Litchman et al., 2015).

EMERGING THEMES AND FUTURE DIRECTIONS FOR DISEASE-MEDIATED NUTRIENT DYNAMICS

The DND model (*Disease-mediated nutrient dynamics*, Figure 2) illustrates the impact of disease-ecosystem feedbacks, highlighting the ways in which model dynamics change with host and pathogen traits and with shifts in the abiotic nutrient environment. Despite the relative simplicity of the DND model (e.g., nutrient-independent transmission rates, similar nutrient uptake dynamics by infected and uninfected hosts), this formulation and parameterization exhibit surprisingly complicated dynamics (e.g., Figures 3–6). While the DND model highlights the exciting dynamical consequences of disease-mediated nutrient recycling for both disease and ecosystems, taken together with the biological examples, a range of important gaps and future directions are brought into focus.

We focus here on the dynamics, and shifts in dynamics, that arise from the structure, assumptions, and parameterization of the DND model, and use these to plot a path forward for the exploration of disease-mediated nutrient dynamics in both theory and empirical systems. As a starting point, the nutrient feedbacks that arise from consumer–resource interactions in both the

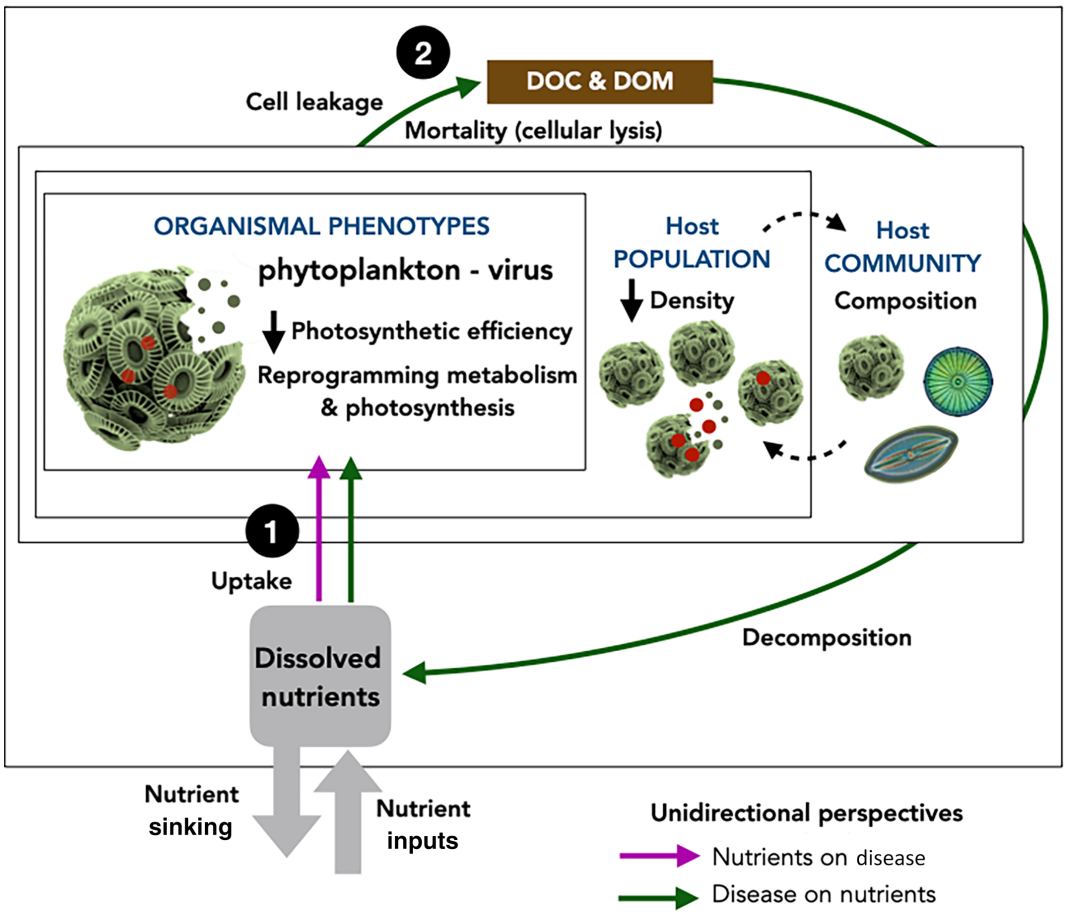

FIGURE 7 Marine systems provide one case study of how environmental nutrients modify, and are modified by, infection. In this case study, these processes include marine phytoplankton uptake of environmental nutrients (purple arrow, 1) that determines infection and disease manifestation in individuals and alters phytoplankton community composition (inner boxes). These infection-induced changes to phytoplankton individuals and communities alter nutrient uptake from the environment (green arrow, 1). Infection feeds back to increase both cell leakage and lysis, releasing dissolved organic carbon (DOC) and other dissolved organic matter (DOM), often containing nitrogen and other elements, and speeding the recycling rate of carbon and nutrients (green arrow, 2)

DND and CND frameworks generate dynamics not seen in unidirectional models (*Disease-mediated nutrient dynamics*; Elser & Urabe, 1999, Atkinson et al., 2017). State transitions are possible where stable equilibria shift to sustained oscillatory dynamics with very small changes in environmental nutrients. In addition, the large cycles in host density, pathogen prevalence, and environmental nutrients only occur when nutrients are recycled, and these cycles also are damped by the addition of small amounts of reproduction by infected hosts even when nutrient recycling is included. The ability of infected hosts to contribute offspring to the host pool is a key biological difference between the CND framework, with consumption and death of prey, and the DND framework, with infection of living hosts. The simple DND model structure thus highlights the role of the feedback loop in the system dynamics, increasing mechanistic understanding (Rastetter, 2017). These dynamic dependencies on small changes in environmental nutrients or small, biologically motivated, departures from the CND model structure also open the door to a new set of knowledge gaps and new questions for nutrient dynamics in empirical host–pathogen systems and the theory of disease-mediated nutrient dynamics.

From an empirical perspective, the predicted cycles also are an important area of focus. Despite the ubiquity of infection, the large magnitude cycles of hosts, infection prevalence, and environmental nutrients predicted by the simple DND model are not frequently documented in natural systems. This apparent mismatch may reflect the general absence of DND-mediated cycles, the importance of additional biological relationships that are not included in this initial model, or may reflect empirical observations that miss key points in temporal dynamics or average across spatial dynamics. While infection can reduce the total mass (Seabloom et al., 2017) and carbon flux rates (Kohli et al., 2021) at the scale of autotroph communities, and can increase environmental nutrients (Cobb et al., 2013), the links between pathogens of autotrophs and temporal cycling of environmental elements are rarely documented. The review of the biology of host–pathogen systems (*The cycle from nutrient supply to host–pathogen interactions and ecosystem nutrient dynamics*) points to a wide array of deviations from the simple DND model structure that may be necessary to predict the dynamics of specific empirical systems. Whether these pathogen-mediated nutrient cycles are rare or simply undocumented, the uncertainty about the relationship between the model predictions and empirical dynamics of DND uncovers gaps in knowledge and points to promising future research directions.

As a starting point, the DND model made the simplifying assumption of a single pathogen species infecting a single host species. While building from simple CND models and providing an important starting point for redefinition by analogy of the CND plant–consumer parameters to host and disease definitions (*Disease-mediated nutrient dynamics*), this assumption ignores the multi-species context of ecological systems (*Variation among species in a community*) and the potential for important dynamic consequences. For example, in a system with two species, there is the potential for compensatory dynamics (Holt & Pickering, 1985), which could allow the epidemic-stimulated release of nutrients from a highly susceptible host species to be rapidly taken up by a less susceptible (or non-host) species, damping the cycles of environmental nutrients. Even within species, if genetic variation exists that favors a subset of host or pathogen genotypes under elevated nutrients, this could also generate compensatory, stabilizing dynamics with ecological and evolutionary implications (Alexander, 2010; Burdon & Laine, 2019; French & Holmes, 2020). Insect vectors of pathogens may differ in nutritional requirements from the pathogens they carry, introducing a new set of stoichiometric constraints on uptake, excretion, and cycling of nutrients (Borer et al., 2010). Pathogens interacting within hosts also may modify host population dynamics, potentially damping or exacerbating cycles (Seabloom et al., 2015). Although not captured in the simplest DND formulation presented here, single host species are frequently infected by multiple pathogens, sometimes highly related (e.g., co-infection by pathogens in the same genus) and sometimes distinctly different (e.g., biotrophic and necrotrophic pathogens). Nutrients also can concurrently increase pathogens while reducing mutualists (e.g., mycorrhizal fungi), shifting nutrient uptake and supply to a host and its pathogens (Lekberg et al., 2021). Further, although we focused here on infection of autotrophic hosts because of their enormous importance for global biogeochemical cycles, models of DND could readily be expanded to examine the dynamic consequences of pathogens at higher trophic levels (Vannatta & Minchella, 2018). Thus, the consequences of the community context of host–pathogen interactions for nutrient dynamics represent a rich future direction. The conditions under which these new model structures would dampen or eliminate cycles will require new model development, empirical parameterization, and analysis.

Although the simple DND model presented here assumes homogeneous mixing, species and nutrients are not homogeneously mixed, even in most aquatic systems, thus raising the important consideration of spatial variation modifying the predicted dynamics. The stability of host–pathogen interactions is strongly influenced by spatial structure, relative dispersal distances, and connectivity of host and pathogen populations (Thrall & Burdon, 1997).

A careful empirical and theoretical exploration of the conditions under which factors such as spatial heterogeneity of nutrient availability, system mixing, vector movement, or relative dispersal distances of hosts and pathogens determines the stability or cycling of environmental nutrients would advance understanding of DND.

In addition to the dynamic consequences of nutrient-dependent host growth examined here, our biological review revealed other key rates that depend on nutrients. For example, host defense, one component of pathogen transmission, varies as a function of environmental nutrient availability (*Defense*). The rate of host nutrient uptake also can decline or increase, depending on the host and type of infection (*Tissue chemistry*), pointing to an additional area warranting exploration because of its potential impact on the pool and cycling of environmental nutrients. Host survival can be prolonged or shortened depending on a combination of pathogen traits (e.g., biotrophic vs. necrotrophic) and nutrient availability (*Growth rate and size*), suggesting the potential for higher-order interactions to modify the resulting dynamics. Addition of nutrient dependence to the model rates could change whether, and the conditions under which, oscillatory behaviors occur.

While the host–pathogen biology reviewed here suggests many opportunities for expanding the DND model, the DND model points to interesting possibilities for examining dynamics in empirical systems, as well. For example, the large cycles of infection prevalence predicted at high nutrients raise the question of whether, like the paradox of enrichment (Rosenzweig, 1971), high resource availability could potentially lead to stochastic extinction of the pathogen because cycles, including extremely low numbers of infected hosts, could potentially reach zero. If so, the system would be fundamentally rewired to exclude the pathogen, leaving only an autotroph and its nutrient resources, thus inducing stability. Typically, host resources are assumed to either benefit or hinder pathogens (*Tissue chemistry*), depending on the relative impacts of host resources on host growth, density, and immunity, as well as pathogen spread (*The cycle from nutrient supply to host–pathogen interactions and ecosystem nutrient dynamics*). The cycles of infection prevalence that arise at elevated nutrient availability when we include nutrient recycling (*Disease-mediated nutrient dynamics*) suggest that there may be situations where lower levels of nutrient availability could increase prevalence, but higher nutrient availability could ultimately cause pathogen loss from the system via stochastic extinction. Empirical tests of these predictions would advance our understanding of the ways in which disease and ecosystems will respond to ongoing environmental change.

Although some of the DND model dynamics play out over very long time periods, we lack long timescales of field data to quantify the linkages and importance of disease and nutrient cycling. Long-term data will be particularly important for understanding the role of DND in long-lived hosts (Borer et al., 2021). Multi-year data sets to understand the mechanisms underlying these processes also will fill a critical gap, particularly in seasonal systems, where nutrients pulsed into systems early in a season stimulate autotroph growth and pathogen build-up, with increasing importance through a season (Kagami et al., 2007). For all ecosystems, however, long-term sampling will be important for understanding the role of DND in because of directional global changes, especially long-term increases in background nutrient inputs to ecosystems (Ackerman et al., 2019).

CONCLUSIONS

Disease and ecosystem nutrient dynamics are clearly linked in biological systems via multiple pathways. Although most work to date has treated these relationships as unidirectional processes in which nutrients impact disease dynamics or infection alters nutrient dynamics, integration of these approaches to explicitly include the bidirectionality and simultaneity of disease–nutrient links demonstrates the potential for feedback loops and emergent dynamics. By distinguishing the broad suite of processes that link disease with ecosystem nutrients and capturing the dynamic effects of biological differences between free-living consumers and pathogens, the DND framework bridges disease and ecosystem ecology and opens new areas of inquiry for both.

The directions suggested by the biology and ecology of hosts and pathogens provide a rich area for both theoretical and empirical exploration of disease-mediated nutrient dynamics. Many potential elaborations on the structure of DND models to better reflect real systems are likely to have dynamic consequences. For example, variation in heterogeneity (e.g., among host and pathogen individuals and species, among spatially distinct host populations, and among species in host communities) and nutrient-dependent rates (e.g., transmission, mortality) are likely to be fruitful areas of inquiry for reconciling apparent differences between modeled and observed dynamics. Additional work to generate a more mathematically robust identification of the necessary and sufficient conditions for sudden shifts in stability and analytically verifying the existence of stable limit cycles will deepen our understanding of the mechanisms underpinning state transitions in DND models. Investigation of model dynamics across parameter ranges

reflecting autotrophic hosts from phytoplankton to trees and the equally wide range of pathogen traits will advance understanding of the importance of absolute and relative parameter values. This type of biologically motivated sensitivity analysis could identify the systems and conditions most likely to exhibit the predicted variation in host, pathogen, and nutrient dynamics. Long-term field sampling and experimental work aimed specifically at creating the conditions to test model dynamics also promise to advance knowledge spanning disease and ecosystem ecology.

ACKNOWLEDGMENTS

This work was supported by a grant to Elizabeth T. Borer from the National Socio-Environmental Synthesis Center (SESYNC) under funding received from the National Science Foundation DBI-1639145.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ORCID

Elizabeth T. Borer https://orcid.org/0000-0003-2259-5853
Rachel E. Paseka https://orcid.org/0000-0003-3656-9496
Angela Peace https://orcid.org/0000-0001-8200-8839
Lale Asik https://orcid.org/0000-0003-0803-155X
Rebecca Everett https://orcid.org/0000-0002-1565-7510
Thijs Frenken https://orcid.org/0000-0002-8989-2804
Angélica L. González https://orcid.org/0000-0002-4636-6329
Alexander T. Strauss https://orcid.org/0000-0003-0633-8443
Dedmer B. Van de Waal https://orcid.org/0000-0001-8803-1247
Lauren A. White https://orcid.org/0000-0003-3852-5374
Eric W. Seabloom https://orcid.org/0000-0001-6780-9259

REFERENCES

Aalto, S. L., E. Decaestecker, and K. Pulkkinen. 2015. "A Three-Way Perspective of Stoichiometric Changes on Host & Parasite Interactions." *Trends in Parasitology* 31: 333–40.

Ackerman, D., D. B. Millet, and X. Chen. 2019. "Global Estimates of Inorganic Nitrogen Deposition across Four Decades." *Global Biogeochemical Cycles* 33: 100–7.

Alderman, S. C., D. D. Coats, F. J. Crowe, and M. D. Butler. 1998. "Occurrence and Distribution of Ergot and Estimates of Seed Loss in Kentucky Bluegrass Grown for Seed in Central Oregon." *Plant Disease* 82: 89–93.

Alexander, H. M. 2010. "Disease in Natural Plant Populations, Communities, and Ecosystems: Insights into Ecological and Evolutionary Processes." *Plant Disease* 94: 492–503.

Anacker, B. L., N. E. Rank, D. Hüberli, M. Garbelotto, S. Gordon, T. Harnik, R. Whitkus, and R. Meentemeyer. 2008. "Susceptibility to Phytophthora Ramorum in a Key Infectious Host: Landscape Variation in Host Genotype, Host Phenotype, and Environmental Factors." *The New Phytologist* 177: 756–66.

Anderson, P. K., A. A. Cunningham, N. G. Patel, F. J. Morales, P. R. Epstein, and P. Daszak. 2004. "Emerging Infectious Diseases of Plants: Pathogen Pollution, Climate Change and Agrotechnology Drivers." *Trends in Ecology & Evolution* 19: 535–44.

Anderson, R. M., and R. M. May. 1979. "Population Biology of Infectious-Diseases.1." *Nature* 280: 361–7.

Anderson, R. M., and R. M. May. 1981. "The Population Dynamics of Microparasites and their Invertebrate Hosts." *Philosophical Transactions of the Royal Society of London B: Biological Sciences* 291: 451–524.

Atkinson, C. L., K. A. Capps, A. T. Rugenski, and M. J. Vanni. 2017. "Consumer-Driven Nutrient Dynamics in Freshwater Ecosystems: From Individuals to Ecosystems." *Biological Reviews* 92: 2003–23.

Banerjee, S., A. S. Perelson, and M. Moses. 2017. "Modelling the Effects of Phylogeny and Body Size on within-Host Pathogen Replication and Immune Response." *Journal of the Royal Society Interface* 14: 20170479.

Barnes, I., A. Fourie, M. J. Wingfield, T. C. Harrington, D. L. McNew, L. S. Sugiyama, B. C. Luiz, W. P. Heller, and L. M. Keith. 2018. "New Ceratocystis Species Associated with Rapid Death of Metrosideros Polymorpha in Hawai'i." *Persoonia* 40: 154–81.

Berger, S., A. K. Sinha, and T. Roitsch. 2007. "Plant Physiology Meets Phytopathology: Plant Primary Metabolism and Plant–Pathogen Interactions." *Journal of Experimental Botany* 58: 4019–26.

Bhaduri, B., J. Harbor, B. Engel, and M. Grove. 2000. "Assessing Watershed-Scale, Long-Term Hydrologic Impacts of Land-Use Change Using a GIS-NPS Model." *Environmental Management* 26: 643–58.

Borer, E., A.-L. Laine, and E. Seabloom. 2016. "A Multiscale Approach to Plant Disease Using the Metacommunity Concept." *Annual Review of Phytopathology* 54: 397–418.

Borer, E. T., L. Asik, R. A. Everett, T. Frenken, A. L. Gonzalez, R. E. Paseka, A. Peace, et al. 2021. "Elements of Disease in a Changing World: Modelling Feedbacks between Infectious Disease and Ecosystems." *Ecology Letters* 24: 6–19.

Borer, E. T., P. R. Hosseini, E. W. Seabloom, and A. P. Dobson. 2007. "Pathogen-Induced Reversal of Native Dominance in a Grassland Community." *Proceedings of the National Academy of Sciences of the United States of America* 104: 5473–8.

Borer, E. T., E. M. Lind, E. J. Ogdahl, E. W. Seabloom, D. Tilman, R. A. Montgomery, and L. L. Kinkel. 2015. "Food-Web Composition and Plant Diversity Control Foliar Nutrient Content and Stoichiometry." *Journal of Ecology* 103: 1432–41.

Borer, E. T., E. W. Seabloom, C. E. Mitchell, and A. G. Power. 2010. "Local Context Drives Infection of Grasses by Vector-Borne Generalist Viruses." *Ecology Letters* 13: 810–8.

Bratbak, G., J. K. Egge, and M. Heldal. 1993. "Viral Mortality of the Marine Alga Emiliania-Huxleyi (Haptophyceae) and Termination of Algal Blooms." *Marine Ecology Progress Series* 93: 39–48.

Brussaard, C. P. D. 2004. "Viral Control of Phytoplankton Populations—A Review." *Journal of Eukaryotic Microbiology* 51: 125–38.

Brussaard, C. P. D., R. S. Kempers, A. J. Kop, R. Riegman, and M. Heldal. 1996. "Virus-Like Particles in a Summer Bloom of

Emiliania Huxleyi in the North Sea." *Aquatic Microbial Ecology* 10: 105–13.

Burdon, J. J. 1991. "Fungal Pathogens as Selective Forces in Plant Populations and Communities*." *Australian Journal of Ecology* 16: 423–32.

Burdon, J. J., and G. A. Chilvers. 1982. "Host Density as a Factor in Plant Disease Ecology." *Annual Review of Phytopathology* 20: 143–66.

Burdon, J. J., and A.-L. Laine. 2019. *Evolutionary Dynamics of Plant-Pathogen Interactions*. Cambridge: Cambridge University Press.

Cable, J. M., B. J. Enquist, and M. E. Moses. 2007. "The Allometry of Host-Pathogen Interactions." *PLoS One* 2: e1130.

Cappelli, S. L., N. A. Pichon, A. Kempel, and E. Allan. 2020. "Sick Plants in Grassland Communities: A Growth-Defense Tradeoff Is the Main Driver of Fungal Pathogen Abundance." *Ecology Letters* 23: 1349–59.

Capps, K. A., and A. S. Flecker. 2013. "Invasive Fishes Generate Biogeochemical Hotspots in a Nutrient-Limited System." *PLoS One* 8: e54093.

Chapin, F. S., P. A. Matson, and P. M. Vitousek. 2011. *Principles of Terrestrial Ecosystem Ecology*, Second ed. New York: Springer.

Chen, Y., and X. Ni. 2011. "Nitrogen Modulation on Plant Direct and Indirect Defenses." In *Recent Advances in Entomological Research*, edited by T. Liu and L. Kang, 86–102. Berlin, Heidelberg: Springer.

Civitello, D. J., B. E. Allman, C. Morozumi, and J. R. Rohr. 2018. "Assessing the Direct and Indirect Effects of Food Provisioning and Nutrient Enrichment on Wildlife Infectious Disease Dynamics." *Philosophical Transactions of the Royal Society of London Series B: Biological Sciences* 373: 20170101.

Clasen, J. L., and J. J. Elser. 2007. "The Effect of Host Chlorella NC64A Carbon: Phosphorus Ratio on the Production of Paramecium Bursaria Chlorella Virus-1." *Freshwater Biology* 52: 112–22.

Clay, K., and C. Schardl. 2002. "Evolutionary Origins and Ecological Consequences of Endophyte Symbiosis with Grasses." *American Naturalist* 160: S99–S127.

Cleland, E. E., and W. S. Harpole. 2010. "Nitrogen enrichment and plant communities." In *Year in Ecology and Conservation Biology 2010*, edited by R.S. Ostfeld and W.H. Schlesinger, 46–61. Malden: Wiley-Blackwell.

Cobb, R. C., V. T. Eviner, and D. M. Rizzo. 2013. "Mortality and Community Changes Drive Sudden Oak Death Impacts on Litterfall and Soil Nitrogen Cycling." *New Phytologist* 200: 422–31.

Cobb, R. C., and D. M. Rizzo. 2016. "Litter Chemistry, Community Shift, and Non-additive Effects Drive Litter Decomposition Changes Following Invasion by a Generalist Pathogen." *Ecosystems* 19: 1478–90.

Cuomo, C. A., C. A. Desjardins, M. A. Bakowski, J. Goldberg, A. T. Ma, J. J. Becnel, E. S. Didier, et al. 2012. "Microsporidian Genome Analysis Reveals Evolutionary Strategies for Obligate Intracellular Growth." *Genome Research* 22: 2478–88.

Dordas, C. 2008. "Role of Nutrients in Controlling Plant Diseases in Sustainable Agriculture. A Review." *Agronomy for Sustainable Development* 28: 33–46.

Droop, M. R. 1973. "Some Thoughts on Nutrient Limitation in Algae." *Journal of Phycology* 9: 264–72.

Elliott, K. J., and W. T. Swank. 2008. "Long-Term Changes in Forest Composition and Diversity Following Early Logging (1919–1923) and the Decline of American Chestnut (Castanea Dentata)." *Plant Ecology* 197: 155–72.

Elser, J. J., and J. Urabe. 1999. "The Stoichiometry of Consumer-Driven Nutrient Recycling: Theory, Observations, and Consequences." *Ecology* 80: 735–51.

Eviner, V. T., and G. E. Likens. 2008. "Effects of Disease on Biogeochemical Cycling." In *Infectious Disease Ecology: The Effects of Ecosystems on Disease and of Disease on Ecosystems*, edited by R.S. Ostfeld, F. Keesing, and V.T. Eviner, 260–83. Princeton, NJ: Princeton University Press.

Falloon, R. E., M. P. Rolston, and D. E. Hume. 1988. "Head Smut of Prairie Grass and Mountain Brome: A Review." *New Zealand Journal of Agricultural Research* 31: 459–66.

Fatima, U., and M. Senthil-Kumar. 2015. "Plant and Pathogen Nutrient Acquisition Strategies." *Frontiers in Plant Science* 6: 750.

Fay, P. A., S. M. Prober, W. S. Harpole, J. M. H. Knops, J. D. Bakker, E. T. Borer, E. M. Lind, et al. 2015. "Grassland Productivity Limited by Multiple Nutrients." *Nature Plants* 1: 15080.

Fenn, M. E., R. Haeuber, G. S. Tonnesen, J. S. Baron, S. Grossman-Clarke, D. Hope, D. A. Jaffe, et al. 2003. "Nitrogen Emissions, Deposition, and Monitoring in the Western United States." *Bioscience* 53: 391–403.

Field, C. B., M. J. Behrenfeld, J. T. Randerson, and P. Falkowski. 1998. "Primary Production of the Biosphere: Integrating Terrestrial and Oceanic Components." *Science* 281: 237–40.

Fischhoff, I. R., T. Huang, S. K. Hamilton, B. A. Han, S. L. LaDeau, R. S. Ostfeld, E. J. Rosi, and C. T. Solomon. 2020. "Parasite and Pathogen Effects on Ecosystem Processes: A Quantitative Review." *Ecosphere* 11: e03057.

Fisher, M. C., D. A. Henk, C. J. Briggs, J. S. Brownstein, L. C. Madoff, S. L. McCraw, and S. J. Gurr. 2012. "Emerging Fungal Threats to Animal, Plant and Ecosystem Health." *Nature* 484: 186–94.

Fleischmann, F., S. Raidl, and W. F. Oßwald. 2010. "Changes in Susceptibility of Beech (*Fagus sylvatica*) Seedlings towards *Phytophthora citricola* under the Influence of Elevated Atmospheric CO_2 and Nitrogen Fertilization." *Environmental Pollution* 158: 1051–60.

Fleischmann, F., D. Schneider, R. Matyssek, and W. F. Oβwald. 2002. "Investigations on Net CO_2 Assimilation, Transpiration and Root Growth of *Fagus sylvatica* Infested with Four Different *Phytophthora* Species." *Plant Biology* 4: 144–52.

Fones, H. N., and S. J. Gurr. 2017. "NOXious Gases and the Unpredictability of Emerging Plant Pathogens under Climate Change." *BMC Biology* 15: 36.

French, R. K., and E. C. Holmes. 2020. "An Ecosystems Perspective on Virus Evolution and Emergence." *Trends in Microbiology* 28: 165–75.

Frenken, T., E. Alacid, S. A. Berger, E. C. Bourne, M. Gerphagnon, H.-P. Grossart, A. S. Gsell, et al. 2017. "Integrating Chytrid Fungal Parasites into Plankton Ecology: Research Gaps and Needs." *Environmental Microbiology* 19: 3802–22.

Frenken, T., R. Paseka, A. L. González, L. Asik, E. W. Seabloom, L. A. White, E. T. Borer, A. T. Strauss, A. Peace, and D. B. Van de Waal. 2021. "Changing Elemental Cycles, Stoichiometric Mismatches, and Consequences for Pathogens of Primary Producers." *Oikos* 130: 1046–55.

Frenken, T., J. Wierenga, A. S. Gsell, E. van Donk, T. Rohrlack, and D. B. Van de Waal. 2017. "Changes in N:P Supply Ratios Affect the Ecological Stoichiometry of a Toxic Cyanobacterium and its Fungal Parasite." *Frontiers in Microbiology* 8: 1015.

Fuhrman, J. A. 1999. "Marine Viruses and their Biogeochemical and Ecological Effects." *Nature* 399: 541–8.

Garcia, N. S., J. A. Bonachela, and A. C. Martiny. 2016. "Interactions between Growth-Dependent Changes in Cell Size, Nutrient Supply and Cellular Elemental Stoichiometry of Marine Synechococcus." *The ISME Journal* 10: 2715–24.

Häffner, E., S. Konietzki, and E. Diederichsen. 2015. "Keeping Control: The Role of Senescence and Development in Plant Pathogenesis and Defense." *Plants (Basel, Switzerland)* 4: 449–88.

Harpole, W. S., L. L. Sullivan, E. M. Lind, J. Firn, P. B. Adler, E. T. Borer, J. Chase, et al. 2016. "Addition of Multiple Limiting Resources Reduces Grassland Diversity." *Nature* 537: 93–6.

Hartmann, F. E., R. C. R. D. L. Vega, F. Carpentier, P. Gladieux, A. Cornille, M. E. Hood, and T. Giraud. 2019. "Understanding Adaptation, Coevolution, Host Specialization, and Mating System in Castrating Anther-Smut Fungi by Combining Population and Comparative Genomics." *Annual Review of Phytopathology* 57: 431–57.

Hatcher, M. J., J. T. Dick, and A. M. Dunn. 2012. "Diverse Effects of Parasites in Ecosystems: Linking Interdependent Processes." *Frontiers in Ecology and the Environment* 10: 186–94.

Heckman, R. W., F. W. Halliday, and C. E. Mitchell. 2019. "A Growth–Defense Trade-off Is General across Native and Exotic Grasses." *Oecologia* 191: 609–20.

Hennes, K. P., C. A. Suttle, and A. M. Chan. 1995. "Fluorescently Labeled Virus Probes Show that Natural Virus Populations Can Control the Structure of Marine Microbial Communities." *Applied and Environmental Microbiology* 61: 3623–7.

Hillebrand, H., E. T. Borer, M. E. S. Bracken, B. J. Cardinale, J. Cebrian, E. E. Cleland, J. J. Elser, et al. 2009. "Herbivore Metabolism and Stoichiometry each Constrain Herbivory at Different Organizational Scales across Ecosystems." *Ecology Letters* 12: 516–27.

Hobara, S., N. Tokuchi, N. Ohte, K. Koba, M. Katsuyama, S.-J. Kim, and A. Nakanishi. 2001. "Mechanism of Nitrate Loss from a Forested Catchment Following a Small-Scale, Natural Disturbance." *Canadian Journal of Forest Research* 31: 1326–35.

Hobbie, S. E. 2015. "Plant Species Effects on Nutrient Cycling: Revisiting Litter Feedbacks." *Trends in Ecology & Evolution* 30: 357–63.

Holfeld, H. 2000. "Infection of the Single-Celled Diatom Stephanodiscus Alpinus by the Chytrid Zygorhizidium: Parasite Distribution within Host Population, Changes in Host Cell Size, and Host–Parasite Size Relationship." *Limnology and Oceanography* 45: 1440–4.

Holt, R. D., and J. Pickering. 1985. "Infectious Disease and Species Coexistence: A Model of Lotka-Volterra Form." *The American Naturalist* 126: 196–211.

Huberty, L. E., K. L. Gross, and C. J. Miller. 1998. "Effects of Nitrogen Addition on Successional Dynamics and Species Diversity in Michigan Old-Fields." *Journal of Ecology* 86: 794–803.

Huot, B., J. Yao, B. L. Montgomery, and S. Y. He. 2014. "Growth–Defense Tradeoffs in Plants: A Balancing Act to Optimize Fitness." *Molecular Plant* 7: 1267–87.

Jones, K. E., N. G. Patel, M. A. Levy, A. Storeygard, D. Balk, J. L. Gittleman, and P. Daszak. 2008. "Global Trends in Emerging Infectious Diseases." *Nature* 451: 990–3.

Kagami, M., A. de Bruin, B. W. Ibelings, and E. van Donk. 2007. "Parasitic Chytrids: Their Effects on Phytoplankton Communities and Food-Web Dynamics." *Hydrobiologia* 578: 113–29.

Keesing, F., R. D. Holt, and R. S. Ostfeld. 2006. "Effects of Species Diversity on Disease Risk." *Ecology Letters* 9: 485–98.

Kohli, M., J. A. Henning, E. T. Borer, L. Kinkel, and E. W. Seabloom. 2021. "Foliar Fungi and Plant Diversity Drive Ecosystem Carbon Fluxes in Experimental Prairies." *Ecology Letters* 24: 487–97.

Koteen, L. E., D. D. Baldocchi, and J. Harte. 2011. "Invasion of Non-native Grasses Causes a Drop in Soil Carbon Storage in California Grasslands." *Environmental Research Letters* 6: 044001.

Kuris, A. M., A. R. Blaustein, and J. J. Alio. 1980. "Hosts as Islands." *American Naturalist* 116: 570–86.

Lacroix, C., E. W. Seabloom, and E. T. Borer. 2017. "Environmental Nutrient Supply Directly Alters Plant Traits but Indirectly Determines Virus Growth Rate." *Frontiers in Microbiology* 8: 2116.

Lehtinen, S., T. Tamminen, R. Ptacnik, and T. Andersen. 2017. "Phytoplankton Species Richness, Evenness, and Production in Relation to Nutrient Availability and Imbalance." *Limnology and Oceanography* 62: 1393–408.

Lekberg, Y., C. A. Arnillas, E. T. Borer, L. S. Bullington, N. Fierer, P. G. Kennedy, J. W. Leff, A. D. Luis, E. W. Seabloom, and J. A. Henning. 2021. "Nitrogen and Phosphorus Fertilization Consistently Favor Pathogenic over Mutualistic Fungi in Grassland Soils." *Nature Communications* 12: 3484.

Lerdau, M., M. Litvak, and R. Monson. 1994. "Plant-Chemical Defense—Monoterpenes and the Growth-Differentiation Balance Hypothesis." *Trends in Ecology & Evolution* 9: 58–61.

Litchman, E., P. de Tezanos Pinto, K. F. Edwards, C. A. Klausmeier, C. T. Kremer, and M. K. Thomas. 2015. "Global Biogeochemical Impacts of Phytoplankton: A Trait-Based Perspective." *Journal of Ecology* 103: 1384–96.

Liu, X., L. Chen, M. Liu, G. García-Guzmán, G. S. Gilbert, and S. Zhou. 2020. "Dilution Effect of Plant Diversity on Infectious Diseases: Latitudinal Trend and Biological Context Dependence." *Oikos* 129: 457–65.

Liu, X., S. Lyu, D. Sun, C. J. A. Bradshaw, and S. Zhou. 2017. "Species Decline under Nitrogen Fertilization Increases Community-Level Competence of Fungal Diseases." *Proceedings of the Royal Society B, Biological Sciences* 284: 20162621.

Lloyd-Smith, J. O., S. J. Schreiber, P. E. Kopp, and W. M. Getz. 2005. "Superspreading and the Effect of Individual Variation on Disease Emergence." *Nature* 438: 355–9.

Loladze, I., Y. Kuang, and J. J. Elser. 2000. "Stoichiometry in Producer-Grazer Systems: Linking Energy Flow with Element Cycling." *Bulletin of Mathematical Biology* 62: 1137–62.

Luo, L., Y. Zhang, and G. Xu. 2020. "How Does Nitrogen Shape Plant Architecture?" *Journal of Experimental Botany* 71: 4415–27.

Maat, D. S., and C. P. D. Brussaard. 2016. "Both Phosphorus- and Nitrogen Limitation Constrain Viral Proliferation in Marine Phytoplankton." *Aquatic Microbial Ecology* 77: 87–97.

Machado, M., S. Steinke, and M. Ganter. 2021. "Plasmodium Reproduction, Cell Size, and Transcription: How to Cope with

Increasing DNA Content?" *Frontiers in Cellular and Infection Microbiology* 11: 660679.

Maekawa, S., N. Inada, S. Yasuda, Y. Fukao, M. Fujiwara, T. Sato, and J. Yamaguchi. 2014. "The Carbon/Nitrogen Regulator ARABIDOPSIS TOXICOS EN LEVADURA31 Controls Papilla Formation in Response to Powdery Mildew Fungi Penetration by Interacting with SYNTAXIN OF PLANTS121 in Arabidopsis." *Plant Physiology* 164: 879–87.

Makarieva, A. M., V. G. Gorshkov, B.-L. Li, S. L. Chown, P. B. Reich, and V. M. Gavrilov. 2008. "Mean Mass-Specific Metabolic Rates Are Strikingly Similar across life's Major Domains: Evidence for life's Metabolic Optimum." *Proceedings of the National Academy of Sciences of the United States of America* 105: 16994–9.

Malmstrom, C. M., C. C. Hughes, L. A. Newton, and C. J. Stoner. 2005. "Virus Infection in Remnant Native Bunchgrasses from Invaded California Grasslands." *New Phytologist* 168: 217–30.

Malmstrom, C. M., A. J. McCullogh, H. A. Johnson, and E. T. Borer. 2005. "Invasive Annual Grasses Indirectly Increase Virus Incidence in California Native Perennial Bunchgrasses." *Oecologia* 145: 153–64.

Matson, P. A., and R. D. Boone. 1984. "Natural Disturbance and Nitrogen Mineralization: Wave-Form Dieback of Mountain Hemlock in the Oregon Cascades." *Ecology* 65: 1511–6.

Mengiste, T. 2012. "Plant Immunity to Necrotrophs." *Annual Review of Phytopathology* 50: 267–94.

Metz, M. R., K. Frangioso, A. C. Wickland, R. Meentemeyer, and D. Rizzo. 2012. "An Emergent Disease Causes Directional Changes in Forest Species Composition in Coastal California." *Ecosphere* 3: 1–23.

Mitchell, C. E., P. B. Reich, D. Tilman, and J. V. Groth. 2003. "Effects of Elevated CO_2, Nitrogen Deposition, and Decreased Species Diversity on Foliar Fungal Plant Disease." *Global Change Biology* 9: 438–51.

Monier, A., A. Chambouvet, D. S. Milner, V. Attah, R. Terrado, C. Lovejoy, H. Moreau, A. E. Santoro, É. Derelle, and T. A. Richards. 2017. "Host-Derived Viral Transporter Protein for Nitrogen Uptake in Infected Marine Phytoplankton." *Proceedings of the National Academy of Sciences of the United States of America* 114: E7489–98.

Mordecai, E. A. 2011. "Pathogen Impacts on Plant Communities: Unifying Theory, Concepts, and Empirical Work." *Ecological Monographs* 81: 429–41.

Moury, B., F. Fabre, E. Hebrard, and R. Froissart. 2017. "Determinants of Host Species Range in Plant Viruses." *Journal of General Virology* 98: 862–73.

Narr, C. F., and P. C. Frost. 2016. "Exploited and Excreting: Parasite Type Affects Host Nutrient Recycling." *Ecology* 97: 2012–20.

Newton, A. C., B. D. Fitt, S. D. Atkins, D. R. Walters, and T. J. Daniell. 2010. "Pathogenesis, Parasitism and Mutualism in the Trophic Space of Microbe-Plant Interactions." *Trends in Microbiology* 18: 365–73.

Ogden, M., R. Hoefgen, U. Roessner, S. Persson, and G. A. Khan. 2018. "Feeding the Walls: How Does Nutrient Availability Regulate Cell Wall Composition?" *International Journal of Molecular Sciences* 19: 2691.

Ostfeld, R. S., F. Keesing, and V. T. Eviner. 2008. *Infectious Disease Ecology: The Effects of Ecosystems on Disease and of Disease on Ecosystems*. Princeton, NJ: Princeton University Press.

Parker, S. S., and J. P. Schimel. 2010. "Invasive Grasses Increase Nitrogen Availability in California Grassland Soils." *Invasive Plant Science and Management* 3: 40–7, 48.

Paull, S. H., S. Song, K. M. McClure, L. C. Sackett, A. M. Kilpatrick, and P. T. Johnson. 2012. "From Superspreaders to Disease Hotspots: Linking Transmission across Hosts and Space." *Frontiers in Ecology and the Environment* 10: 75–82.

Preston, D. L., J. A. Mischler, A. R. Townsend, and P. T. J. Johnson. 2016. "Disease Ecology Meets Ecosystem Science." *Ecosystems* 19: 737–48.

Rasconi, S., N. Niquil, and T. Sime-Ngando. 2012. "Phytoplankton Chytridiomycosis: Community Structure and Infectivity of Fungal Parasites in Aquatic Ecosystems." *Environmental Microbiology* 14: 2151–70.

Rastetter, E. B. 2017. "Modeling for Understanding v. Modeling for Numbers." *Ecosystems* 20: 215–21.

Rastetter, E. B., and G. R. Shaver. 1992. "A Model of Multiple-Element Limitation for Acclimating Vegetation." *Ecology* 73: 1157–74.

Riedell, W. E., S. L. Osborne, and A. A. Jaradat. 2007. "Crop Mineral Nutrient and Yield Responses to Aphids or Barley Yellow Dwarf Virus in Spring Wheat and Oat." *Crop Science* 47: 1553–60.

Rohrlack, T., G. Christiansen, and R. Kurmayer. 2013. "Putative Antiparasite Defensive System Involving Ribosomal and Nonribosomal Oligopeptides in Cyanobacteria of the Genus Planktothrix." *Applied and Environmental Microbiology* 79: 2642–7.

Rosenzweig, M. L. 1971. "Paradox of Enrichment: Destabilization of Exploitation Ecosystems in Ecological Time." *Science* 171: 385–7.

Rúa, M. A., J. Umbanhowar, S. Hu, K. O. Burkey, and C. E. Mitchell. 2013. "Elevated CO_2 Spurs Reciprocal Positive Effects between a Plant Virus and an Arbuscular Mycorrhizal Fungus." *New Phytologist* 199: 541–9.

Ruardij, P., M. J. W. Veldhuis, and C. P. D. Brussaard. 2005. "Modeling the Bloom Dynamics of the Polymorphic Phytoplankter *Phaeocystis globosa*: Impact of Grazers and Viruses." *Harmful Algae* 4: 941–63.

Sanders, A. J., and B. W. Taylor. 2018. "Using Ecological Stoichiometry to Understand and Predict Infectious Diseases." *Oikos* 127: 1399–409.

Seabloom, E. W., E. T. Borer, K. Gross, A. E. Kendig, C. Lacroix, C. E. Mitchell, E. A. Mordecai, and A. G. Power. 2015. "The Community Ecology of Pathogens: Coinfection, Coexistence and Community Composition." *Ecology Letters* 18: 401–15.

Seabloom, E. W., E. T. Borer, and L. L. Kinkel. 2018. "No Evidence for Trade-Offs in Plant Responses to Consumer Food Web Manipulations." *Ecology* 99: 1953–63.

Seabloom, E. W., L. Kinkel, E. T. Borer, Y. Hautier, R. A. Montgomery, and D. Tilman. 2017. "Food Webs Obscure the Strength of Plant Diversity Effects on Primary Productivity." *Ecology Letters* 20: 505–12.

Sheik, A. R., C. P. D. Brussaard, G. Lavik, P. Lam, N. Musat, A. Krupke, S. Littmann, M. Strous, and M. M. M. Kuypers. 2014. "Responses of the Coastal Bacterial Community to Viral Infection of the Algae Phaeocystis Globosa." *The ISME Journal* 8: 212–25.

Smith, V. 2007. "Host Resource Supplies Influence the Dynamics and Outcome of Infectious Disease." *Integrative and Comparative Biology* 47: 310–6.

Smith, V. H., and R. D. Holt. 1996. "Resource Competition and within-Host Disease Dynamics." *Trends in Ecology & Evolution* 11: 386–9.

Sterner, R. W. 1990. "The Ratio of Nitrogen to Phosphorus Resupplied by Herbivores - Zooplankton and the Algal Competitive Arena." *American Naturalist* 136: 209–29.

Sterner, R. W., and J. J. Elser. 2002. *Ecological Stoichiometry: The Biology of Elements from Molecules to the Biosphere*. Princeton, NJ: Princeton University Press.

Sun, Y., M. Wang, L. A. J. Mur, Q. Shen, and S. Guo. 2020. "Unravelling the Roles of Nitrogen Nutrition in Plant Disease Defences." *International Journal of Molecular Sciences* 21: 572.

Suttle, C. A. 2005. "Viruses in the Sea." *Nature* 437: 356–61.

Suttle, C. A. 2007. "Marine Viruses—Major Players in the Global Ecosystem." *Nature Reviews Microbiology* 5: 801–12.

Thrall, P. H., and J. J. Burdon. 1997. "Host-Pathogen Dynamics in a Metapopulation Context: The Ecological and Evolutionary Consequences of Being Spatial." *Journal of Ecology* 85: 743–53.

Underwood, W. 2012. "The Plant Cell Wall: A Dynamic Barrier against Pathogen Invasion." *Frontiers in Plant Science* 3: 85–5.

van de Waal, D. B., J. M. Verspagen, M. Lürling, E. van Donk, P. M. Visser, and J. Huisman. 2009. "The Ecological Stoichiometry of Toxins Produced by Harmful Cyanobacteria: An Experimental Test of the Carbon-Nutrient Balance Hypothesis." *Ecology Letters* 12: 1326–35.

van Donk, E., and J. Ringelberg. 1983. "The Effect of Fungal Parasitism on the Succession of Diatoms in Lake Maarsseveen I (The Netherlands)." *Freshwater Biology* 13: 241–51.

Vannatta, J. T., and D. J. Minchella. 2018. "Parasites and their Impact on Ecosystem Nutrient Cycling." *Trends in Parasitology* 34: 452–5.

Wang, Z. Y., A. Göttlein, H. Rodenkirchen, F. Fleischmann, and W. Oßwald. 2003. "The Influence of *Phytophthora citricola* on Rhizosphere Soil Solution Chemistry and the Nutritional Status of European Beech Seedlings." *Journal of Phytopathology* 151: 365–8.

Whitaker, B. K., M. A. Rúa, and C. E. Mitchell. 2015. "Viral Pathogen Production in a Wild Grass Host Driven by Host Growth and Soil Nitrogen." *New Phytologist* 207: 760–8.

Woolhouse, M. E. J., D. T. Haydon, and R. Antia. 2005. "Emerging Pathogens: The Epidemiology and Evolution of Species Jumps." *Trends in Ecology & Evolution* 20: 238–44.

Woolhouse, M. E. J., L. H. Taylor, and D. T. Haydon. 2001. "Population Biology of Multihost Pathogens." *Science* 292: 1109–12.

How to cite this article: Borer, Elizabeth T., Rachel E. Paseka, Angela Peace, Lale Asik, Rebecca Everett, Thijs Frenken, Angélica L. González, Alexander T. Strauss, Dedmer B. Van de Waal, Lauren A. White, and Eric W. Seabloom. 2022. "Disease-Mediated Nutrient Dynamics: Coupling Host–Pathogen Interactions with Ecosystem Elements and Energy." *Ecological Monographs* 92(2): e1510. https://doi.org/10.1002/ecm.1510