Trends in Parasitology

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Opinion

Ecological Stoichiometry for Parasitologists

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Ecological stoichiometry (ES) is an ecological theory used to study the imbalances of chemical elements, ratios, and flux rates among organisms and the environment to better understand nutrient cycling, energy flow, and the role of organisms in ecosystems. Parasitologists can use this framework to study phenomena across biological scales from genomes to ecosystems. By using the common currency of elemental ratios such as carbon:nitrogen:phosphorus, parasitologists are beginning to explicitly link parasite–host interactions to ecosystem dynamics. Thus, ecological stoichiometry provides a framework for studying the feedbacks of parasites on the environment as well as the effects of the environment on parasites and disease.

Highlights

ES uses the balance of multiple elements and energy in organisms and their environment to understand nutrient cycling and energy flow in ecological systems.

ES is a powerful framework for parasitologists because it uses a common currency that cuts across biological scales from genes to ecosystems.

Parasitologists can use ES to answer questions ranging from topics that have already been well studied, but from new angles, to new frontiers in disease ecology and epidemiology.

Why Ecological Stoichiometry?

Ecological stoichiometry (ES) (see Glossary) is a framework for understanding ecological dynamics (i.e., the changing nature of ecological systems) by using first principles of chemistry and the balance among multiple elements and energy [1]. As a theory, ES has matured to help provide predictions about cellular, organismal, evolutionary, and ecosystem dynamics across a range of systems [2]. Parasitology is a field that can benefit from an ES approach by providing a basis for directly linking parasites to the broader ecological systems in which they are embedded, as well as understanding parasite–host interactions at multiple levels of organization. By framing parasite–host interactions in elemental ratios, as ES does, parasitologists can directly scale-up across biological levels by using the same metrics of nutrient cycling and energy flow as those used by ecosystem ecologists. Thus, key environmental drivers of parasitism and the potentially important feedbacks of parasites on ecosystems can be better understood using ES. In this Opinion article, we (i) give a brief primer on ES for parasitologists, (ii) present a conceptual framework of ES that illustrates the potential ways in which parasitologists can use ES, and (iii) outline ongoing and future questions that can be addressed with ES while reviewing a handful of recent examples from the literature.

What Is Ecological Stoichiometry?

Stoichiometry is the study of patterns of mass balance in the chemical conversions of different types of matter [3]. Many people are introduced to, and use, stoichiometry when balancing chemical reactions in introductory chemistry classes. These principles of mass balance are also widely used by ecologists to study nutrient cycling and energy flow in natural systems [1,3].

Carbon, nitrogen, and phosphorus are the elements most studied using the ES framework as they comprised the **Redfield ratio** [4], and C can be a useful proxy for energy while N and P are often limiting nutrients for organisms and ecosystems. Vannatta and Minchella [5] built a strong framework on which to understand parasite effects on ecosystem nutrient cycling. This framework involves focusing on one nutrient at a time and can be a starting point for incorporating multiple nutrients and their ratios, as well as alterations in nutrient flux rates associated with altered host physiology and behavior. Additionally, other elements besides C, N, and P may be limiting in other cases and thus worthy of explicit attention in an ES framework. For example, potassium has been

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linked to fungal epidemics [6], and iron has long been studied for its role in infectious disease [7]. The ratios of these and other micronutrients may play a role in both host and parasite homeostasis.

Many organisms are adapted to maintain a **homeostasis** of elements needed for growth and reproduction, deviations from which reduce fitness [8]. In other words, many animals need to obtain a consistent ratio of essential nutrients from their food. When food nutrient ratios differ from the consumer's homeostatic needs, a nutritional imbalance may result where one or more elemental nutrients limit growth or impair fitness. The animal then conserves the limiting nutrient while removing excess nonlimiting nutrients (Figure 1). Thus, animals often release or regenerate (through excretion or egestion) nutrient elements at ratios different from those at which they ingest, leading to differential nutrient availability in the environment [1]. These limitations can be predicted using the mass balance of the elements.

The relative amounts of essential elements or their ratio can determine nutrient use and cycling rates rather than their absolute amounts. In turn, differential nutrient regeneration at one trophic level can affect other trophic levels and the broader ecosystem processes of nutrient cycling and energy flow [3]. Importantly, ES has provided insights into large-scale biogeochemical couplings of organisms at the ecosystem scale [9] while also guiding questions at the genomic and cellular end of the biological scale (reviewed in [1]). For example, freshwater snails exacerbated phosphorus limitation in a stream ecosystem through high N:P excretion ratios (i.e., less P per unit N) of individual snails, thus linking individual elemental use and ecosystem elemental cycling [10]. At the genomic scale, the elemental content of proteins is a function of the level of their encoding genes such that proteins associated with highly expressed genes in plants are low in nitrogen compared to proteins encoded by low-expression genes [11]. **Consumer-driven nutrient recycling (CNR)** [12,13], **threshold elemental ratios (TERs)** [14], and the **growth rate hypothesis (GRH)** [15] have all developed as key ecological concepts through ES [16]. More recently, efforts to understand the evolutionary dynamics of stoichiometric traits have further expanded the scope of ES as a theory [2]. For example, populations of rotifers fed P-deficient algal diets rapidly adapted to P-limiting conditions in which they had greater fitness compared to individuals from populations on P-rich diets [17]. Ecological stoichiometric approaches have been primarily developed in aquatic systems, while the analogous framework of **nutritional geometry (NG)**, which also centers on organismal homeostasis and functionally relevant biochemical currencies, has matured from behavioral ecology and terrestrial insect ecology [16]. Additionally, the **metabolic theory of ecology (MTE)**, which uses energy as a currency that scales across biological levels, has a number of common assumptions and goals as ES and NG [18–21]. Current efforts are underway to synthesize these frameworks to potentially arrive at a powerful perspective to link organisms with their environment via the common currencies of materials and energy at many levels of biological organization [16]. These theories have not been developed using parasites, but we contend that using parasites and their hosts to test hypotheses within these frameworks will refine and inform general ecological theory and advance parasitology. Many opportunities exist to not only test hypotheses from these theories using parasite systems, but to also inform more traditional epidemiological approaches to parasitology and disease ecology. Thus, we can look at traditional parasitology through a new lens or from a slightly different angle [22]. Here, we focus on ES because it reduces the biochemicals of NG and MTE to elements and ratios of elements (C:N:P) that are common currencies at all scales of biological organization.

An Ecological Stoichiometry Framework for Parasitology

Parasites, by definition, obtain energy and nutrients from their hosts. Thus, we can study the effects of parasites on their hosts from the ES standpoint using the parasite as the consumer

Glossary

Connectance: in a food web, connectance is the proportion of realized feeding links out of all the possible feeding links.

Consumer-driven nutrient recycling (CNR): the feedback mechanism linking consumer dynamics and producer nutritional status.

Ecological stoichiometry (ES): the balance of multiple chemical elements during ecological interactions.

Food chain length: the number of species encountered as energy or nutrients move from plants to top predators in a food web. The number of links between the base of the web and the top predator.

Growth rate hypothesis (GRH): differences in organismal C:N:P ratios are caused by differential allocations to RNA necessary to meet protein synthesis demands of rapid biomass growth and development.

Homeostasis: maintenance of constant internal conditions in the face of externally imposed variation.

Metabolic theory of ecology (MTE): the fundamental biological rate that governs most patterns in ecology is organism metabolic rate. This theory is based on relationships among metabolic rate, body size, and temperature.

Nestedness: in a food web, the degree to which species with few links are a subset of the links of other species, rather than a different set of links.

Nutritional geometry (NG): framework of nutritional ecology linking animal physiology, behavior, and demography with macronutrients and micronutrients such as carbohydrates, lipids, and proteins.

Redfield ratio: the atomic ratio of C, N, and P found in ocean plankton (C:N:P = 117:14:1). Named after Alfred C. Redfield who first described the ratio.

Threshold elemental ratios (TERs): the nutrient ratio of an organism's food where that organism switches from limitation by one of these elements to limitation by another.

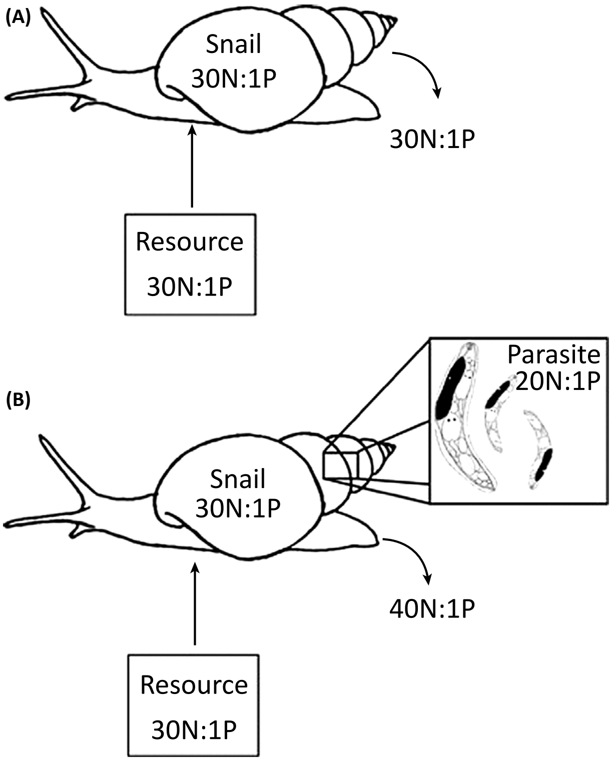

Figure 1. Conceptual Diagrams (A) Representing the General Concept of Nutrient Cycling through a Resource and Snail Consumer, and (B) How the Balance of N:P May Shift among a Resource, Snail Consumer, and Trematode (Snail Parasite) within the Snail (Data from [15]). A freshwater snail's resource often include periphyton, which is a complex of algae, bacteria, and fungi. The nitrogen (N) and phosphorus (P) content of this resource can vary and depends on nutrient availability in the environment. The N and P ratio (N:P) of the snail body is relatively homeostatic. When snails ingest resources with nonhomeostatic N or P content, this imbalance results in differential N:P regeneration (excretion and egestion) by the snail.

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and the host as the resource (Figure 1). We can then link processes at multiple biological levels, from the cellular to the individual to the ecosystem, because of the common currencies of nutrient elemental content and flux. At the individual level, many animals maintain a homeostatic ratio of C:N:P or at least N and P [1]. Parasites may have different C:N:P requirements than their hosts, creating a potential imbalance in homeostatic needs between consumer and resource [23,24]. Indeed, the extent of the mismatch between host and parasite elemental ratios may contribute to parasite virulence. Anthropogenic nutrient enrichment could possibly exacerbate this mismatch if parasites can steal nutritional elements before they are used by the host for immune defense or other functions [24]. While the concepts of nutrient limitation [25] and nutrient eutrophication [26] on parasite dynamics have been studied, explicitly incorporating multiple elements that feedback into the environment is the basis for ES and we argue will lead to a fuller understanding of the role of parasites in ecosystems.

At the cellular and tissue levels, different tissues within a single organism often exhibit differences in elemental content. For example, the gonads of freshwater snails in the genus *Physa* contain a lower N:P ratio compared to the head or foot tissue [23]. Trematodes that target *Physa* gonads contained similar P content and N:P ratios as host gonads. Thus, parasites that infect specific host tissues may have evolved to feed on tissues that meet their stoichiometric homeostatic needs. Conversely, these parasites may have evolved homeostatic needs that match those of the host tissue they exploit. Comparative ES studies of related parasite taxa that differ in the host tissue they infect may help to resolve the forces driving the evolution of parasite tissue specificity. In addition, ES may shed new light on the extent to which certain parasites truly are parasites. For instance, gut-dwelling tapeworms and acanthocephalans, which have no mouth or gut and absorb food through their external surfaces, may follow more closely to the stoichiometry of the food digested by their host that that of host tissues; the degree to which they compete with the host, rather than feed on it, could be resolved by ES.

The advantages of using ES as a framework for addressing parasitology questions include all the reasons that ecologists use it, and it also provides a straightforward framework for studying how parasites affect ecosystems by using the same first principles, elements, and rate dynamics that ecosystem ecologists measure. The indirect effects of parasites on communities have been studied in a phenomenological manner where a parasite affects a host or a set of hosts and the net change in host behavior, life history, morphology, etc. cascades through the community [27–29]. For example, trematode-infected freshwater snails grazed more rapidly than other snails, resulting in a change in algal communities presumably due to the change in grazing pressure [28]. Wood *et al*. [30] found that marine snails graze more slowly when they are infected by trematodes, this also resulting in an effect on macroalgal communities. While both of these studies found a link between parasite-altered behaviors and the broader ecological community, neither used the common currency of nutrients to more directly link snail physiology, behavior, and ecosystems. Conversely, the environmental drivers of parasite prevalence and intensity are studied from a disease triangle framework by studying how the environment affects both the parasite and the host [31], and increasingly from a community ecology angle [32]. For example, the studies reviewed in Johnson *et al*. [32] aim to understand the environmental factors associated with disease. An ES approach allows us to account for the feedbacks of disease on the environment. Both of these approaches are somewhat limited in that individual traits and community attributes are measured in many different units and currencies, making emergent patterns and phenomena across systems difficult to detect.

ES can be used to make clear hypotheses and predictions that more succinctly link feedbacks of parasites on ecosystems. For example, a handful of recent studies have used ES to link the effects of parasites on host nutrient regeneration. Bernot [23] measured the changes in nitrogen and phosphorus excretion and egestion by a freshwater snail due to infection by a castrating trematode that absorbed phosphorus at a faster rate than the host needed for growth. The result was that infected snails excreted phosphorus at a slower rate than uninfected snails, thereby exacerbating phosphorus limitation in the system. Additionally, infected snails fed phosphorus-deficit food shed fewer trematode cercariae presumably due to less phosphorus available to the parasite via its host. Different effects of trematodes on other freshwater snails include faster metabolic rates that can influence nutrient cycling rates [33]. Mischler *et al*. [34] focused on changes in nitrogen excretion by infected snails and extended these organismal-level parasite effects to whole-lake ecosystems. In this case, trematodes caused snails to excrete nitrogen more rapidly, thereby altering nitrogen cycling at the pond level. Similarly, freshwater crustacean nutrient recycling is also affected by parasites [35,36]. These studies have followed the traditional use of ES in aquatic systems. Future studies can address whether the effects of parasites' feedback to nutrient pools and fluxes in terrestrial and marine ecosystems, particularly where keystone species experience high infection prevalence and altered host stoichiometry, is likely to have large cumulative effects [5]. Studies in other systems have already taken an ES approach in weevil–tree [37], and fungus–cyanobacterium [38] dynamics. In these cases, limiting nutrients were studied as limitations on parasite success. Detailed elemental contents of some terrestrial organisms, like insects, are already well documented [39], providing the basis for fruitful research using an ES approach. Additionally, while more studies are including parasites in food webs [40,41], ES can link food-web metrics like **connectance**, **nestedness**, and **food chain length** to functional components of empirical ecosystems like nutrient pools, nutrient fluxes, and trophic efficiency [42]. Similarly, ES can also be used to make clear hypotheses and predictions about how ecosystem and community-level process affect parasites and their hosts [43,44]. For instance, in a P-limited ecosystem, a parasite may not be able to acquire sufficient P from its host, reducing its fitness, the fitness of its host, or both.

Concluding Remarks

In conclusion, ES uses the conservation of matter of essential nutrients such as C, N, and P to understand pools and fluxes of nutrients involved in interactions across all biological scales. For parasitology, using common nutrient currencies such as N:P can help to frame parasite–host interactions at multiple levels, including the ecosystem level where current disease ecology and parasite ecology efforts are heading. We contend that ES provides a fruitful framework to ask many parasitology questions ranging from topics that have already been well studied to new frontiers in disease ecology and epidemiology (see Outstanding Questions).

Of particular importance and priority should be the use of ES to better standardize effects and phenomena across scales from parasites to ecosystems. For example, asking whether nutrients in the environment limit or promote epidemics, and then whether the effects of an epidemic have reciprocal effects on the environment can be asked by following multiple elements through pools of ecosystem compartments. The elements that are followed through the ecosystem do not need to be the traditional C, N, or P, but could also include elements like calcium, that limits host fitness, or iron, that may limit parasite fitness. This approach offers the advantage of explicitly accounting for feedbacks of elements into and out of different organisms while using the measures and currency of ecosystem ecologists. Experimental studies where key nutrient limitations are introduced and then followed through hosts, parasites, food webs, and ecosystems can inform broader field studies of nutrient cycling in ecosystems differing in parasite diversity or prevalence.

Additionally, at an organismal level, the physiological effects of resource limitation on hosts and their parasites can be studied within an ES framework. Do parasites amplify the negative effects of resource limitation? Do limiting nutrients affect host immune system function (production of cells, function of cells, etc.)? The balance of key elements can be used to predict and potentially weaken the effects of parasites on their hosts.

Outstanding Questions

How does the environment limit or not limit epidemics? Is there a nutrient threshold (in environment or host) above which triggers an epidemic (or below which keeps disease/parasite rare)?

How do parasite effects on hosts feedback to affect communities and ecosystems?

How and why do parasites affect host diet and allocation of limiting nutrients to immune system function (production of cells, function of cells, etc.)?

Are there other limiting elements to parasites or their hosts? Calcium? Iron?

Are elements limiting or are larger nutritional compounds (lipids, proteins, carbohydrates, etc.) more important in affecting hosts and/or their parasites?

What are the physiological effects of resource limitation on hosts and their parasites? Do parasites amplify the negative effects of resource limitation?

Do parasites alter host elemental composition?

Do parasites affect the rates or ratios of excreted or egested elements from hosts?

Do parasites affect the point at which nutrients become toxic to a host?

Does parasite prevalence and diversity affect ecosystem function and trophic efficiency through altered nutrient cycling or limitation?

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