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The context of host competence: a role for plasticity in host–parasite dynamics

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Even apparently similar hosts can respond differently to the same parasites. Some individuals or specific groups of individuals disproportionately affect disease dynamics. Understanding the sources of among-host heterogeneity in the ability to transmit parasites would improve disease management. A major source of host variation might be phenotypic plasticity – the tendency for phenotypes to change across different environments. Plasticity might be as important as, or even more important than, genetic change, especially in light of human modifications of the environment, because it can occur on a more rapid timescale than evolution. We argue that variation in phenotypic plasticity among and within species strongly contributes to epidemiological dynamics when parasites are shared among multiple hosts, which is often the case.

Heterogeneity in host competence

Predicting disease risk to humans, wildlife, and domestic animals has become ever more crucial as the frequency and magnitude of emergence events continue to increase [1,2]. Although host abundance and density strongly influence whether or not a parasite will establish and persist in a population [3,4], a growing body of evidence also suggests that host competence, defined as the proficiency with which a host transmits a parasite to another susceptible host or vector (Box 1), is a key determinant of epidemiological dynamics for parasites with more than one host [5–13]. Thus, a productive step toward improving predictions of such dynamics would include a framework for understanding how heterogeneity in host competence arises and persists.

Competence represents the functional role of an individual or group of individuals (e.g., of the same sex, age, size, life-history stage, population, or species) for infection dynamics in an ecological community [8–10,14,15] (Box 1). In other words, competence is often a relative term because different hosts and combinations of hosts can act to facilitate epidemics or maintain the presence of a parasite in the environment. Although mediated by individual behavioral, physiological, and immunological factors, host competence links what happens inside a host to what happens among hosts comprising communities [16–19]. Crucially, however, competence is governed not only by genetic variation of hosts, parasites, or vectors (Box 1) but also by the environments in which such genetic variants occur [15,20,21]. Consequently, how competence drives variation in community infection dynamics will be mediated by feedbacks among higher and lower levels of biological organization, from individuals to ecosystems [17,18]. We focus here on phenotypic plasticity as a mediator of variation in host competence and environmentally dependent disease risk.

Phenotypic plasticity: a context for host competence?

The environment works on organisms in two ways: it sorts genetic variation via natural selection and it exposes genetic variation via plasticity [22]. Phenotypic plasticity describes the ability of one genotype to express different phenotypes across environmental contexts [22]. Depending on spatial or temporal heterogeneity in the environment, organisms adjust their morphology, physiology, and behavior, often in an adaptive manner [22]. The evolution of phenotypically plastic traits depends in large part on the type and magnitude of spatial and temporal heterogeneity in the environment [22]. When reliable cues accurately signal impending changes in the environment, species may evolve a highly plastic repertoire of traits, including those tied directly and indirectly to their interactions with parasites and vectors [22]. Thus, our insight into disease dynamics might be improved if we consider how different environments affect hosts plastically. For example, resource-rich environments fuel rapid replication of a fungal parasite in its water flea host, *Daphnia dentifera*. This plastic shift in host competence can drive large epidemics in *Daphnia* populations that cause larger host die-offs and more intense parasite-mediated selection for costly resistance to the parasite [15,23–25]. Environmentally mediated epidemics in this system may produce cascading effects on the rest of the ecosystem because the abundance of *Daphnia* also affects the abundance and composition of algal and fish communities [26]. Simply put, plasticity could often underlie unique host (individual, population, and species) contributions to parasite dynamics across contexts but, in general, the role of plasticity has been minimally considered, especially in terms of parasites with more than one host (including zoonoses).

A plasticity-mediated framework for disease dynamics

Figure 1 illustrates how variation in parasite transmission potential or risk of infection (depicted as the transmission coefficient, β) might be driven by plasticity in host competence among individuals, nested within species, nested

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Box 1. Heterogeneity in host competence

Host competence is the ability of a host to transmit infection to another susceptible host or vector effectively. Behaviors of hosts, parasites, and vectors affect the frequency and magnitude of host–parasite encounters [step **(1)** in Figure I], whereas genetic, molecular, and cellular processes generally mediate within-host post-exposure host responses, including susceptibility to infection (e.g., whether hosts become infected upon exposure or not) **(2)**, as well as duration and magnitude of infectiousness and probability and rate of recovery after infection **(3)**. Variation in the way that individual hosts cycle through a progression of exposure, infection, disease, and recovery has obvious individual-level consequences (e.g., life or death), but these individual-level responses are also directly linked to transmission to other susceptible hosts, to vectors, or into the physical environment **(4)**. Host competence at an individual level mediates intraspecific population level (**5**) and interspecific community level (**6**) parasite prevalence and spread. The proficiency with which a parasite is transmitted among susceptible hosts is crucial because it ultimately influences community-level dynamics, including whether a parasite invades, spreads, and persists in a multihost environment.

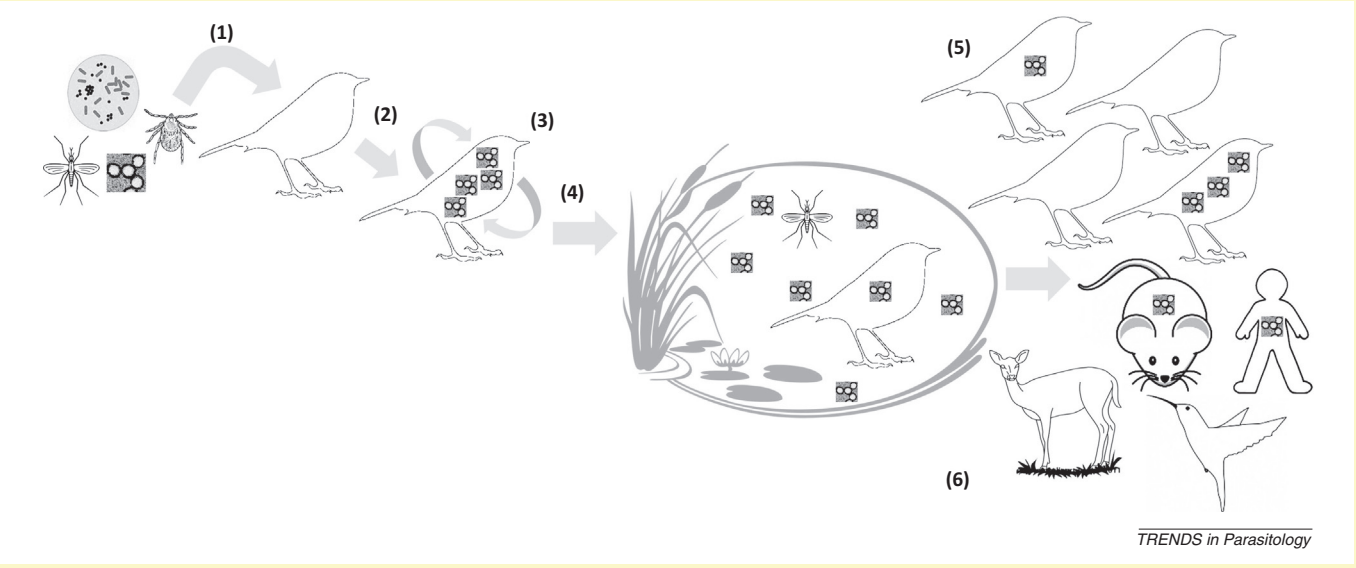

Figure I. Heterogeneity in host competence.

within ecological communities (Figure 1) [27,28]. In this hypothetical example, individuals vary in competence-related traits contributing to transmission depending on their genotype, the environment, and gene–environment interactions (e.g., plasticity including but not limited to epigenetic regulation of gene expression, acquired immunity, and parental effects) (Figure 1A) [27,28]. At the species level (Figure 1B), the range of genotypes present in the population determines the mean and variance of a host species' contribution to parasite transmission potential. In this particular example, despite variation in shape, all reaction norms for all three species have the same average contribution to β across all environments. However, β and variation in β via host competence differs among species, depending on environment. Some species will therefore transmit consistently, whereas others might transmit differently across environments or be extremely variable in particular environments. Host energetics, immunity, behavior, and other traits could mediate differences in these reaction norms [29–31]. At the community level (Figure 1C), species composition and plasticities within and among species differ across environments, thus giving a different community value of β (e.g., the contributions of all species to parasite transmission among a multi-host community) contingent on the site considered. Figure 1C highlights a surprising outcome about β when both community composition and heterogeneity in plasticities are considered: two identical communities can have very different β values contingent on how the species respond to variable environments. For example, in Environment 4, average β is double that of Environment 3 simply as a result of different plasticities among species in different contexts.

To further illustrate the consequences of plasticity in host competence on disease dynamics, we developed a general susceptible-infected (SI) epidemiological compartment model [3]. This classic modeling formalism categorizes hosts by their infection status, and tracks changes in these groups as individuals 'move' through them via births, deaths, and infective contacts, which occur at rates depending on traits and densities [3]. From this model we can calculate the parasite reproductive ratio, R_0, a fundamental index of the potential for parasite spread. Parasites can initiate epidemics when $R_0 > 1$, and larger values of R_0 generally produce larger epidemics with greater effects on host density [3] (Box 2). We show here that a plastic increase in host competence, and thus the contribution to β in one species across an environmental gradient, can facilitate parasite invasion ($R_0 > 1$), increase equilibrial infection prevalence, and increase infected host density. Without this plasticity, the potential for parasite invasion is reduced; with plasticity, the parasite can establish in environments that were previously unsustainable. The qualitative behavior of this model is robust to allowing host species to compete and variation in parasite virulence. This example illustrates only one possibility.

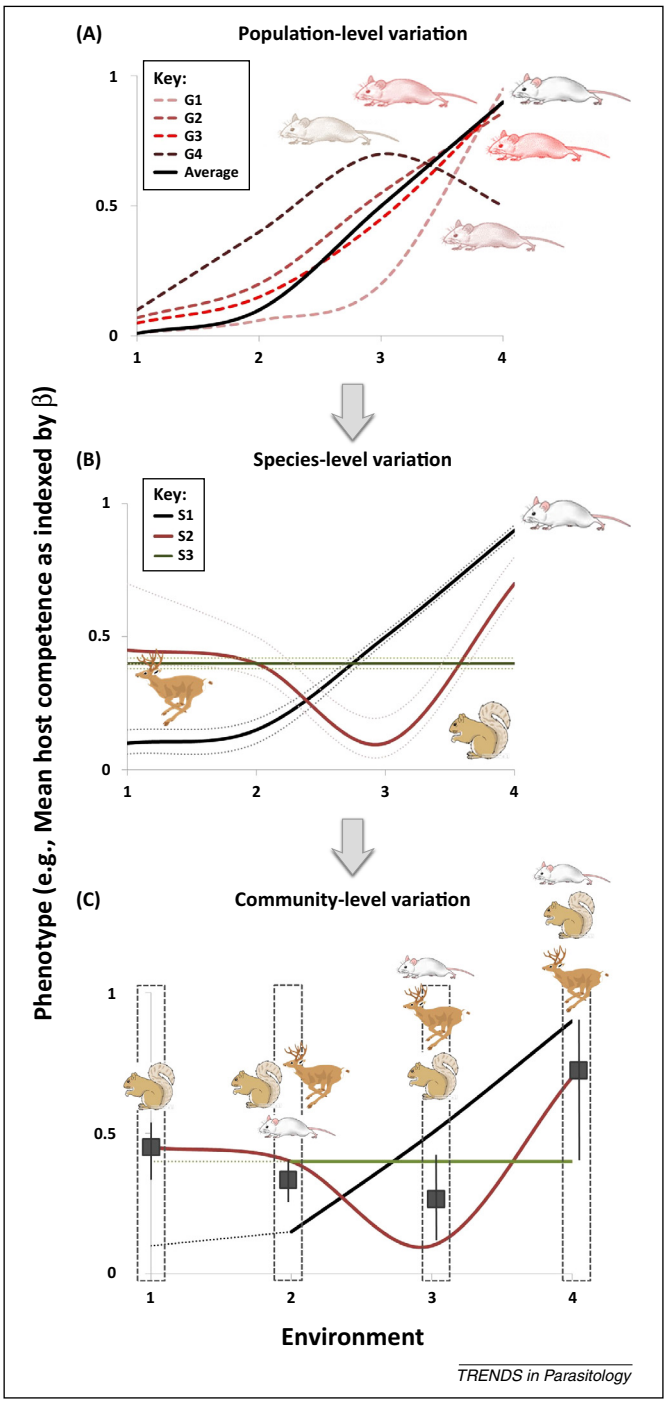

Figure 1. Plasticity in host competence and its potential effects on disease dynamics. Disease risk is a product of a hierarchy of host traits arising via fixed and plastic genetic differences at the level of the individual but extending to a multi-host community of species. The figure illustrates how the risk of parasite transmission (denoted as the transmission coefficient, β, shown on the *y* axis) for a hypothetical population (A), species (B), or community (C) varies as host competence changes along an environmental gradient (*x* axis). Importantly, variation in transmission risk is fundamentally derived from processes at the individual level. In **(A)** the solid black line shows the average contribution to transmission of individuals (e.g., mice) of genotypes 1–4 (G1–G4) across an environmental gradient (i.e., a single reaction norm for the population), but the dashed lines emphasize the extent of variation in reaction norms for host competence among individual genotypes, such that the contributions of individuals to transmission through variation in competence might be very distinct. At the species level **(B)** the range of genotypes present in the population determines the mean and variance in transmission potential. S1–S3 denote three example species (e.g., a deer, a mouse, and a squirrel). Broken lines depict variation in β in three species across environments. Despite variation in shape, all reaction norms for all three species have the same mean β. However, average β and variation in β differ among species depending on their position along the environmental gradient. At the community level **(C)** both species composition (i.e., host identity) and plasticities within species differ across the environment and shape the community value of β. Broken lines indicate species absence, unbroken lines indicate species presence, and dashed boxes encompass particular environment types. Black boxes denote the mean ± SD community-level β.

Across natural systems, plasticities in host competence may produce a variety of epidemiological outcomes, for example facilitating or damping epidemics contingent on how genotypes and species respond to environmental heterogeneity [15,23]. Thus, plasticity can qualitatively and quantitatively change the outcome of host–parasite interactions at an individual level, which can percolate to affect population and community-level dynamics [15,23–25,27,28].

From key hosts to key host–environment interactions

For a growing number of host–parasite systems, a few host species are emphasized as key drivers of community-level transmission dynamics and human disease risk because they act to amplify the amount of parasite circulating among hosts [7–14,32,33]. Conversely, the presence of other less-competent hosts could dilute community-level disease risk [14]. However, different plasticities within species may explain why community-level phenomena, such as the dilution or amplification effect, are not always observed, as well as why some individuals within species are more prone to create new infections than others (i.e., superspreaders). In the forests of Northeastern USA, one species, the white-footed mouse (*Peromyscus leucopus*), is integral to Lyme disease risk for the entire community. In part its impact is mediated by its high relative abundance, but its immunological profile and capacity to tolerate high tick burdens are also important [32,34–36]. Moreover, compared to other species in the community (e.g., songbirds, white-tailed deer, and other small mammals), white-footed mice bitten by infected ticks accrue a sufficiently high burden of *Borrelia burdorferi* to facilitate subsequent mouse-to-tick transmission [32]. If the identity of 'amplifiers' and 'diluters' changes with environmental context, the varying magnitude of the diversity–disease risk relationship observed across host–parasite systems might be explained by different plasticities among species [37]. It would be informative to discern whether plasticity can explain the presence, absence, or degree of dilution across other systems because many parasites have expanded their geographic ranges and phenology in association with changing climate [38].

Another opportunity to evaluate the role of plasticity involves West Nile virus (WNV), a disease that is driven by the preference of mosquito vectors for specific hosts [39]. The American robin (*Turdus migratorius)* is bitten most often by mosquitoes that transmit WNV, making robins a key link in the enzootic transmission cycle [10]. For this reason, infection profiles of robins in an area tend to be predictive of human disease risk in the same areas [10,39]. Robins are migrants, however, meaning that temporal elongation or amplification of WNV cycles must involve other hosts once robins have emigrated. As resident passerines are well known to change plastically across a year to cope with the various stressors that accompany different seasons [40], some hosts may be more preferred

than others by the remaining vectors of WNV. Indeed, even when robins are present, different plasticities among species may modify the disease risk within a community if bites directed at robins are amplified or diluted by plasticities in other species. Further, environmentally mediated changes in host epidemiological traits, including susceptibility and the magnitude and duration of infectiousness, may mitigate or exacerbate the relative effect of vector preferences on transmission dynamics in different locations or at different times.

Several other areas of emerging concern might benefit from considering a possible role of plasticity in community disease dynamics. First, there has been an enormous interest in bats as reservoirs for a range of viral parasites that cause deadly human diseases such as Marburg virus, rabies, and Ebola [41–44]. While it is typically the case that variation among species is greater than variation within a species, plasticity among individuals could be as important as species-level differences (Figure 1A). In other words, the differences between a bat and another mammal might be less important epidemiologically than the differences between a bat living near humans where food is plentiful and another bat living in a natural environment where resources are scarcer [45]. Hosts occupy diverse environments, and their genotypes, physiological condition, and other factors all affect whether any individual within a host species/population succumbs to infection or lives to transmit it to another susceptible host [45]. In this light, bats might either be a particular risk because of invariant competence across environments or because of exceptionally high competence (e.g., viral shedding) in particular environments [43,45]. Obviously the management implications of the two alternatives can differ dramatically [45].

A final phenomenon to consider with respect to individual-level plasticity is superspreading, such as in the case of HIV [5] and severe acute respiratory syndrome (SARS) [9], whereby disproportionate contact rates and viral shedding among some highly connected individuals make them drivers of epidemics. On the one hand, superspreading may involve fixed, genetic variants; some individuals might interact consistently and extensively with other hosts, vectors, or contaminated resources no matter where they occur. On the other, superspreading may only emerge in contexts where the behavior and physiology of individuals interact to produce amplified transmission potential and disease risk. If environments could buffer the effects of

Box 2. How plasticity in host competence can affect parasite dynamics: a simple model

Heterogeneity in host competence might alter disease dynamics across environmental gradients through two mechanisms: changes in the composition of the community and changes in host traits via plasticity. We illustrate here the potential effects of these compositional and plastic trait changes on parasite dynamics with a multi-host SI model across an environmental gradient (e.g., resource availability).

The model tracks the changes in the density of susceptible, S_i, and infected, I_i, individuals for three species ($i = 1$, 2, or 3):

$$\frac{dS_i}{dt} = b_i(E)(S_i + I_i)(1 - c_i(S_i + I_i)) - dS_i - S_i \sum_{i=1,2,3} \beta_{i,j} I_j \quad [I]$$

$$\frac{dI_i}{dt} = S_i \sum_{i=1,2,3} \beta_{i,j} I_j - (d + v) I_i \quad [II]$$

The model allows host community composition to change over the environmental gradient in the absence of parasitism (Figure IA) by specifying host maximal birth rate, b_i, as a function of an environmental covariate, E (ranging from 0 to 1). The model assumes intraspecific density-dependence of host birth rates, at strength c_i, but no interspecific competition (although allowing interspecific variation does not qualitatively alter the results). Hosts can die at a background death rate, d (common to all species), and are lost through density-dependent transmission, with species-pair specific transmission rates, β_{ij}. We assumed that values of β_{ij} depend on an underlying competence trait, σ_i, for each species, which act multiplicatively to determine β (and yielding a symmetric matrix of transmission coefficients):

$$\beta = \begin{matrix} \sigma_1^2 & \sigma_1\sigma_2 & \sigma_1\sigma_3 \\ \sigma_2\sigma_1 & \sigma_2^2 & \sigma_2\sigma_3 \\ \sigma_3\sigma_1 & \sigma_3\sigma_2 & \sigma_3^2 \end{matrix} \quad [III]$$

Infected hosts arise from these transmission events, but die at an elevated death rate owing to the (common) virulent effects, v, of the parasite. We determined the parasite's R_0 (i.e., the reproductive ratio of the parasite, or the number of secondary infections produced by the first infected individual) using the next-generation matrix method [53], and simulated the model using the lsoda function in the R computing language to determine equilibrial infection prevalence and density of infected hosts [54].

We examined the consequences of compositional and trait changes on parasite dynamics by considering two scenarios. In scenario 1, host community composition (in the absence of parasitism) changes across the environmental gradient, but all host traits except birth rate remain constant (Figure IB), regardless of community composition and environment (e.g., no plasticity). Thus, any changes in the mean competence of the host community (grey line in Figure IB) and parasite dynamics across the environmental gradient (black line in Figure ID–F) are driven entirely by community composition. In scenario 2 (Figure IC), composition changes exactly as before, but now one of the three host species also exhibits plasticity in its competence (blue line in Figure IC). Consequently, mean competence within the community (grey line in Figure IC) changes as a function of host community composition and plasticity. Changes in parasite dynamics along the environmental gradient reflect altered composition and traits (red line in Figure ID–F).

Comparing the red and black lines across the gradient (Figure ID–F) reveals the potential influence of plasticity in one species on community-level parasite dynamics. Without plasticity (e.g., scenario 1), competence increases along the environmental gradient due entirely to a compositional change in the host community. Increases in mean transmissibility across the gradient facilitate parasite invasion, and increase equilibrial infection prevalence and density of infected hosts (black lines, Figure ID–F). However, with scenario 2, competence at the community level is enhanced by the plasticity exhibited by one host. In this example, this plastic increase in competence increases the community mean competence in intermediate environments (compare grey lines in Figure IB,C). This increase in community-wide competence facilitates greater values of R_0 and increases in the equilibrial prevalence and density of infected hosts in this community, especially at intermediate environmental values (red lines Figure ID–F). However, at higher values along this environmental gradient, this plastic host species is lost from the community (Figure IA), and this diminishes the effects of its plasticity. In this example, plasticity facilitated epidemics under conditions in which risk would have otherwise been low. However, it is notable that, in other situations, plasticity in host competence might also prevent or diminish the magnitude and duration of epidemics. By integrating mechanistic understanding of host and parasite plasticity with epidemiology, we may better anticipate disease outbreaks across environmental gradients. Parameters used in the simulations: scenario 1: $b_1(E) = \exp(-2*E)$, $b_2(E) = 1$, $b_3(E) = (E/(0.9 + E)$, $d = 0.1$, $c_1 = c_3 = 0.01$, $c_2 = 0.02$, $v = 0.2$, $\sigma_1 = 0.04$, $\sigma_2 = 0.08$, $\sigma_3 = 0.12$. Scenario 2: as in scenario 1, except $\sigma_1(E) = 0.04 + 0.16*E$.

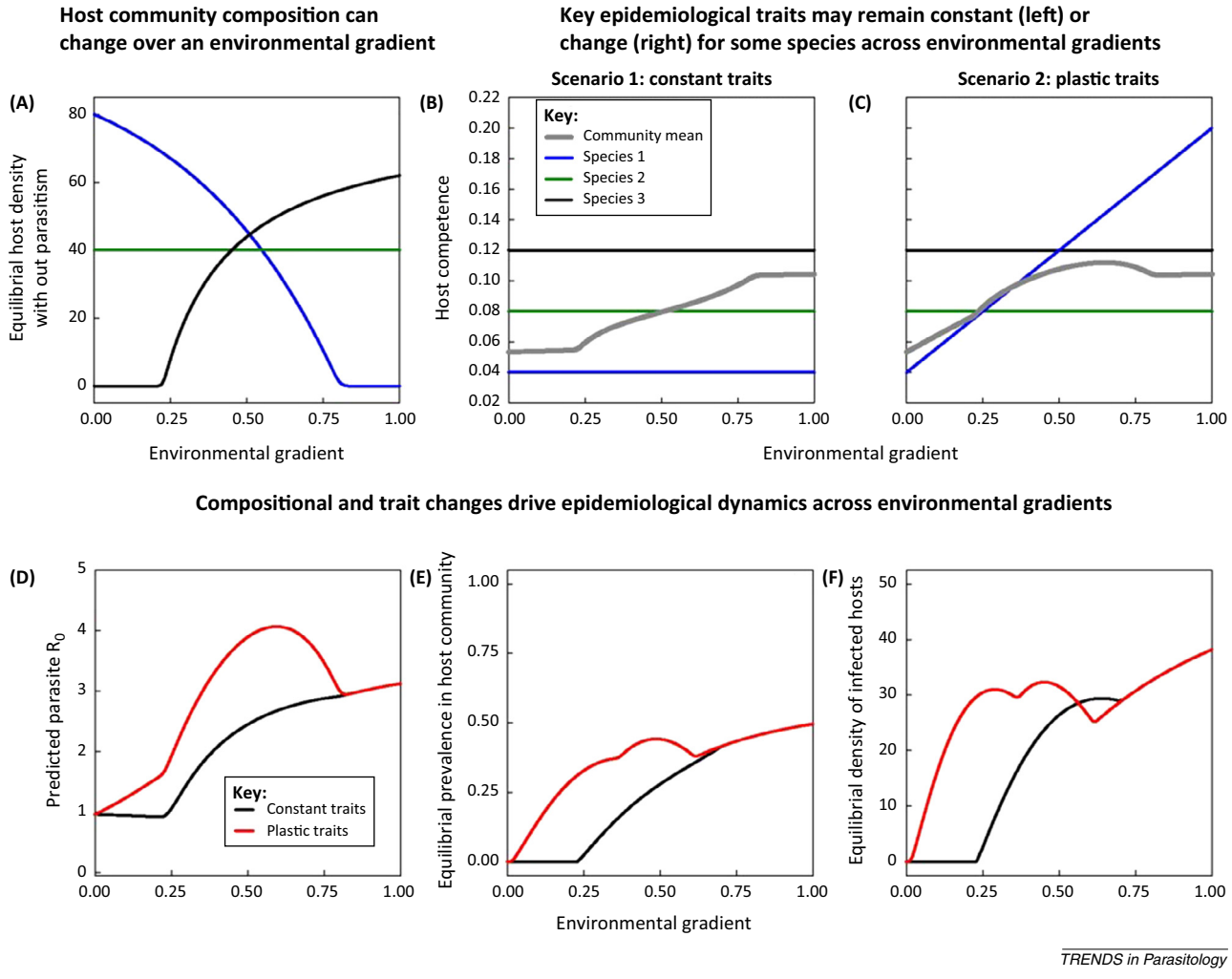

Figure I. How plasticity in host competence can affect parasite dynamics: a simple model.

parasite burden on host performance (i.e., environmentally enhanced tolerance of parasites via better nutritional conditions in resource-rich locations), hosts may disproportionately generate new infections through high contacts with uninfecteds [45]. Likewise, in stressful environments, adversity may reduce immune defenses and/or defensive behaviors such that some hosts are more prone to become infected and infectious to others [45]. Such outcomes may be particularly likely at sites where humans, livestock, and wildlife all come into contact. Farms, open-air markets, zoos, and other similar sites may exacerbate disease risk for reasons involving the coming-together of competent species; however, risk may be exacerbated (or damped) in light of different plasticities among hosts driven by food resources, coinfection, and excessive use of antibiotics, which could polarize the microbiota of each potential host [45,46].

Future directions

We expect that our framework for integrating plasticity into studies of host competence for parasites will improve our understanding and control of infectious diseases that threaten conservation or human health. Concerted research at multiple biological levels, using this framework as a guide, holds much promise. At the individual level, it could reveal whether the physiological mediators of transmission are more plastic in some hosts than others among geographic sites, seasons, genotypes, or age classes; such hosts might dilute risk in some contexts and amplify it in others. At the population and species levels, genetic/epigenetic variation in reaction norms (Box 3) may mediate the development of particular immune system configurations and behavioral repertoires [30,34,35], some more conducive to parasite transmission than others. At the community level, changing environments might influence ecological interactions, the timing of life events, and the allocation of resources among various processes [15,47,48], which could enable some species to play greater roles in infectious disease dynamics at some times and places than others [49]. Importantly, our framework applies not only to hosts but also to vectors and pathogens themselves, which may also exhibit phenotypically plastic responses to their external environments [20,21,50,51]. An additional dimension of complexity worthy of note pertains to the role of coinfection in mediating host competence and infection dynamics [19]. We have discussed plasticity in host competence to transmit a single parasite type shared among multiple hosts. However, coinfections as well as previous

Box 3. Drivers of host heterogeneity and differential disease dynamics: a role for epigenetics?

Heterogeneity in some host traits can be attributed solely to genetic variation [55]; however, much, if not most, of the variation in traits arises from interactions between genotype and environment (i.e., plasticity) [56]. One possible mechanism by which environmental factors can contribute to heterogeneity in host competence is epigenetics, defined here as potentially heritable molecular-level mechanisms that affect gene expression without altering the underlying DNA sequence [57]. Unlike genetic variation, epigenetic variation, such as DNA methylation, is more evolutionarily labile and responds quickly to external environmental factors [58]. In other words, epigenetic marks might often act as molecular mechanisms of plasticity. Several studies have provided evidence for the importance of DNA methylation as a mediator of both immunological [59] and behavioral variation [56]. DNA methylation alters gene expression predominantly by affecting the ability of transcription factors to bind to promoters. Thus, environmentally induced epigenetic modifications provide a source of variation that might allow organisms to adjust their phenotypes more rapidly than would be possible via genetic variation alone [57]. Because individuals vary in their capacity to respond epigenetically to the environment [22], selection may act on this variation to influence population-level patterns of epigenetic responsiveness and hence plasticity. Moreover, evidence suggests that such environmentally-sensitive changes in DNA methylation not only have the potential to influence disease susceptibility but these differences in epidemiological traits can also persist across several generations [60]. Transgenerational epigenetic inheritance of traits associated with host competence could have significant implications for disease dynamics in multi-host parasite communities. For instance, epigenetic inheritance of traits conferring immunological resistance could exert selection pressure on parasite traits (e.g., virulence, immune-evasion mechanisms, etc.), thus potentially leading to more rapid host–parasite evolution than would be possible through the accumulation of genetic variants alone.

infection history may play a vital role in determining the context of host competence, particularly across environmental gradients of different parasite richness, abundance, and distribution.

Concluding remarks

Some of the biggest concerns of epidemiologists, disease ecologists, and medical scientists involve how to predict where and when diseases will spill into new hosts or locations [2,52]. Such insight is fundamentally based on understanding the hosts that support infectious organisms as well as the environments in which host–parasite interactions occur. Hosts, vectors, and parasites all respond and adjust to their environments to remain viable in light of the entirety of the challenges they face. Future infectious disease research would benefit not only from being multi-disciplinary but also being multi-scalar, integrated, and considerate of plasticity.

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