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Opinion

Co-circulation and co-infection: parasite interactions across scales

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Parasite–parasite interactions occur both within and between hosts, but the two scales are rarely considered together. Consequently, there is a gap in our ability to predict the integrated effects of interactions occurring across scales, disentangle their relative contributions to key ecological outcomes, and accurately identify the drivers of host–parasite evolutionary responses. Here, we extend the standard susceptible–infected framework of theoretical epidemiology to explicitly incorporate parasite–parasite interactions across scales. We identify where – in each step of the transmission process – such interactions may occur, at the within- or between-host levels, providing empirical examples where possible. Thus, we demonstrate how integrating the two scales provides a more complete understanding of the evolutionary ecology of multi-parasite systems and suggest future avenues of investigation.

Highlights

Climate change and human activities are shifting parasite distributions, and thus causing novel parasite co-occurrences.

Multiple parasites (strains or species) co-circulating within a host population often cause co-infections, that is, the simultaneous infection of an individual host by multiple parasites.

Co-circulating parasites can interact at both the host individual and host population scales, with crucial implications for transmission, host health, host–parasite evolution and disease management. However, interactions at one scale are often investigated without considering the other.

We present a conceptual framework that explicitly recognises the two scales of parasite–parasite interactions. This framework identifies multiple pathways by which parasites interact and highlights the ecological, epidemiological, and evolutionary consequences of these interactions.

Parasite interactions across scales

A single population can host multiple parasites (strains or species). This **co-circulation** (see Glossary) of parasites can lead to the **co-infection** of individual hosts. Co-infecting parasites interact through a range of mechanisms, with implications for host health, population dynamics, and host–parasite evolution [1–3]. Co-circulating parasites can also interact at the host population level, without necessarily co-infecting the same host individual. For example, measles and whooping cough can interfere with each other by removing susceptible individuals from the host population via effects on host behaviour and mortality [4,5]. Although interactions among parasites occur both **within hosts** (**individual level**) and **between hosts** (**population level**), these distinct scales of interaction are rarely considered concomitantly [6,7].

We argue that focusing on individual- and population-level parasite–parasite interactions as independent phenomena has resulted in a fundamental gap in our understanding of their ecological, epidemiological, and evolutionary consequences. Indeed, interactions at one scale may compound, confound or obscure interactions at another (Figure 1). To address this gap, we use a susceptible–infected (SI) transmission framework to delineate the range of ways that parasite–parasite interactions at the individual and population levels can affect parasite transmission dynamics. We illustrate these concepts with specific examples at both levels across diverse host–parasite systems. We then discuss the broader implications: why studying individual- and population-level interactions in combination generates novel insights into infectious disease ecology and evolution; how consideration of both scales may be necessary for successful disease control; and how appropriate modelling and experiments can help to disentangle when interactions at one scale affect those at another. Finally, we identify outstanding questions and future directions for building a more holistic perspective on parasite–parasite interactions.

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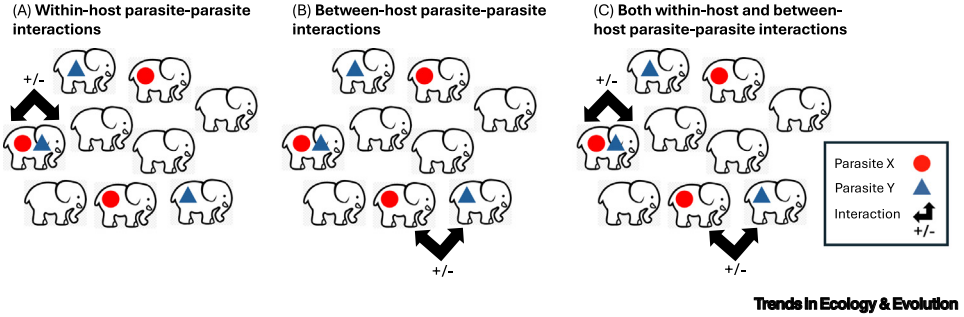

Figure 1. Parasite–parasite interactions. Here, a host population (elephants) can be infected with two parasites (X, red circle; and Y, blue triangle). Parasites can interact (double-headed arrow) at different levels in the host population. (A) Most research has focused on interactions that occur within a co-infected host (within-host parasite–parasite interactions), as illustrated by the co-infected elephant (red circle and blue triangle). (B) By contrast, two parasites that co-circulate in the host population can interact at the population level (between-host parasite–parasite interactions), a process which does not necessarily involve parasites ever infecting the same host. (C) Importantly, interactions among parasites infecting the same host population can occur simultaneously at both levels, with interactions at one level potentially affecting interactions at the other. The importance of considering such cases is at the heart of this paper.

A transmission framework for individual- and population-level interactions

We use the SI transmission framework (Box 1) to illustrate how both individual- and population-level interactions among parasites determine epidemiological dynamics [8]. In this framework, transmission is conceptualised as a three-step process. First, a susceptible host must make contact with an infected one; next, the infective stage of the parasite must then be successfully transferred from the infected to the susceptible; finally, the parasite must become established within the new host [9]. Although the precise details and mechanisms at play in each of these

Box 1. Individual- and population-level interactions in a susceptible–infected (SI) transmission framework

In the SI transmission framework, widely used in theoretical epidemiology [8], the density of infected individuals I in a host population is governed by the equation

$$\frac{dI}{dt} = \beta SI + \dots \quad [I]$$

with S being the density of susceptible individuals and β the transmission coefficient. We limit ourselves to density-dependent transmission for brevity, but the ideas herein are readily translatable to frequency-dependent transmission. The term βSI encodes transmission as being proportional to the product of the densities of susceptible and infected individuals; the ellipsis represents processes such as population turnover and recovery, the details of which are system-specific.

This framework is formulated for a single parasite (the focal parasite), whose transmission we are interested in. We consider this in the context of a background parasite, whose transmission we do not explicitly incorporate, but which may affect the focal parasite's transmission dynamics. Thus, S and I are, respectively, the susceptible and infected host subpopulations for the focal parasite, some of which may also be infected by the background parasite. We therefore write

$$S = U + I_B \quad [II]$$

$$I = I_F + I_C \quad [III]$$

where U are hosts uninfected by either parasite, I_B are infected by only the background parasite, I_F by only the focal parasite, and I_C are co-infected. The transmission coefficient of the focal parasite can be decomposed into

$$\beta = \kappa \times \iota \times \sigma \quad [IV]$$

where κ is the contact rate between individuals, ι is the infectiousness of focal-infected individuals and σ is the susceptibility of focal-uninfected individuals [9]. The values of κ, σ, and ι may differ depending on infection status by the background parasite, but we do not codify this mathematically for the present purpose. Thus, the transmission function βSI comprises seven pathways by which the background parasite may affect transmission of the focal parasite (Table 1 in the main text): three traits (contact rate, susceptibility, and infectiousness) and four subpopulations (uninfected, the two singly infected and co-infected hosts). How parasites may interact along these pathways, at both the WH and BH levels, is explored in more detail in the main text.

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steps will differ between systems, this sequence highlights the elements determining transmission: the susceptible and infected host subpopulations, their **contact rate rate**, host **susceptibility**, and host **infectiousness**.

Here, we extend this framework from a single parasite (the **focal parasite**, *i.e.*, the one whose transmission we are interested in) to incorporate a **background parasite**. Although we do not explicitly consider transmission of this background parasite, its presence may affect the focal parasite's transmission dynamics via any of the elements of transmission. Particularly, the presence of a background parasite divides the focal-susceptible subpopulation into uninfected and background singly-infected, and the focal-infected subpopulation into focal singly-infected and co-infected. This framework therefore yields seven pathways (four subpopulations and three traits) by which the background parasite may affect transmission of the focal parasite (Box 1). Table 1 illustrates how these pathways may include both within-host (WH) or between-host (BH) interactions. Note that we consider only two-parasite systems for illustrative purposes, but the ideas are readily extended to more via the consideration of multiple background parasites and their possible interactions with the focal parasite (see subsequent text).

By definition, WH interactions occur between parasites infecting the same host, but not necessarily at the same time. Thus, this category includes WH interference competition between parasites, and indirect interactions mediated by a shared host, such as via the WH resources or the host immune response [10]. By contrast, BH interactions occur at the population level, via hosts but not within them. By altering host behaviour, condition or abundance, a background parasite may indirectly affect the transmission of the focal parasite [5]. Theoretical and empirical examples of interactions at both levels are outlined in Table 1.

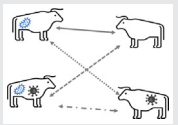
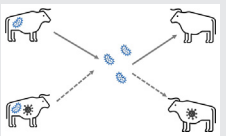
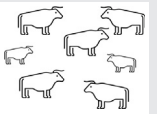
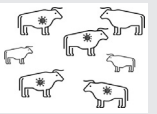
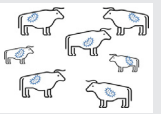
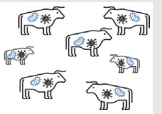
Although rarely investigated (but see [11]), contact rates may decrease as a consequence of co-infection promoting convalescence or conspecific avoidance, such as through increased pathology [12] (Table 1, WH1). At the population level, host behavioural defences against one parasite could affect transmission-relevant contact rates for others (Table 1, BH1). For example, the use of face masks, self-isolation, lockdown, and several other non-pharmaceutical interventions against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) reduced contact rates and thereby the circulation of other respiratory viruses [13]. Similar behavioural modifications may be seen in non-human animals: garden ant colonies (*Lasius niger*) exposed to the fungus *Metarhizium brunneum* altered their behaviour and social networks, which may inhibit the transmission of the fungus [14], and possibly other parasites. Parasites can also directly affect host behaviour via host manipulation [15,16]. Whether co-infecting parasites benefit from this will depend on whether their interests align. For example, the protozoan *Toxoplasma gondii* modifies behaviour of infected rats to enhance predation by cats, its definitive host [17]; the consequences for transmission of a co-infecting parasite then depends on whether it also infects the same definitive host.

Susceptibility and infectiousness are also sensitive to co-infection. Infection by the background parasite can make a host more or less susceptible to the focal parasite by weakening its immune response, depleting its condition, or priming the immune system to resist the focal parasite. The same processes might increase or decrease infectiousness in co-infected hosts. Research supports host infectiousness and susceptibility being impacted by WH interactions (Table 1, WH2,3). For instance, narrow-leafed plantain (*Plantago lanceolata*) plants co-infected with two different strains of powdery mildew (*Podosphaera plantaginis*) released more spores than were released by singly infected plants [18]. In humans, acquired immunity to paramyxoviruses reduced susceptibility to infections from other strains [19]. Susceptibility can also be affected by population-level interactions (Table 1, BH3), such as the release of volatiles by infected plants, upregulating

Glossary

Background parasite: the parasite that co-circulates within the same host population as the focal parasite, possibly but not necessarily co-infecting the same individuals.
Between-host or population-level interactions: parasites affect one another indirectly, through their hosts, without necessarily infecting the same host individual.
Co-circulation: the presence of two or more parasite species (or strains) within the same host population at the same time, but not necessarily within the same individual hosts.
Co-infection: the presence of two or more parasite species (or strains) within the same host, at the same time.
Contact rate: the rate at which encounters of sufficient length to transmit parasite infective stages occur between uninfected and infected individuals or infective stages (depending on transmission mode).
Focal parasite: the parasite currently being considered, the focus of study.
Force of infection: the rate at which susceptible hosts acquire infections.
Infectiousness: the propensity of an infected individual to transmit infection to another individual upon contact.
Susceptibility: the propensity of a host to become infected upon exposure.
Within-host or individual-level interactions: parasites affect one another, directly or indirectly, due to their presence within the same host individual. Infection can be concurrent (co-infection) or not (sequential, non-overlapping infections by different parasites of the same host).

Table 1. WH and BH interactions among parasites – theoretical and empirical examples

Transmission of focal parasite	***β*: Transmission coefficient**			***S*: Focal-susceptible density**		***I*: Focal-infected density**	
	Contact rate	'Donor' infectiousness	'Recipient' susceptibility	Uninfected	Background singly-infected	Focal singly-infected	Co-infected
How does the background parasite affect transmission of the focal parasite?							
Within-host interactions (**WH**)	**WH1**	**WH2**	**WH3**	**WH4**	**WH5**	**WH6**	**WH7**
	↑*β* Vector attraction or deterrence ↓*β* Inactivity, convalescence	↑*β* Immune suppression, reduced host condition ↓*β* WH competition, cross-immunity	↑*β* Immune suppression, reduced host condition ↓*β* WH competition, cross-immunity, immune priming	↓***S*** Reduced fecundity	NA	NA	↑***I*** Impedes recovery ↓***I*** Co-infection mortality, promotes recovery ↑↓***I*** Alters host competitiveness
	↑*β* Vectors prefer co-infected *Solanum tuberosum* (potato) [11] ↓*β* Hospitalisation of co-infected *Homo sapiens* (human) [49]	↑*β* Increased infective stage output (ISO) in co-infected *M. musculus* [50], *H. sapiens* [51] ↓*β* Reduced ISO in co-infected *Blattella germanica* (cockroach) [52]	↑*β* Background parasite increases susceptibility to focal in *M. musculus* [50], *H. sapiens* [51] ↓*β* Background parasite reduces susceptibility to focal in *Daphnia dentifera* (water flea) [53]	↓***S*** Reduced fecundity in co-infected *Aedes aegypti* (mosquito) [54], *D. galeata* [21], and *Hordeum vulgare* (barley) [22]	NA	NA	↑***I*** Inter-parasite competition reduces mortality in *M. musculus* [23] ↓***I*** Co-infection increases mortality in *H. sapiens* [49], *S. lycopersicum* (tomato) [55], *D. dentifera* [53]
Between-host interactions (**BH**)	**BH1**	**BH2**	**BH3**	**BH4**	**BH5**	**BH6**	**BH7**
	↑*β* Boldness, promiscuity ↓*β* Inactivity, convalescence ↑↓*β* vector attraction or deterrence	NA	↑↓*β* Signalling affects susceptibility of neighbouring hosts	↑***S*** Birth stimulation (release from host density-dependent limitation) ↓***S*** Reduced fecundity	↓***S*** Background infection mortality ↑↓***S*** Alters host competitiveness relative to focal infected	↑↓***I*** Alters host competitiveness relative to background infected	NA
	↑*β* Vectors infected with one virus prefer *S. lycopersicum* infected with another [55] ↓*β* Social distancing reduces respiratory disease transmission in *H. sapiens* [13] ↑↓*β* Parasites affect host behaviour (reviews), [15,16,56][a]	NA	↑↓*β* Background parasite affects neighbouring plants susceptibility (reviews) [20,57][a]	↑***S*** Fecundity compensation in *Poecilia reticulata* (guppy) and *Biomphalaria alexandrina* (snail) [58,59][a]	↓***S*** Background parasite increases mortality, reducing focal-susceptible pool in *H. sapiens* [4,5][a]	↑***I*** Focal phage infections alter host competitiveness relative to background infected in *Pseudomonas aeruginosa* (bacteria) [60][a]	NA

[a]Mechanisms predicted to have consequences for parasite–parasite interactions by our framework, but under investigated.

immune responses in neighbouring conspecifics, thus reducing susceptibility to co-circulating parasites [20].

The sizes of susceptible or infected subpopulations are critical determinants of transmission. WH interactions may: reduce fecundity, thereby diminishing the uninfected pool, decreasing transmission (Table 1, WH4); impede recovery, lengthening the time an individual is infected, increasing transmission (Table 1, WH7); or increase mortality, reducing transmission (Table 1, WH7). *Daphnia galeata* co-infected with a protozoan (*Caullerya mesnili*) and a fungus (*Metschnikowia* sp.) showed increased mortality (shorter transmission window) and reduced fecundity (fewer susceptibles) compared with single infections [21], reducing transmission. Similarly, co-infection with two viruses resulted in high disease severity and low fecundity in barley (*Hordeum vulgare*) [22]. However, co-infection might also decrease mortality, as observed in co-infecting *Trypanosoma brucei* strains in mice (*Mus musculus*), promoting host survival through apparent competition via the host immune response [23]. At the population level (Table 1, BH4–6), increased host mortality due to the background parasite may decrease both focal-susceptible and focal-infected subpopulations via reductions in background singly-infected and co-infected hosts. If increased mortality releases the wider host population from density-dependent constraints, promoting an influx of new individuals via increased births or immigration, this may increase the susceptible pool [24]. Host competition also provides opportunity for BH interactions; if infection by a background parasite alters host competitiveness relative to hosts singly infected by the focal parasite, the corresponding subpopulations will change in abundance [25].

Consequences and implications

Co-infection interactions can have dramatic consequences for the transmission and population dynamics of parasites. These effects can manifest by altering the parasite basic reproduction number, changing the regions of parameter space that lead to coexistence, and hence probabilities of parasite co-circulation, and altering host and parasite population dynamics, quantitatively and qualitatively [26–28]. Importantly, the magnitude and direction of these effects can depend on the specific nature of the co-infection [29]. Work in wood mice (*Apodemus sylvaticus*) found a strong negative WH interaction between co-infecting nematodes (*Heligmosomoides polygyrus*) and coccidians (*Eimeria hungaryensis*) [30]. However, analysing population-level patterns of association between these two parasites revealed no signal of the interaction; instead, infection levels of the two parasites were positively correlated across hosts [31]. This likely arises from correlated exposure due to their shared transmission route (faecal–oral), swamping the signal of the WH interaction. Hence, population-level patterns of parasite co-circulation may poorly reflect the occurrence or direction of WH interactions [32]. Only when data were examined at local spatial scales around co-infected hosts did the negative WH effect become apparent [33]. Further empirical evidence of conflicting relationships between scales was found in African buffalo (*Syncerus caffer*) infected with bovine tuberculosis (bTB). bTB increased individual susceptibility to brucellosis (*Brucella* sp.), but given a concomitant increase in mortality among co-infected individuals, models predicted that the presence of brucellosis should reduce the prevalence of bTB at the population level [34]. These examples demonstrate how designing experiments and combining approaches which are explicitly multiscale in scope leads to a fuller understanding of host–parasite dynamics, and is necessary to properly investigate hypothesised parasite interactions. Research that focuses strictly on one level of interaction may erroneously attribute observed phenomena to interactions at that level, thus leading to flawed interpretations of the dynamics and consequences of co-circulating parasites (see also Box 2).

When two or more parasites are present, interdependence between co-circulation and co-infection interactions may generate complex and nonlinear fitness landscapes [28,29]. Interactions

Box 2. Application of our framework to spider mites (*Tetranychus* spp.)

Spider mites are ectoparasites that feed on several plant species, causing damage to agricultural and natural ecosystems. Within this group, *Tetranychus urticae* (a generalist) co-circulates in the Mediterranean region with several other spider mite species [61], including *T. evansi* (a specialist on plants of the family *Solanaceae*) [62]. Spider mites are easy to manipulate in controlled conditions (Figure I), making them an ideal system for the application of our framework.

In laboratory experiments, *T. evansi* suppresses the defences of the tomato plant (*Solanum lycopersicum*) [63], facilitating infection by *T. urticae* [64], (Table 1, WH2). However, on whole plants, *T. urticae* is generally excluded, unless it arrives first [65], possibly because *T. evansi* webs prevent *T. urticae* from accessing leaves [66]. This exclusion could have population-level consequences if *T. evansi* infection prevents *T. urticae* from accessing immunocompromised plants (Table 1, BH5). Thus, we might conclude that *T. evansi* is a better competitor, and should always exclude *T. urticae*. However, results from a field work study only partially corroborate this: during 10 years of co-circulation in eastern Spain, *T. evansi* tended to displace *T. urticae* from non-crop plants but did not completely exclude them; both mites still occurred in co-infection (on 4.2% of sampled plants) [67].

Applying our conceptual framework can provide further insights and reconcile these experimental and large-scale patterns. For instance, in laboratory settings, the presence of *T. evansi* increases the rate at which *T. urticae* infects new leaf discs [68] (*e.g.*, contact rate). This could facilitate its spread to new hosts (Table 1, BH1) while avoiding or reducing WH competition. Interestingly, lima bean plants (*Phaseolus lunatus*) infected with *T. urticae* emit volatile compounds that trigger immune-related responses in unexposed neighbouring plants, thus increasing defences against further conspecific infections [69] (Table 1, BH3). Although lima bean is not a suitable host for *T. evansi*, the shared tomato host emits similar volatiles upon infection [70], which could be further investigated following infection with both spider mite species.

These WH and BH interactions highlight that this is a fertile system for exploring how interaction mechanisms at different scales contribute to parasite epidemiology (Figure I). It nicely illustrates how neglecting one level could produce an incomplete depiction of actual infection dynamics, or even erroneous interpretations (exclusion vs. coexistence). The full picture requires both levels to be considered, alongside factors such as parasite genetic background, multi-host communities, environmental conditions, and evolution.

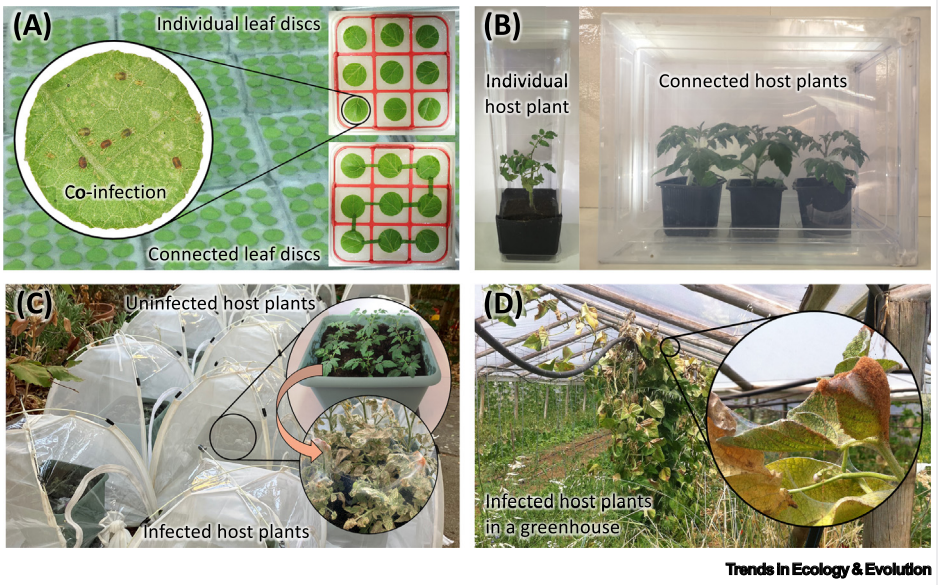


Figure I. Spider mite parasite system across scales. Illustrative pictures of how spider mite co-infections and co-circulation can be studied at WH and BH levels in laboratory settings on (A) leaf discs and (B) entire plants, in (C) semi-field, and (D) field conditions. Photo credits: (A, B, D) Flore Zélé (author); (C) Alison Duncan (author). All photos used with permission.

that change population-level prevalence or mean parasite abundance will quantitatively affect the overall **force of infection**, and therefore the risk and implications of (co-)infection for individual hosts [28,29]. Bidirectional cross-scale effects may occur across various parasite systems

whenever co-infection interactions shape population-level transmission dynamics, and co-circulation interactions, in turn, shape co-infection risk. This type of feedback has potential consequences for disease control and evolutionary dynamics. Transmission reduction or eradication of a focal parasite may unintentionally remove constraints on a background parasite, a notorious example being pneumococcal serotype replacement post-vaccination, in which the prevalence of target serotypes decreases but that of non-target serotypes increases [35]. To understand the outcomes of such multilevel interactions will therefore require dynamic frameworks, either in the form of individual-based models with explicit interactions [36], mathematical models along the lines of the 'essentially nested' models [37], or co-infection-replicator systems with mechanistic fitness [28,29]. This should be informed and tested, whenever possible, by field data and experimental systems.

Concluding remarks and future perspectives

Given the range of possible interactions between parasites and the complex nature of their emergent multiscale effects, mathematical models play a vital role in studying their occurrence and consequences. Existing models of co-circulating parasites with and without co-infection provide a well-developed theoretical foundation to build upon [29,38]. Such models are generally restricted to microparasites (*e.g.*, viruses, bacteria) or different parasite strains, with direct (contact) transmission and SI-type dynamics, including their extension to include recovery and/or reinfection. There is clear potential to broaden the scope of these models to include different host traits (resistance, tolerance, dispersal) and parasite types (micro- and macroparasites, parasites with different transmission modes) [39], revealing generalities and/or specificities of any conclusions, and advancing our understanding of host–parasite dynamics and their predictability [28,40]. For example, macroparasite-specific models generally extend SI theory, in which infection status is binary, to explicitly incorporate parasite load [41], thus allowing transmission, mortality, *etc.* to be load-dependent. Interactions among parasites may themselves be load-dependent, perhaps via increased parasite–parasite encounter rates or host behavioural modification at high loads, leading to complexities only captured by such models. Simple predictions could also be obtained by considering whether co-infecting parasites have aligned interests, especially when sharing a transmission route [42]. Apart from the recognised conflict between horizontal and vertical transmission strategies (the latter better matches host interests as it exploits host fecundity [43]), parasites with complex life cycles also illustrate such conflicts [44]. For parasites co-infecting the same intermediate host but having different definitive hosts (e.g., fish vs. bird), there will be a strong selective pressure to reach the 'correct' host and avoid a dead-end route, no matter the interests of the other parasites.

Our framework has been developed with a single host species in mind. However, the concepts have important implications for multi-host systems too, particularly in the context of biological invasions and disease management with spillover and spillback among host species [25]. In such a context, parasite–parasite interactions like those already discussed may occur in both host species, but with the added complication of how the background parasite affects interspecies transmission of the focal parasite. For instance, if a background parasite reduces the density of optimal hosts for the focal parasite, the focal may switch onto alternative, sub-optimal hosts [45]. A related process is apparent competition, in which one parasite suppresses a dominant host species, thereby allowing a less competitive host to persist. In such cases, specialised parasites that depend exclusively on the subdominant host may, in effect, rely on the presence of the first parasite in order to persist. The consequences of such interactions will be complex, depending on the precise relationships between the multiple host and parasite species.

The framework may also be applied to multi-parasite communities (*i.e.*, those with more than two parasites, see Box 2). Using time–series data in natural populations can allow the building of a

Outstanding questions

How do parasite interactions at the host individual and population scales affect one another?

What are the consequences of cross-scale interactions for parasite coexistence, host population dynamics, and individual host infection risk and health?

How can we differentiate between co-infection and co-circulation interactions in real-world systems?

What is the relative importance of WH and BH interactions in explaining epidemiological dynamics?

How can we better evaluate outcomes of potential disease management strategies and improve predictability in multi-parasite systems?

How can we best integrate theory, field and experimental data on parasite interactions? Which empirical results require new or adapted theory to help explain them, and which theories have not yet been sufficiently tested empirically?

Do interactions occurring at both scales affect basic theoretical predictions?

How do parasite interactions shift along environmental or ecological gradients?

Can other biotic and abiotic factors modify transmission opportunities and epidemiological dynamics for co-circulating and co-infecting parasites?

Some pathways of interaction between parasites predicted by our framework are yet to receive much consideration; are they rare or simply overlooked?

complete web of parasite interactions within the community for different transmission components, such as susceptibility [46]. As suggested by our framework, this requires, as a first step, considering all possible combinations of focal and background parasites, and precise knowledge on all pairwise WH and BH interactions with their direction and magnitude. However, multiple background parasites result in correspondingly more possible interactions with the focal; these interactions may be enhanced or confounded by interactions between background parasites. Furthermore, introducing a third parasite could feasibly result in interactions between parasites that were previously unaffected by one another (*i.e.*, high-order interactions). Thus, simply including additional background parasites in an additive manner may not fully reflect the true nature of the composite web of interactions [46].

Multiscale parasite–parasite interactions also have evolutionary implications [47]. For instance, if a background parasite increases the fecundity (Table 1, BH4) or mortality (Table 1, BH5) of a suitable host, these changes in host availability could, in turn, affect patterns of local adaptation of a focal parasite. At the same time, interactions increasing the probability of co-infection, such as a background parasite making a host more attractive to a focal parasite (Table 1, WH3), may make (co)evolution in co-infections more likely, with consequences for virulence and transmission [48].

In conclusion, multiparasite systems cannot be fully understood without taking into account interactions among parasites at both the individual and population levels. To achieve this will require multiscale experimental design, with data collected at both levels and across temporal scales, in conjunction with carefully designed statistical and mathematical models. Our framework should therefore be employed to (i) inform methodological approaches that incorporate the different levels and types of parasite–parasite interaction, and (ii) interpret the resulting data. Cross-disciplinary approaches among ecologists, epidemiologists, and evolutionary biologists – including sampling natural populations together with controlled eco-evolutionary (e.g., mesocosm) experiments – will help to generate new research questions and refine predictions (see Outstanding questions). This will advance our knowledge of host–parasite interactions across scales and their consequences for the parasites involved, and their hosts.

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Declaration of interests

No interests are declared.

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