

Speciation in parasites: a population genetics approach

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Parasite speciation and host–parasite coevolution should be studied at both macroevolutionary and microevolutionary levels. Studies on a macroevolutionary scale provide an essential framework for understanding the origins of parasite lineages and the patterns of diversification. However, because coevolutionary interactions can be highly divergent across time and space, it is important to quantify and compare the phylogeographic variation in both the host and the parasite throughout their geographical range. Furthermore, to evaluate demographic parameters that are relevant to population genetics structure, such as effective population size and parasite transmission, parasite populations must be studied using neutral genetic markers. Previous emphasis on larger-scale studies means that the connection between microevolutionary and macroevolutionary events is poorly explored. In this article, we focus on the spatial fragmentation of parasites and the population genetics processes behind their diversification in an effort to bridge the micro- and macro-scales.

Species and speciation

Understanding the general patterns and processes of speciation is fundamental to explaining the diversity of life. Parasites represent ideal models for studying speciation processes because they have a high potential for diversification and specialization, and some groups live in conditions that are ripe for sympatric speciation (see Glossary). The host represents a rapidly changing environment and a breeding site, which makes the number of diversifying factors potentially larger for parasitic than for free-living organisms [1]. However, parasites are almost totally ignored in the general evolutionary literature on speciation processes. Even in the parasitology literature, fundamental studies of parasite speciation are scarce (reviewed in [2–4]). Most parasite-population studies concern parasites of humans and domestic animals, and studies on natural, undisturbed populations are needed [3]. Because ecological factors that shape microevolutionary patterns might also reinforce long-term macroevolutionary trends [2,5,6], we focus on parasite life histories, and parasite population

dynamics and their influence on population genetics. The first step toward identifying the evolutionary processes that promote parasite speciation is to compare existing studies on parasite populations. Crucial, and novel, to this approach is consideration of the various processes that function on each parasite population level separately (from intrapopulation to metapopulation). Patterns of genetic differentiation over small spatial scales provide information about the mode of parasite dispersal and their evolutionary dynamics. Parasite population parameters inform us about the evolutionary potential of parasites, which affects macroevolutionary events. For example, small effective population size (N_e) and vertical transmission can initiate founder-event speciation, whereas natural selection can cause either adaptive or ecological speciation in parasite species with a large N_e (transience versus divergence speciation [7], see later). In 1995, Nadler [2] considered the various microevolutionary processes that structure parasite populations and summarized all the empirical evidence available at the time. Subsequently, the wider use of molecular techniques has achieved major advances and prompted a new synthesis.

Glossary

Adaptive radiation: the evolution of ecological and phenotypic diversity within a rapidly multiplying lineage.

Allopatric speciation: the formation of new species following either the geographical or the physical separation of populations of the ancestral species. In the case of parasites, allopatric speciation includes speciation following host-switching and parasite speciation following host speciation.

Deme: a randomly mating population that is isolated from other such populations. Depending on the parasite species, this is not always the same as the intrapopulation.

Ecological speciation: the evolution of reproductive isolation caused by divergent natural selection in different environments (e.g. different hosts or different niche on host).

F_{st} : fixation index that describes the distribution of genetic variation among populations (generally known as F -statistics).

Intrapopulation: all individuals of one parasite species that occur either in or on the same host individual.

Metapopulation: assemblage of populations in a larger area, among which migration of individuals can occur.

Reconciliation analyses: a method to compare and reconcile the phylogenies of hosts and their parasites to determine which evolutionary events (extinction, intra-host speciation and host-switching) explain any incongruence between them.

Sympatric speciation: the formation of new species in the absence of either a geographical or a physical barrier that isolates populations of the ancestral species. For parasites, sympatric speciation can occur on the same host species, in which case it is synonymous with intra-host speciation, synxenic speciation and parasite duplication.

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Here, we concentrate on metazoan parasites and our review of the recent literature also serves as a basis to formulate appropriate frameworks for future studies.

Special features of parasites

Parasitism is one of most successful modes of life, measured by the number of times it has evolved independently and the diversity of extant parasite species [8]. Practically every animal species is infected by at least one parasite species and, even without strict host specificity, there are at least as many (and possibly more) parasitic than free-living species. According to Price [9] the most extraordinary adaptive radiations have been among parasitic organisms, and he was one of the first to stress the need for studies on their evolutionary biology. Although other authors agree [1,10], relatively few have taken advantage of this purported opportunity. However, an increased interest for host–parasite cospeciation studies has paralleled the development of software programs for testing cospeciation [11].

Parasites represent a diverse group of biologically different organisms that are united only by their common lifestyle, which is spent either in or on the host, feeding on the tissues of the latter and causing it harm. Generally, parasites differ from free-living animals in their more-specialized feeding behaviour and intimate host associations. Although some features that are considered unique to parasites are also present in other small, specialized animals, we can identify some general characteristics: (i) hermaphroditic, parthenogenetic and asexual reproduction are common; (ii) the generation time is usually short; and (iii) parasite populations are highly fragmented, with many populations also experiencing strong seasonal fluctuations in size. These features will influence the N_e , evolutionary rate and other population genetics parameters which, in turn, affect microevolutionary and macroevolutionary processes (see later and Box 1).

The strong potential for diversification can also be ascribed partly to more frequent opportunities for sympatric speciation in parasites than in free-living organisms [1,9,10,12,13]. These might result from narrow habitat selection either within or between host species [14]. Furthermore, many host–parasite relationships might evolve according to coevolutionary arms races, which fuel speciation as predicted by Thompson and Cunningham [15] and by the models of Kawecki [16]. Ecological specialization can lead to speciation if certain conditions are fulfilled, and pea aphids are a well-known example of this [17]. However, Kawecki shows that genetic trade-offs for performance on different host species are not necessary in the case of coevolutionary interactions between a host and a specialized parasite species. Another modelling approach [18] confirms that parasites have the characteristics required for the evolution and maintenance of adaptive diversity, with especially strong specialization and diversification expected in parasites with direct life cycles that spend several generations on the same host individual (such as pinworms and lice). Indeed, examples of ecological speciation in animal parasites such as the blood fluke *Schistosoma* [13] are available, but controlled, comparative experiments are needed.

Box 1. Population genetics factors

Speciation in parasites can be accelerated by coevolutionary arms races [15,16] and by adaptive radiations, such as after host switching [49]. However, speciation might also be triggered by non-adaptive processes, depending on N_e (see below). Although the overall population can be extremely large, aggregated distribution in the host population might make infrapopulations too small to minimize the role of genetic drift compared with gene flow and/or natural selection. Wahlund effects can occur (subdivided populations that contain fewer heterozygotes than predicted) [50], whereas colonization of a new host individual and seasonal change in prevalence can cause systematic founder events. This might stimulate speciation by drift, which is described as the transience speciation concept by Templeton [7], but its role in speciation is still debated (peak shift models are reviewed in [51]).

For a neutral allele, the probability of fixation (P) in a deme increases as N_e decreases, roughly following Equation I [52]:

$$P = 1/2N_e \quad (I)$$

but

$$N_e = 4FM/F + M \quad (II)$$

(F =number of females; M =number of males) [53].

N_e decreases as the skew in the sex ratio increases, following Equation II. Thus, if two males mate with 50 females, $N_e \approx 8$. Also, asexuality reduces N_e because of the increased linkage of the genome [54]. N_e is expected to be decreased further by the aggregated transmission of infective stages, and when the contribution of infrapopulations is disproportionate to their effective size [55]. Criscione and Blouin have developed a conceptual framework using a subdivided-breeders model to estimate N_e . A recent model [56] highlights the impact of variance in the clonal reproductive success of trematode larvae and the rate of adult selfing on N_e . Previously, this first parameter has been overlooked in population genetics models and shows that, in general, parasitic life cycles are unlike those used in classical models.

Many parasite species also have a shorter generation time than their host, which results in a faster turnover (either per year or per host generation) of either neutral or slightly deleterious alleles. The average conditional fixation time (t) of a selectively neutral allele depends on N , the population size [57], as shown by Equation III:

$$(t) = 4N \text{ generations} \quad (III)$$

The average fixation time for a neutral mutation in an organism with a generation time of a month and a population size of 40 (and $N \approx N_e$) is ~ 13 years. Thus, the genetic composition can change rapidly in small populations, which enables speciation by peak shifts to occur. However, mutations that are selectively advantageous will be lost through drift, and their probability of fixation will increase as N_e increases (see also Refs [2,4]).

Do parasites have a higher evolutionary potential than free-living species?

It has been demonstrated that endosymbiotic bacteria and fungi have higher rates of molecular-sequence evolution than closely related, free-living lineages [19]. The combination of population fragmentation, extinction and recolonization patterns, regular bottlenecks, and asexual reproduction reduces the N_e and should lead to an increased rate of fixation of nearly neutral and slightly deleterious mutations. As discussed previously, many parasite species have these characteristics so the genetic composition can change rapidly in small populations (Box 1). Several cophylogenetic studies show a higher rate of sequence evolution for the parasite than the host [20–23]. In case of the chewing lice, this is linked to frequent founder events because of the small population

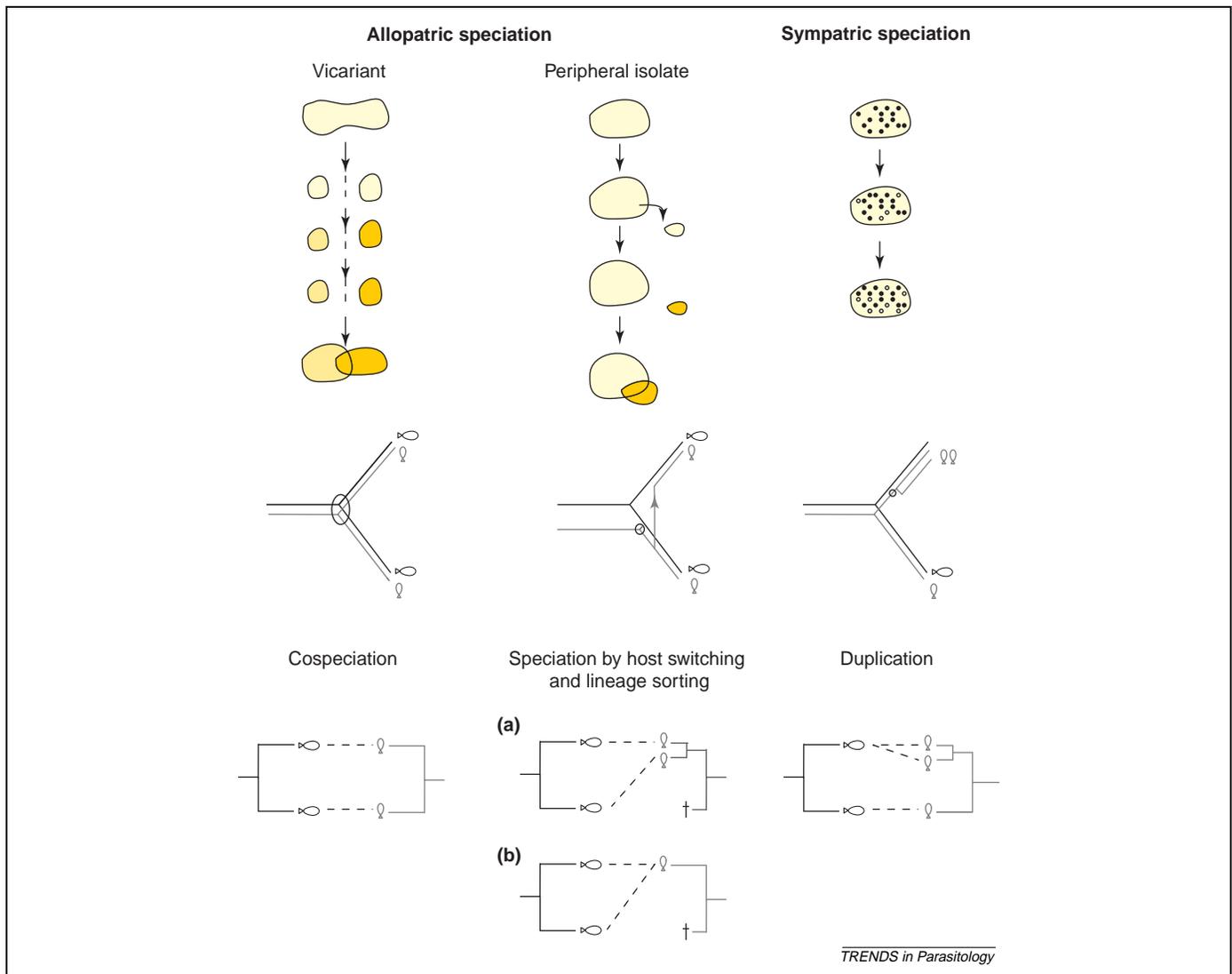


Figure 1. The geography of speciation and the major speciation modes and their phylogenetic correlates applied to parasites (by analogy to [47]). An ancestral parasite species can be subdivided geographically together with its ancestral host species (vicariance). Although repeated speciation of both host and parasite results in mirror-image phylogenies (vicariant allopatric cospeciation), two other possibilities exist (see main text). **(a,b)** Host-switching involves the movement of a small subset of a species into a new geographical area. This can be followed by speciation through a peripheral-isolates mode (a) or the new host will be added to the species range of the parasite (b). In free-living organisms, the reduction in gene flow depends on their dispersal capabilities and the magnitude of the geographical barrier, whereas, in parasites, the magnitude of gene flow depends on the transmission mode and dispersal capabilities of the parasite and the degree of sympatry between the old and the new host species. Finally, sympatric speciation occurs when species arise in the absence of a physical barrier. Brooks and McLennan [47] define sympatric speciation as speciation on the same host species, which is equivalent to synxenic speciation defined by Combes [36]. Other frequently used terms in coevolutionary studies are intra-host speciation and parasite duplication [11]. Here, we define speciation by host-switching as allopatric speciation but, depending on the parasites involved, this might also be a form of sympatric speciation when infective, free-living stages of both host-adapted populations are in syntopy. (For a more thorough discussion, see Ref. [14].) It is important to establish whether intrinsic mechanisms (evolved in the parasite) or extrinsic barriers to gene flow are involved. However, as indicated by Le Gac and Giraud [48], the study of speciation modes might benefit from including the mechanisms that prevent gene flow, rather than geography alone.

size and vertical transmission between their pocket gopher hosts [21]. Another correlation between an increased evolutionary rate and the transition to parasitism has been described for parasitic wasps [24]. Again, the authors associate the parasitic lifestyle with an increased frequency of founder events and an increased selection pressure fuelled by coevolutionary arms races.

Macroevolution: the geography of parasite speciation

Phylogenetic trees provide an indirect record of the speciation events that led to present-day species. By constructing species-level phylogenies and comparing the geographical distribution of sister taxa, the relative contribution of the different speciation modes can be inferred (reviewed in [25]). The main problem with this

approach is that the current distribution of a species is not necessarily a reliable indicator of its historical geographical range because the geographical range of a species evolves and can change considerably over short time periods (e.g. post-glacial expansion induced by the Quaternary Ice Ages). Therefore, it is possible that inter-specific phylogenies cannot rigorously test alternative hypotheses concerning the geography of speciation [26].

Because the host constitutes the principal environment of a parasite, the geography of speciation might be inferred more readily in host–parasite systems. Tracking the evolutionary path of the host seems to be more clear-cut than tracking an entire ecosystem for a free-living species [22]. Several statistical methods can reconstruct the ancestral host by reconciling the

phylogenetic trees of host and parasite [11,22]. However, results of reconciliation analyses should be interpreted with caution. Frequent host-switching can both obscure and mimic phylogenetic congruence [27,28]. Absolute or relative timing of host and parasite trees can assess the possibility of synchronous speciation and, similarly, branch lengths can be taken into account in the latest version of TreeMap (<http://taxonomy.zoology.gla.ac.uk/~mac/treemap/>). Nevertheless, it is difficult to discriminate between some scenarios. For example, two parasite sister taxa found on a single host species can arise by either sympatric speciation or allopatric speciation in geographically isolated host populations followed by secondary contact. However, different solutions can be tested statistically because gene trees are amenable to mathematical modeling, and the multitude of methods available provides additional tests. Also, life-history information about the host and parasite (such as distribution range and parasite-dispersing capability) can be taken into account to choose among the optimal solutions obtained by TreeMap 2.

Generally, the speciation modes are classified according to either the geographic scale at which they occur [29] or the population genetics events underlying them [7]. Figure 1 reflects the first view, although we stress that population genetics parameters must also be included (Box 1). The figure shows the influence of the different parasite-speciation modes on the phylogenetic branching pattern, and, thus, on the degree of congruence between host and parasite phylogenies. In addition to speciation by host-switching, sorting and duplication events also produce incongruent patterns. In most associations studied to date, phylogenetic congruence is either imperfect or absent; most associations represent a combination of cospeciation and host-switching [27,28,30,31]. These macro-evolutionary trends are influenced by the life-history features of both host and parasite, such as host specificity and mobility [5,6,32]. Examples of strict cospeciation occur in systems in which host-switching is prevented by the asocial lifestyle of the host and the low mobility of the parasite. Examples include the rodent (lice) [30,33], and insect-symbiont associations where the bacteria that are needed for host reproduction are transmitted maternally [34].

Cospeciation has been studied mainly at the macro-evolutionary level but this process is also observed at the population level. Rannala and Michalakis [35] studied the effect of population-level processes on patterns of cospeciation using the coalescent theory of population genetics. Demographic parameters such as N_e and transmission rate heavily influence both the occurrence and the probability of detecting cospeciation (i.e. identical host and parasite gene trees). Again, this shows that ecology has an important role in speciation processes, and stresses the need for complementary information on basic demographic parameters for both parasite and host.

Microevolution: fragmentation of parasite populations

The fragmented nature of parasite populations can be observed on many levels. Combes [36] distinguishes

fragmentation along three scales: space; host species; and host individual. Further subdivision includes the various intermediate and paratenic host species that are used by many parasites, their aggregated distribution in the host population and the site specificity. This fragmentation greatly complicates the ecological genetics of parasites. In particular, the influence of gene flow, genetic drift and natural selection differs between levels. Therefore, we focus on the infrapopulation and metapopulation levels, predict which host and parasite traits influence genetic diversity, gene flow and population structure at each of these levels (Figure 2), and compare this with empirical data from the literature (Boxes 2 and 3) to review current population genetics studies in parasites. Principally, we consider spatial fragmentation of the adult parasites.

Infrapopulation level: effective population size and mating system

An important component of speciation theory is the deme concept [29] because this is the unit on which either selection or drift operates. Demes are random mating populations, so when applied to parasites this denotes the adult ('sexually' reproducing) parasites that usually inhabit an individual host organism (the infrapopulation). However, the infrapopulation on one host can either comprise several demes at different sites on the host individual or it can be part of a deme when gene flow between host individuals is high [4]. Demes are affected by inbreeding, mortality and immigration from other demes. The relative influence of natural selection and genetic

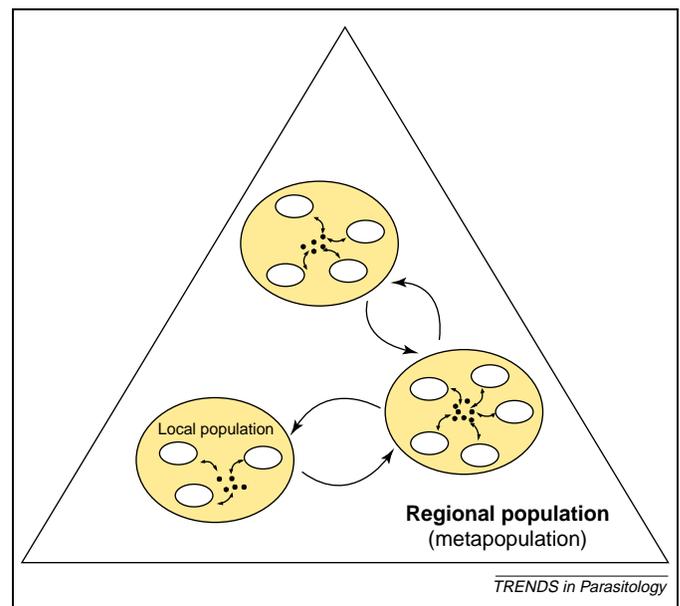


Figure 2. Simplified representation of parasite populations that are fragmented at the host level (infrapopulation – small white circles) and the spatial level (local population at regional scale – large yellow circles). The hypothetical parasite has a direct life cycle (no intermediate hosts), with infective stages (black dots) leaving infrapopulations to be recruited in others. In intestinal helminths, for example, parasite eggs released in the faeces of one host individual will subsequently join infrapopulations in other host individuals. Note that, if all populations are connected by arrows (parasite gene flow), the population structure equals panmixia, with random mating between all individuals. In this case, the regional population (metapopulation) rather than the local population is the unit of evolution. The other extreme is completely isolated local populations, which all evolve independently.

Table 1. Ecological and natural-history factors that might influence the population genetics structure of parasites^a

Factors that increase genetic structure	Factors that decrease genetic structure
Immobile or asocial hosts	Highly mobile hosts (definitive, intermediate and paratenic) or vectors
Unstable heterogeneous external environment	Stable, homogeneous, external environment
Complex life cycle with many specific, obligate hosts	Persistent (long-lived) life-cycle stages in environment or definitive host
Suitable parasite niches patchily distributed in space or time	Uniform availability of parasite niches in space and time
Small effective parasite population size	Large effective population size
Highly aggregated distribution among hosts	Uniform distribution of parasites among hosts
Parasite is predominantly self-fertilizing	Parasite predominantly outcrossing
Frequent population extinction followed by reestablishment	Stable populations with rare extinctions
Equilibrium between migration and natural selection	Non-equilibrium between migration and natural selection
Short generation time (non-coding DNA)	Long generation time
High host specificity	Low host specificity and/or many reservoir hosts
Host-to-host transfer or host-mediated dispersal (vertical transmission)	High parasite mobility (horizontal transmission)

^aModified from Ref. [2].

drift depends on the parasite N_e , gene flow and mating system (Box 1). Therefore, factors that influence inbreeding, gene flow and N_e must be evaluated to predict the deme structure (Table 1).

Box 2. Factors influencing the genetic structure of infrapopulations

Typically, the F_{st} index is used to describe population differentiation. However, interpreting F_{st} among parasite infrapopulations is difficult because it is influenced by factors such as drift, inbreeding and gene flow. Nevertheless, here are some examples:

(i) Infrapopulation size: the two nematodes *Ascaris suum* and *Ostertagia ostertagi* have similar life cycles, infect livestock and are obligately outcrossing. Infrapopulation sizes in *A. suum* are smaller (a few dozen per host) than in *O. ostertagi* (thousands per host) and, thus, are more susceptible to genetic drift. This results in stronger population subdivision than in *O. ostertagi* [2]. The large N_e is assumed to be the main factor behind the unusually high within-population diversities observed for trichostrongylid nematodes [58].

(ii) Reproduction mode: outcrossing trichostrongylid nematodes have large N_e , which results in high within-population diversity. By contrast, hermaphroditic juveniles of *Heterorhabditis marelatus* produce clumped patches of offspring that mate and leave the insect host. As a consequence, infrapopulations originate from a few maternal founders, which results in extremely low N_e and low within-population diversity [59]. Parasitic nematodes of plants have a mainly parthenogenetic mode of reproduction and much lower overall mitochondrial DNA diversity than either *Ascaris suum* or trichostrongylids [59]. In mixed-mating systems the frequency of selfing can depend on the number and size of other individuals in the infrapopulation (e.g. cestodes, [60]). Self-fertilization in *Echinococcus granulosus* results in infrapopulations with substantial heterozygote deficiencies [61]. Asexual amplification of *Schistosoma mansoni* in intermediate hosts (snails) has little effect on the overall genetic diversity that characterizes adult infrapopulations in the vertebrate hosts (*Rattus rattus*) [62] but slightly increases the genetic differentiation between infrapopulations at the local scale [63]. The presence of a second intermediate host in the life cycle can serve to assemble packets of metacercariae representing many different clones, thus, ensuring genetically diverse infrapopulations of adult worms in the definitive host [64]. By contrast, with the digenean *Fascioloides magna*, the persistence of aggregated encysted metacercariae of the same clone in the environment, is responsible for the presence of identical multilocus genotypes within hosts and a strong genetic differentiation between infrapopulations [65].

(iii) Premunition: in schistosomes, premunition (immunological cross-reaction stimulated by resident adult schistosomes against incoming larval parasites) was thought to restrict the genetic composition of the deme to the initial colonizers [2]. However, concomitant immunity might operate in a genotype-specific manner, which selects for more genetic heterogeneity in male than female schistosomes, and contributes to a sex-specific genetic structure with evolutionary implications [66].

Demes, or infrapopulations, of parasites are usually short-lived and survive no longer than an individual host. New demes are formed continuously in new hosts from subsets of parasite larval stages drawn from the population gene pool. Only a few parasite taxa, in which offspring re-infect the same, long-lived, hosts as their parents over several generations, have demes that are somewhat permanent over time. Establishing the deme structure helps to predict the speciation mode. As discussed in Box 1, deme size is an important factor in determining whether speciation evolves by selection or drift. For example, small, isolated demes of parasites with a direct life cycle are more likely to show population genetics patterns similar to that of their host resulting in host-parasite cospeciation at the macroevolutionary scale than demes enlarged by immigrants from other hosts (Box 2).

Metapopulation level: host and parasite mobility

At this level we assess how differences arise between parasite populations from various localities. Local adaptation is an important step towards speciation that is influenced by the interaction between gene flow and natural selection. If N_e is extremely small, genetic drift will swamp local adaptation. Simulation studies [37,38] highlight the importance of host and parasite dispersal and infrapopulation processes. Higher parasite migration relative to host migration is predicted to increase the local adaptation of the parasite [38]. Thus, gene flow and N_e are the main players at this level. Gene flow is influenced by several characteristics of the parasite, the host and the habitat (Box 3 and Table 1), and some factors also correlate (e.g. life cycle pattern and parasite mobility). Because these factors are species-specific, patterns in different parasite groups vary accordingly.

Concluding remarks

We have shown that parasite population ecology and population genetics are linked tightly. More specifically, we argue that the structure of parasite populations correlates with (i) host mobility, (ii) mode of reproduction of the parasite, (iii) complexity of the parasite life cycle, (iv) parasite infrapopulation size and (v) host specificity. The importance of these factors varies from one parasite species to the next. Therefore, a comparative approach with a phylogenetic perspective is crucial to disentangle the various processes that drive parasite diversification.

Box 3. The importance of mobility in the host and parasite, and the parasite life cycle

Studies of coevolution in local populations are insufficient; understanding the coevolutionary dynamics of interactions requires a geographic view [67]. The process of coevolution depends on the subdivision of populations into demes, geographic differences in outcome, adaptation, specialization and the combined effects of drift, gene flow and extinction. Thus, important factors are:

(i) Host movement: in trichostrongylids movement of the host influences parasite gene flow. Parasites of wild hosts display higher differentiation than those of domestic ruminants [58,59]. Host-dependent gene flow between parasite populations has also been demonstrated for bird-tick systems [68]. Dispersal of *S. mansoni* seemed to be determined mainly by definitive host dispersal [62,69]. However, parasite genetic differentiation is twice that of the definitive hosts, which indicates that rat migration might correlate negatively with the age or the infection status of the host. Of four freshwater digenean species in salmon, three digeneans cycle exclusively in aquatic hosts and are more genetically subdivided than the fourth species from the same location but whose life cycle includes highly mobile terrestrial hosts [70]. Extensive host movement might overcome the effect of selfing in *E. granulosus*, resulting in high within-population and low between population differentiation [61].

(ii) Biological traits of host and parasite: pocket gopher hosts are asocial, and their chewing lice spend their entire life on the host and are transmitted strictly by contact. Therefore, seasonal bottlenecks in population size occur. As a consequence, parasite population differentiation is almost identical to that of the host. This micro-geographic pattern is apparent at the macro-level in mirror-image phylogenies for hosts and parasites [30]. In this case, host-gene flow seems to be the upper boundary for parasite-gene flow. Comparing four louse–host associations [6] indicates that dispersal is a more fundamental barrier to host-switching than establishment. Dispersal in itself depends on the ecology and behaviour of the lice, and the ability to hitch a ride on species such as flies [32].

(iii) Host specificity: avian body lice (genus *Physoconelloides*) are more host-specific than wing lice (genus *Columbicola*) and show more population genetics structure and cospeciation with the host [5]. Host-race formation has also been described for the tick *Ixodes uriae* of sympatric seabird species [68].

(iv) Abiotic factors: during the dry season, relatively more schistosome infrapopulation pairs are genetically differentiated than during the rainy season. The restricted displacement of rats, patchy spatial aggregation of infected snails and limited cercarial dispersion in standing water are thought to be responsible for this [62].

For metazoan parasites we propose an approach that is similar to that used by Burdon and Thrall [39] with plant pathogens, which monitors the genetic structure of host and pathogens at the various spatial (and temporal) scales. Such studies are challenging but feasible, and can be combined with simulation models [37,38,40] and experimental studies [41] to provide the best way forward in this field. Ideally, this approach will be complemented by experiments to elucidate whether and how reproductive isolation is achieved; at present, there are few such studies.

The importance of including demographic parameters in pathogen speciation studies is recognized increasingly, mainly in the fields of epidemiology [42] and plant pathology [43]. This new combination has been coined ‘evolutionary epidemiology’ [42] and ‘phylogenetics’ [44]. The latter term denotes the melding of immunodynamics, epidemiology and evolutionary biology. According to these authors, ‘a key priority for infectious disease research is to clarify how pathogen genetic variation, modulated by host immunity, transmission bottlenecks, and epidemic

dynamics, determines the wide variety of pathogen phylogenies observed at scales that range from individual host to population’.

As stated by McDonald and Linde [42], the evolutionary potential of pathogens is reflected in their population genetics structure. According to their framework, pathogens with a mixed reproduction system, a high potential for gene flow, large N_e and high mutation rates pose the highest risk of breaking down resistance genes. They also found that life-history traits of the pathogen (in particular the potential for long-distance migration) predict the evolution of fungicide resistance better than chemical characteristics (B.A. McDonald, personal communication). Thus, although phylogenetic and cospeciation studies are necessary to investigate the origin and evolution of pathogen species [45], population genetics studies are needed to document the evolutionary origin of drug resistance in pathogens [46] and to study the effect of disease management on the evolution of parasite populations. Ultimately, this will enable prediction of the factors that govern the evolution of parasite populations, which is crucial for parasite-control programs.

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