bioRxiv preprint doi: https://doi.org/10.1101/2021.11.27.470149; this version posted November 28, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Effect of host-switching on the eco-evolutionary patterns of parasites

[1*]Elvira D'Bastiani, [2]Débora Princepe, [1,3]Karla M Campião, [2]Flavia MD Marquitti, [1,3]Walter A Boeger, [1,4]Sabrina LB Araujo

[1,3,4]Laboratório de Interações Biológicas, Universidade Federal do Paraná, UFPR

[3]Departamento de Zoologia, Universidade Federal do Paraná, UFPR

[2]Departamento de Física, Universidade Estadual de Campinas, UNICAMP

[4]Departamento de Física, Universidade Federal do Paraná, UFPR

***Corresponding author**: Elvira D'Bastiani e-mail: elviradbastiani@gmail.com

Authorship statement:

Conceived and designed the experiments: EDB, SBLA and DP

Performed the experiments and analysed the data: EDB, SBLA and DP

Wrote the paper: EDB, SLB, KMC, DP, WB, FMDM

Other contributions: EDB, DP, FMDM, WB, KMC and SLBA

Emails:

Elvira D'Bastiani <elviradbastiani@gmail.com>

Débora Princepe <deborapr@gmail.com>

Karla M. Campião <kcampiao@gmail.com>

Flavia MD Marquitti <flamarquitti@gmail.com>

Walter A Boeger <wboeger@gmail.com>

Sabrina LB Araujo <araujosbl@gmail.com>

bioRxiv preprint doi: https://doi.org/10.1101/2021.11.27.470149; this version posted November 28, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

ABSTRACT

Increasing empirical evidence has revealed that host-switching is more common than cospeciation in the history of parasites. Here, we investigated how the intensity of host-switching, mediated by opportunity and compatibility, affects the phylogenetic history and ecology of the parasites. We developed a theoretical model to simulate the evolution of populations of parasites that can explore and colonize new hosts under variable host-switching intensities. Eco-evolutionary patterns (beta diversity/normalized Sackin index) obtained from parasite simulations were compared to nine empirical cases. Our model reproduced the empirical patterns, and such simulations varied in host-switching intensity according to the analysed case. This intensity does not differ among cases of ecto and endoparasites, but it was stronger in local cases when compared to a regional scale. Our results highlight the importance of contact opportunity, and suggest that host-switching intensity mediates the exploration and colonization of new hosts promoting variation in the eco-evolutionary patterns.

Key-words: dispersion of parasites, opportunity and compatibility of interaction, phylogenetic conservatism and structure of community of parasites.

bioRxiv preprint doi: https://doi.org/10.1101/2021.11.27.470149; this version posted November 28, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

INTRODUCTION

The dispersion of parasite individuals followed by colonization of a new host lineage, known as host-switching, is a common event observed during the evolutionary trajectory of many lineages of parasites (De Vienne et al. 2013). Initially, host-switching results in the increase of the host repertoire of a parasite (Braga et al. 2021) which, subsequently, when new hosts can impose reproductive isolation it may result in speciation of parasite lineages. This is the dynamic of the oscillation hypothesis (Nylin & Soren 2018). Empirical examples showing high levels of host-switching include symbiotic interactions ranging from host-parasite and plant-insect systems to microbial pathogens, brood parasitism, plant-feeding insects, and even parasitic plants (Nylin et al. 2014; Fecchio et al. 2019; Hayward et al. 2021). Consequently, understanding the factors influencing the success of host-switching and subsequent speciation events is critical for understanding the parasite diversification.

A recently proposed theoretical framework that accommodates the evolutionary dynamics of host-parasite associations, the Stockholm Paradigm (Brooks et al. 2014; Brooks et al. 2019), suggests that parasites perform host-switching by ecological fitting (Agosta & Klemmens 2008; Agosta & Brooks 2020). Ecological fitting is the process whereby organisms colonize and persist in novel environments, use novel resources or form novel associations with other species through a set of traits they already possess (Agosta & Klemmens 2008). The expression of these unexplored capabilities is mediated by the opportunity of interaction (temporal, spatial, ecological), which determines the possibility of encounters between hosts and unfamiliar parasites. After the encounter, and if the interaction is compatible, it is followed by the resolution of subsequent conflicts that emerge from the basic dynamics of “living together”, which should result in co-accommodation (Brooks & McLennan 2012; Araujo et al. 2015).

bioRxiv preprint doi: https://doi.org/10.1101/2021.11.27.470149; this version posted November 28, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

The chances of parasites dispersing from one host species to another are influenced also by ecological and life-history traits. These include characteristics of all organisms within the interaction system, such as niche similarity among host species, modes of transmission of parasites, dietary preferences of the vector (if there is one), and also ecosystemic characteristics as the host community composition and shared phylogenetic history are relevant factors that define the chances of host-switching (Bush et al. 2006; Jaramillo & Rivera-Parra 2018). Niche similarity among host species is one fundamental element constraining the incorporation of new host species by ecological fitting. This is because the capacity of a parasite species to use new resources is related to the phylogenetic conservatism of the resource provided by the host species. Phylogenetic distance between the original and new host species represents an adequate proxy for the nature of the resource which is tracked by the parasite lineage (Charleston & Robertson 2002; Agosta & Klemmens 2008; Engelstädter & Fortuna 2019). Consequently, the host phylogenetic conservatism can define the arena of possibilities for host-switching.

Several studies have indicated the ubiquity and relevance of host-switching in nature (Engelstädter & Hurst 2006; De Vienne et al. 2007; Cuthill & Charleston 2013; De Vienne et al. 2013; Engelstädter & Fortuna 2019). Although, few have explored the relationship between the switches and the evolutionary histories of host species (see Cuthill & Charleston 2013; Engelstädter & Fortuna 2019). Moreover, the effect of compatibility and interaction opportunity for parasite propagation between host species, as well as the influence of such factors in the patterns of parasite communities remain unexplored. Here, we aim to fill these unexplored gaps by proposing a novel approach to investigate how the intensity of host-switching, mediated by opportunity and compatibility of interaction, affects the phylogenetic history and ecology of the parasites.

bioRxiv preprint doi: https://doi.org/10.1101/2021.11.27.470149; this version posted November 28, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

We proposed a theoretical model based on parasite individuals that can switch among host species during their evolution according to phylogenetic conservatism; that is, the probability of parasites switching hosts decreases with increasing divergence in the evolutionary time of the host. We compared the eco-evolutionary pattern that emerged from the model to nine empirical communities of parasites to predict their intensity of host-switching. These communities were classified by the parasitism type (ecto or endoparasites) and their spatial scale (local or regional). We analysed how the predicted host-switching varied over these classifications and discussed how they are mediated by opportunity and compatibility of interaction.

MATERIAL AND METHODS

Model general overview

We modeled the eco-evolutionary trajectories of parasites influenced by their host evolutionary history and host-switching events. Thus, we assumed that the evolutionary history of the host can represent a proxy for the resources for parasite species (Agosta et al. 2010; Imrie et al. 2021). We also assumed that the probability of host-switching decreases as the phylogenetic distance between the species of host involved in the event (original and new host species) increases. Finally, the model assumes that parasite evolution occurs at the same evolutionary time scale as the host, which increases possibilities for host-switching as host speciation occurs. Parasite individuals are explicitly modeled and characterized by their used host species and genetic identity, following the description of the model proposed by Higgs & Derrida (1991) and Manzo & Peliti (1994). This approach allows us to model parasite speciation. The host species are modeled as resources that impose a carrying capacity to parasite species, analogous to islands in the Manzo-Pelit model (Manzo & Peliti 1994), but in the present model, the

bioRxiv preprint doi: https://doi.org/10.1101/2021.11.27.470149; this version posted November 28, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

islands (hosts species in our case) emerge (as a new host species that speciate) and the distance between them varies over time, according to a predetermined time host diversification (e.g. based on ultrametric empirical phylogenies). The model does not consider the selection pressure imposed by parasites on the evolution of the resource. Therefore, we are not modeling a process of reciprocal evolution, or co-evolution.

Host and parasite characterization

Following the model proposed by Higgs & Derrida (1991), parasite individuals are explicitly modeled by biallelic sequences of infinite sites, a simplified form to represent their genomes and heritable trait. Individuals are monoic and engage in sexual reproduction, with non-overlapping generations. The empirical data have evolutionary times in the order of millions of years, and to maintain this time scale in the model would demand a higher computational cost. As proposed by Costa et al. (2019), in our approach we adopted a higher value of mutation rate in order to decrease the number of iterations necessary for speciation (time steps or generations) to happen. Furthermore, we assumed that, due to the shorter life cycle of parasites, they have a faster speciation rate (Dowton & Austin 1995; Light & Hafner 2007). To satisfy these conditions, we rescaled the whole host phylogeny assuming that the smaller branch length consists of the minimal time for parasites to speciate in allopatry (τ_a generations - see the details in supplemental information I). The simulation starts with a clonal parasite population using a unique host species. The first host speciation occurs only after τ_a generations, accumulating genetic variation before the first host speciation (the root of the host phylogeny). Each host species imposes a carrying capacity of K parasite individuals. Thus, the overall carrying capacity increases by K individuals at each new host speciation.

bioRxiv preprint doi: https://doi.org/10.1101/2021.11.27.470149; this version posted November 28, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Parasite reproduction

Reproduction is sexual and occurs between parasite individuals that are in the same host and that have a minimum genetic similarity, q_{min}, measured based on the Hamming distance between genomes. In each host species, *K* offspring are born, replacing the parental population. We establish a maximum of *K* random trials with reposition to find one compatible partner. The offspring is generated by *locus* recombination of the parents and each *locus* has a probability μ of mutation. We set $q_{min} = 0.5q_0$, where q_0 is the expected mean similarity within one population in equilibrium, because it avoids the occurrence of parasite speciation within the same host species. Consequently, parasite speciation only happens when more than one host species is used. For a more detailed description of the method, see the supplemental information I.

Host-switching

After the first host speciation, parasite individuals in a host species can switch to another host. For each parasite individual, we randomly selected a host species, including the one in use. If the selected host species is not the original host (donor), we follow a probability function for the host-switching event. This probability of host-switching events (P_{hs}) decreases over time, representing the loss of opportunity and/or compatibility of parasites associated with the evolutionary history of hosts. The probability of a parasite individual successfully migrate (host-switching) from one host to another host species, in a given generation *n*, is defined as:

$$P_{hs}(n)=exp[-r * (n - n_s)] \,, \qquad (1)$$

where *r* is a positive parameter that controls the decay of the host-switching probability, and n_s is the generation that the common host ancestor had speciated (then, n-n_s is how

bioRxiv preprint doi: https://doi.org/10.1101/2021.11.27.470149; this version posted November 28, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

long the two host species had diverged). If $r = 0$, these probabilities are equal to 1 regardless of the host divergence time, meaning that there is no restriction to host-switching. As a consequence, parasite gene flow is continuous and speciation does not occur. At the other extreme, for sufficiently large r values (P_{hs}~0), host-switching is absent, and cospeciation between hosts and parasites is expected. For intermediary r value, some parasite individuals can eventually switch hosts. This will increase the host repertoire of the parasitic species, and also enable speciation by isolation (by host use), similar to the speciation by founder's effect (Mayr 1999; Gavrilets & Hastings 1996). In order to better interpret the effect of parameter r on the trajectories and compare the results between the communities, we do not present our results in terms of r, but how much it changes the overall host-switching events. To obtain this overall metric, we calculated the expected percentage of parasite individuals that switch hosts over the entire simulation and we call it as **host-switching intensity**.

Empirical database

Nine studies from empirical communities of parasite-host associations (Table 1) were used for comparative purposes. Selection criteria was that, in addition to information on species interaction, these communities essentially needed to have published phylogenies for hosts and parasites (see the details in supplemental information II). We separated these communities according to the parasitism type and spatial scale (Table 1 - Fig. S5-S13). For all empirical studies selected, parasite groups are monoxenic (both ecto-endoparasites), with simple life cycles that encompasses a single host species. All ectoparasites analysed herein can be transmitted during the larval and adult stages while endoparasites can be transmitted only during the larval stage. Hence, ectoparasites are likely more prone to explore and colonize new hosts (Boeger et al. 2005; Malcicka et al.

bioRxiv preprint doi: https://doi.org/10.1101/2021.11.27.470149; this version posted November 28, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

2015). A total of 50 runs were performed with 250 individuals of carrying capacity, for each configuration of the parameters of host-switching intensity.

Characterization of the ecological and evolutionary patterns of parasites

We expected that the ecological and evolutionary processes leave signatures in the resulting composition of parasite species and phylogenetic trees of parasites; thus, we compared both the structure of phylogenies and the composition of the parasite species in the empirical data with those resulting from the simulations. We compared the species composition using the beta diversity of multiple-site dissimilarities (β - Baselga 2010; 2013a, b). The structure of the phylogenetic trees was characterized by measuring the tree imbalance, using the normalized Sackin index (I_n - Blum & François 2005). As each empirical case represents particular ecological and evolutionary processes, we analysed whether there was an optimal range of host-switching intensity that reproduced each composition (β) and normalized Sackin index (I_n). To reproduce the scenarios that best fit the empirical situations, we assumed that the simulations needed to reproduce both the β and the I_n metrics simultaneously (with a ±5%confidence interval). Then we compared the resulting host-switching intensity among the empirical cases analysed to understand how it varied for different evolutionary histories. Statistical analyses were performed using 'ape' (Paradis & Schliep 2019), 'betapart' (Baselga et al. 2018) 'picante' (Kembel et al. 2010), 'phytools' (Revell 2012) and 'vegan' (Oksanen et al. 2013) R packages.

Statistical analysis

To test whether the parasitism type and spatial scale modulates the host-switching intensity in the empirical cases analysed, a linear mixed-effects model (LMM) was performed using the lmer function from the 'lme 4' package (Bates et al. 2015). For this analysis the host-switching intensity, the type of parasitism as well as the spatial scale as

bioRxiv preprint doi: https://doi.org/10.1101/2021.11.27.470149; this version posted November 28, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

fixed variables were included, and empirical cases were treated as random variables. After performing the LMM analysis, an analysis of variance (ANOVA) was used to determine significant differences (p-value ≤ 0.01) using the Anova function in the 'car' package (Fox & Weisberg 2019). All statistical analyses were performed in R v.4.0.0 (R Core Team 2020) and Rstudio v.1.3.959 (RStudio Team 2020).

RESULTS

The beta diversity and normalized Sackin index of parasites varied according to the host-switching intensity (e.g. the expected percentage of parasite individuals that switch hosts during the entire history of the host community). To illustrate the prevalent beta diversity and normalized Sackin index according to the host-switching intensity, we presented the case of feather mites associated with birds (ID. 1 - Fig. 1). As expected, beta diversity decreases as host-switching intensity increases regardless of the studied case (Fig. 1a and Fig. S14). It occurs because the increase of host-switching promotes the interaction of different host species with the same parasite species. Additionally, for each value of host-switching intensity, there is a small variation in the beta diversity (Fig. 1a and Fig. S14). The only exception was ID. 4, which resulted in a wide variation in beta diversity under high host-switching intensity (Fig. S14).

When host-switching intensity is low (below 5%), the normalized Sackin index (I_n) for the simulated parasite phylogenies assumes exactly the same value of the one obtained from the empirical phylogeny of the host (note the dashed line in Fig. 1b and also Fig. S15). This low host-switching intensity does not allow the establishment of a population in a new host. As a consequence, the simulated parasite phylogenies have the same normalized Sackin index of the empirical host phylogeny. For higher host-switching intensity, colonization followed by speciation is more likely to occur and the normalized

bioRxiv preprint doi: https://doi.org/10.1101/2021.11.27.470149; this version posted November 28, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Sackin index varies over simulations even when they are under the same host-switching intensity (Fig. 1b and Fig. S15). The wide variation in the normalized Sackin index for a given host-switching intensity reveals that stochastic host-switching events, even if more likely occurring between closely related species, can change the structure of the resulting phylogenetic tree. The normalized Sackin index tends towards zero (balanced tree) as host-switching intensity goes to one, regardless of the community (Fig. S15), resembling a neutral speciation scenario Yule model (Yule 1924; Aldous 2001).

For all cases, there is a host-switching intensity that simultaneously reproduces the empirical beta diversity and the parasite normalized Sackin index (Fig. 2). As mentioned before, both metrics are sensitive to host-switching intensity, but still restricted to some combinations of beta diversity and Sackin index (see in Fig. 2, the graphs showing the beta diversity *vs.* normalized Sackin index are not fully filled). Generally, the beta diversity and the parasite normalized Sackin index obtained under high host-switching intensity (greater than 50%) are far from the empirical pattern (see Fig. 2, the yellow dots rarely approach the intersection of the solid lines). Then, host phylogeny is an important proxy for host-switching events.

The simulated host-switching intensity that simultaneously fit beta diversity and parasite normalized Sackin index of each empirical case ($\pm$5% confidence interval) recovered a range of 0.06% to 22.07% of host-switching intensity. Within this range, the associations between mammals and lice presented the lowest host-switching intensity (case ID. 2 with 0.07% - 1.13%), followed by that involving birds and feather mites (case ID. 1 with 0.06% - 8. 17%), wildlife and arthropod parasites (case ID. 3 with 0.82% - 2.69%), frogs and Polystomatidae (case ID. 7 with 0.22% - 3.71%), frogs and *Rhabdias* spp. (case ID. 8 with 1.99% - 4.94%), frogs and *Oswaldocruzia* spp. (case ID. 9 with 5.29% - 5.91%), fish and Gyrodactylidae (case ID. 6 with 9.35%), - the highest intensities

bioRxiv preprint doi: https://doi.org/10.1101/2021.11.27.470149; this version posted November 28, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

of host-switching were observed between rodents and fleas (case ID. 5 with 13.47% - 16.87% and case ID. 4 with 0.43% - 22.07%). For ectoparasites, the switching intensity of hosts observed in the simulations was 0.06% to 22.07% and, for endoparasites, it was in the range of 0.22% to 5.91% but no significant correlation was observed between host-switching intensity and parasitism type (LMM: beta= -0.007, SE= 0.018, df = 5.98, t= -0.6, p = 0.70, ANOVA: F=0.16, p = 0.69, Fig. 3). The host-switching events are more frequent in studies conducted in a local scale (blue color in Fig. 3) than in regional scales (salmon color in Fig. 3) (LMM: effect of host-switching intensity on spatial scale: beta= 0.08, SE= 0.18, df = 6.12, t= 4.66, p = 0.003, ANOVA: F = 21.75, p = 0.003, Fig. 3).

DISCUSSION

In this study, we proposed a theoretical model to investigate how the intensity of host-switching, mediated by opportunity and compatibility of interaction (using host phylogenetic distance as proxy), shapes the phylogenetic history and ecology of the parasites. Our results indicated that different host-switching intensities can drive distinct ecological and evolutionary patterns of the parasite lineages. The model reproduced the eco-evolutionary pattern of all analysed empirical cases, but the range of predicted host-switching intensity varied among them. The parasitism type did not explain this variation, but the extent of the spatial scales of the empirical cases analysed present some correlation with the predicted intensity of host-switching. Host-switching intensity was higher for local empiric cases when compared to regional scale cases.

Variation in host-switching intensity through history influences the resulting eco-evolutionary patterns of the parasites involved. When the frequency of host-switching is sufficiently high, parasites can maintain the gene flow among infrapopulations of distinct hosts and speciation does not occur. On the other hand, if the gene flow is reduced, reduction in host-switching favours parasite speciation (see the eco-evolutionary

bioRxiv preprint doi: https://doi.org/10.1101/2021.11.27.470149; this version posted November 28, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

dynamics in the movie available in supplemental information III S16 and S17). This was the general pattern observed for all simulated communities, strongly suggesting that host-switching is an important driver for parasite evolution. During simulations, in line with the oscillation hypothesis, species first increase their host repertoire (generalize) and then speciate (specialize) (Janz & Nylin 2008; Braga et al. 2018).

Our results also support that host phylogenetic relationship is a good predictor of host-switching - i.e. host-switching is most likely to occur between related host species. There is probably some common trait, such as a specific physiological mechanism that has evolved and may be being expressed through phylogeny. The dispersion of parasites followed by colonization of a new host lineage has been increasingly investigated in the Stockholm Paradigm (Agosta et al. 2010; Araujo et al. 2015; Nylin et al. 2018; Brooks et al. 2019). For a parasite lineage, the closer (phylogenetically) the species of the original and new host, the greater the possibility that the necessary combination of elements that compose the adequate resource is conserved or, is at least quali- and quantitatively similar. Hence, phylogenetic proximity has been widely recognized as a potential criterion to anticipate the emergence of new associations (Streicker et al. 2010; Damas et al. 2020). However, this is not a universal criterion, as compatibility appears to be also modulated by other biological elements (e.g. morphology, genetics, ecology) associated with the opportunity of encounters between hosts and parasites. This theoretical framework has provided evidence on how the host-switching mediated by compatibility and opportunity of interaction influence the dynamics of parasitic interactions leading to species diversification (Agosta et al. 2010; Nylin et al. 2018; Brooks et al. 2019). The possibility of encounter between potential symbionts in time and space, emerges from geographic distributions, ecology, and inherent biological traits of the associates. Compatibility emerges from the ancestral capacity in which both must be physiologically

bioRxiv preprint doi: https://doi.org/10.1101/2021.11.27.470149; this version posted November 28, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

compatible to establish a long-term association. Compatibility and opportunity should occur simultaneously to allow the establishment of new associations. Thus, any factor that influences the compatibility and/or the opportunity among hosts and parasites may affect the intensity of host switching by parasites. Such factors can include biological and/or spatial variations, which may explain the varied predicted intensities of host-switching among analysed communities.

The parasitism type (ecto *vs* endoparasites) had no effect on the predicted intensity of host-switching by parasites. Ectoparasites have direct contact with the external environment, while endoparasites may have free-living infective stages but spend most of their life without direct contact with the environment (Bush et al. 2001). Because of this, higher host-switching intensity could be expected in ecto rather than endoparasites due to the amount of time under variable environmental conditions that could lead to a stronger selective pressure to use a broader array of hosts. In addition, all parasites analysed here are monoxenic and differ by the transmission strategy: ectoparasites can transmit between host individuals during adult stages, while the endoparasites only during the larval stage. Hence, the strategy of transmission of the ectoparasites allows successive host-switching by an individual parasite, while endoparasites are restricted to less host-switching events. This wider possibility of transmission was assumed to favor a higher intensity of host-switching by ectoparasites than by endoparasites (Boeger et al. 2005). Consequently, as we could not detect significant differences between the empirical networks analysed herein, our results do not support these hypotheses. For instance, an alternative explanation may be linked to the generalization that propagule size compensates for the wider possibility of transmission. Moreover, there is great heterogeneity in the characteristics of both ecto and endoparasites. Each parasitism type includes a great diversity of organisms, with profound differences in their evolutionary

bioRxiv preprint doi: https://doi.org/10.1101/2021.11.27.470149; this version posted November 28, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

history and biological characteristics (for example, by comparing species of the genus fleas, lice, feather mites, helminths, platyhelminthes), which may be more influential to host-switching intensity than the general site of parasitism type itself. Expanding the analyses to a broader sample of empirical networks, including variations in the reproductive strategies may provide important insights on this question.

Unlike parasitism type, our results indicate that host-switching intensity is higher on local than regional spatial scale. The opportunity for interaction is increased in host communities at a local scale, as this reduces the likelihood that geographic barriers exist, hampering the possibility of encounter. This is evident when comparing rodent and flea cases at regional (ID. 4) and local spatial scales (ID. 5). Similarly, since the cases of *Rhabdias* spp. and frogs (ID. 8) are defined geographically (and not by host taxa) it was assumed that host-switching and ecological fitting were evolutionarily more important than association with particular host taxa (Kuzmin et al. 2014; Müller et al. 2018). However, the majority of the empirical cases analysed herein and elsewhere suggest that switches are responsible for parasite diversification and distribution (see Krasnov et al. 2016; Dona et al. 2017; Patella et al. 2017).

Although the model can reconstruct eco-evolutionary patterns of empirical cases, it has some limitations. First, there is no variation of the carrying capacity imposed by each host species; second, variation in abundance and spatial distribution are not explicitly considered; third, the parasites compete for the same resource (in contrast, each parasite species would have a carrying capacity); and finally, selective pressure is not explicitly modelled. The solutions to these limitations would make the model more realistic but also demand more computational time and increase the number of parameters to be evaluated. Thus, quantitative comparisons of predicted host-switching intensities should not be done, but the qualitative implications, as already discussed. Furthermore,

bioRxiv preprint doi: https://doi.org/10.1101/2021.11.27.470149; this version posted November 28, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

we emphasize the need for empirical phylogenetic studies, since the availability of phylogenetic data on parasites is still scarce. Phylogenetic data on parasites are extremely important to clarify the role of host-switching in the ecological and evolutionary patterns of parasite lineages.

Our results indicate that the intensity of host-switching, mediated by opportunity and compatibility of interaction, influence the phylogenetic history and ecology of the parasites. As suggested by the Stockholm Paradigm, parasites may already carry the ancestral capabilities to switch to new hosts, and here we showed that the host evolutionary history, when associated with opportunity for contact and interaction compatibility (opportunity + compatibility are represented by the parameter *r*), creates the possibility for the colonization of a new host species. Our study represents a first attempt to model and evaluate the empirical evolutionary history of hosts as a proxy for parasite resources and offers a new approach to understanding the eco-evolutionary patterns of parasite species. This model has important implications for predicting changes in host lineages in situations of environmental or climatic changes or yet in cases of emerging diseases where the parasitic host switches can cause disease outbreaks.

ACKNOWLEDGEMENTS

We thank the researchers who collected and reported the field data, our institutions and the many colleagues who helped us in different ways during this project for their comments and suggestions, especially to Professor Dr. Marcus Aguiar. EDB is grateful for the Ph.D. degree scholarship provided by Capes (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior). EDB and SBLA acknowledge the computational support from Professor Carlos M. de Carvalho at LFTC-DFis-UFPR.

bioRxiv preprint doi: https://doi.org/10.1101/2021.11.27.470149; this version posted November 28, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

FINANCIAL SUPPORT

This study was supported by Brazilian Coordination for the Improvement of Higher Education Personnel (CAPES). DP was supported by the São Paulo Research Foundation (FAPESP), grants #2018/11187-8 and #2016/01343-7 (ICTP-SAIFR).

CONFLICT OF INTEREST

The authors declare that they have no conflict of interests.

DATA ACCESSIBILITY STATEMENT

The model, phylogenies and interactions of all analysed cases are available at https://github.com/elviradbastiani/host_switching_model.

REFERENCES

Agosta, S.J., & Brooks, D.R. (2020). The major metaphors of evolution: Darwinism then and now (Vol. 2). Springer Nature, Switzerland AG. pp. XVII - 273.

Agosta, S.J. & Klemens, J.A. (2008). Ecological fitting by phenotypically flexible genotypes: implications for species associations, community assembly and evolution. Ecology Letters, 11, 1123-1134.

Agosta, S.J., Janz, N. & Brooks, D.R. (2010). How specialists can be generalists: resolving the" parasite paradox" and implications for emerging infectious disease. Zoologia, 27, 151-162.

Aldous, D.J. (2001). Stochastic models and descriptive statistics for phylogenetic trees, from Yule to today. Statistical Science, 16, 23-34.3

Araujo, S.B., Braga, M.P., Brooks, D.R., Agosta, S.J., Hoberg, E.P., von Hartenthal, F.W. & Boeger, W.A. (2015). Understanding host-switching by ecological fitting. PLoS One, 10, e0139225.

bioRxiv preprint doi: https://doi.org/10.1101/2021.11.27.470149; this version posted November 28, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Badets, M., Whittington, I., Lalubin, F., Allienne, J.F., Maspimby, J.L., Bentz, S. & Verneau, O. (2011). Correlating early evolution of parasitic platyhelminths to Gondwana breakup. Systematic Biology, 60, 762-781.

Baselga, A. (2010). Partitioning the turnover and nestedness components of beta diversity. Global ecology and biogeography, 19, 134-143.

Baselga, A. (2013a). Separating the two components of abundance-based dissimilarity: balanced changes in abundance vs. abundance gradients. Methods in Ecology and Evolution, 4, 552-557.

Baselga, A. (2013b). Multiple site dissimilarity quantifies compositional heterogeneity among several sites, while average pairwise dissimilarity may be misleading. Ecography, 36, 124-128.

Baselga, A., Orme, D., Villeger, S., De Bortoli, J., Leprieur, F., Logez, M. & Henriques-Silva, R. (2017). Partitioning beta diversity into turnover and nestedness components. R package betapart, Version, 1-4.

Bates, D., Maechler, M., Bolker, B., Walker, S., Christensen, R.H.B., Singmann, H. & Grothendieck, G. (2011). Package 'lme4'. Linear mixed-effects models using S4 classes. R package version, 1(6).

Becker, D.J., Streicker, D.G. & Altizer, S. (2018). Using host species traits to understand the consequences of resource provisioning for host–parasite interactions. Journal of Animal Ecology, 87, 511-525.

Blum, M.G. & François, O. (2005). On statistical tests of phylogenetic tree imbalance: the Sackin and other indices revisited. Mathematical biosciences, 195, 141-153.

Boeger, W.A., Kritsky, D.C., Pie, M.R. & Engers, K.B. (2005). Mode of transmission, host switching, and escape from the Red Queen by viviparous gyrodactylids (Monogenoidea). Journal of Parasitology, 91, 1000-1007.

bioRxiv preprint doi: https://doi.org/10.1101/2021.11.27.470149; this version posted November 28, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Braga, M.P., Araujo, S.B., Agosta, S., Brooks, D., Hoberg, E., Nylin, S. & Boeger, W.A. (2018). Host use dynamics in a heterogeneous fitness landscape generates oscillations in host range and diversification. Evolution, 72, 1773-1783.

Braga, M.P. & Janz, N. (2021). Host repertoires and changing insect–plant interactions. Ecological Entomology, 46, 1241–1253.

Brooks, D.R. & McLennan, D.A. (2012). The nature of diversity. University of Chicago Press, pp. 676.

Brooks, D.R., Hoberg, E.P., Boeger, W.A., Gardner, S.L., Galbreath, K.E., Herczeg, D. & Dursahinhan, A.T. (2014). Finding them before they find us: informatics, parasites, and environments in accelerating climate change. Comparative Parasitology, 81, 155-164.

Brooks, D.R., Hoberg, E.P. & Boeger, W.A. (2019). The Stockholm paradigm: climate change and emerging disease. University of Chicago Press, pp. 400.

Bush, A.O., Fernandez, J.C., Esch, G.W. & Seed, J.R. (2001). Parasitism: the diversity and ecology of animal parasites. Cambridge university press, pp. 540.

Bush, S.E., Sohn, E. & Clayton, D.H. (2006). Ecomorphology of parasite attachment: experiments with feather lice. Journal of Parasitology, 92, 25-31.

Charleston, M.A. & Robertson, D.L. (2002). Preferential host switching by primate lentiviruses can account for phylogenetic similarity with the primate phylogeny. Systematic biology, 51, 528-535.

Costa, C.L., Lemos-Costa, P., Marquitti, F.M., Fernandes, L.D., Ramos, M.F., Schneider, D.M. & de Aguiar, M.A. (2019). Signatures of microevolutionary processes in phylogenetic patterns. Systematic biology, 68, 131-144.

bioRxiv preprint doi: https://doi.org/10.1101/2021.11.27.470149; this version posted November 28, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Cuthill, J.H. & Charleston, M.A. (2013). A simple model explains the dynamics of preferential host switching among mammal RNA viruses. Evolution: International Journal of Organic Evolution, 67, 980-990.

Damas, J., Hughes, G.M., Keough, K.C., Painter, C.A., Persky, N.S., Corbo, M. & Lewin, H.A. (2020). Broad host range of SARS-CoV-2 predicted by comparative and structural analysis of ACE2 in vertebrates. Proceedings of the National Academy of Sciences, 117, 22311-22322.

De Vienne, D.M., Giraud, T. & Shykoff, J.A. (2007). When can host shifts produce congruent host and parasite phylogenies? A simulation approach. Journal of evolutionary biology, 20, 1428-1438.

De Vienne, D.M., Refrégier, G., López-Villavicencio, M., Tellier, A., Hood, M.E. & Giraud, T. (2013). Cospeciation vs host-shift speciation: methods for testing, evidence from natural associations and relation to coevolution. New Phytologist, 198, 347-385.

Doña, J., Sweet, A.D., Johnson, K.P., Serrano, D., Mironov, S. & Jovani, R. (2017). Cophylogenetic analyses reveal extensive host-shift speciation in a highly specialized and host-specific symbiont system. Molecular phylogenetics and evolution, 115, 190-196.

Dowton, M. & Austin, A.D. (1995). Increased genetic diversity in mitochondrial genes is correlated with the evolution of parasitism in the Hymenoptera. Journal of Molecular Evolution, 41, 958-965.

Engelstädter, J. & Fortuna, N.Z. (2019). The dynamics of preferential host switching: Host phylogeny as a key predictor of parasite distribution. Evolution, 73, 1330-1340.

Engelstädter, J. & Hurst, G.D. (2006). The dynamics of parasite incidence across host species. Evolutionary Ecology, 20, 603-616.

Fecchio, A., Wells, K., Bell, J.A., Tkach, V.V., Lutz, H.L., Weckstein, J.D. & Clark, N.J. (2019). Climate variation influences host specificity in avian malaria parasites. Ecology Letters, 22, 547-557.

bioRxiv preprint doi: https://doi.org/10.1101/2021.11.27.470149; this version posted November 28, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Fox, J. & Weisberg, S. (2019). Nonlinear Regression, Nonlinear Least Squares, and Nonlinear Mixed Models in R. population, 150, 200.

Gavrilets, S. & Hastings, A. (1996). Founder effect speciation: a theoretical reassessment. The American Naturalist, 147, 466-491.

Hayward, A., Poulin, R. & Nakagawa, S. (2021). A broadscale analysis of host-symbiont cophylogeny reveals the drivers of phylogenetic congruence. Ecology Letters, 24, 1681–1696.

Higgs, P.G. & Derrida, B. (1991). Stochastic models for species formation in evolving populations. Journal of Physics A: Mathematical and General, 24, L985.

Imrie, R. M., Roberts, K. E. & Longdon, B. (2021). Between virus correlations in the outcome of infection across host species: Evidence of virus by host species interactions. Evolution letters, 5, 472-483.

Nylin, S. & Janz, N. (2008). 15. The Oscillation Hypothesis Of Host-Plant Range And Speciation. In Specialization, Speciation, and Radiation. University of California Press, 203-2015.

Jaramillo, M. & Rivera-Parra, J. L. (2018). Host-Switching: How It Starts. In Disease Ecology. Springer, Cham, pp. 139-156.

Kembel, S.W., Cowan, P.D., Helmus, M.R., Cornwell, W.K., Morlon, H., Ackerly, D.D. & Webb, C.O. (2010). Picante: R tools for integrating phylogenies and ecology. Bioinformatics, 26, 1463-1464.

Krasnov, B.R., Shenbrot, G.I., Khokhlova, I.S. & Degen, A.A. (2016). Trait-based and phylogenetic associations between parasites and their hosts: a case study with small mammals and fleas in the Palearctic. Oikos, 125, 29-38.

Kuzmin, Y., de Vasconcelos Melo, F.T. & Dos Santos, J.N. (2014). A new species of Serpentirhabdias Tkach, Kuzmin & Snyder, 2014 (Nematoda: Rhabdiasidae) parasitic in the

bioRxiv preprint doi: https://doi.org/10.1101/2021.11.27.470149; this version posted November 28, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

brown ground snake Atractus major Boulenger (Reptilia: Serpentes: Dipsadidae) in Brazil. Systematic Parasitology, 89, 101-106.

Light, J.E. & Hafner, M.S. (2007). Cophylogeny and disparate rates of evolution in sympatric lineages of chewing lice on pocket gophers. Molecular phylogenetics and evolution, 45, 997-1013.

Malcicka, M., Agosta, S.J. & Harvey, J.A. (2015). Multi level ecological fitting: indirect life cycles are not a barrier to host switching and invasion. Global change biology, 21, 3210-3218.

Manzo, F. & Peliti, L. (1994). Geographic speciation in the Derrida-Higgs model of species formation. Journal of Physics A: Mathematical and General, 27, 7079.

Mayr, E. (1999). Systematics and the origin of species, from the viewpoint of a zoologist. Harvard University Press, pp. 372.

Müller, M.I., Morais, D.H., Costa-Silva, G.J., Aguiar, A., Avila, R.W. & da Silva, R.J. (2018). Diversity in the genus *Rhabdias* (Nematoda, Rhabdiasidae): Evidence for cryptic speciation. Zoologica Scripta, 47, 595-607.

Nylin, S., Agosta, S., Bensch, S., Boeger, W.A., Braga, M.P., Brooks, D.R. & Janz, N. (2018). Embracing colonizations: a new paradigm for species association dynamics. Trends in ecology & evolution, 33, 4-14.

Nylin, S., Slove, J. & Janz, N. (2014). Host plant utilization, host range oscillations and diversification in nymphalid butterflies: a phylogenetic investigation. Evolution, 68, 105-124.

Oksanen, J., Blanchet, F.G., Kindt, R., Legendre, P., Minchin, P.R., O'hara, R.B. & Oksanen, M.J.(2013). Package 'vegan'. Community ecology package, version, 2, 1-295.

Paradis, E. & Schliep, K. (2019). ape 5.0: an environment for modern phylogenetics and evolutionary analyses in R. Bioinformatics, 35, 526-528.

bioRxiv preprint doi: https://doi.org/10.1101/2021.11.27.470149; this version posted November 28, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Patella, L., Brooks, D.R. & Boeger, W.A. (2017). Phylogeny and ecology illuminate the evolution of associations under the Stockholm paradigm: Aglaiogyrodactylus spp. (Platyhelminthes, Monogenoidea, Gyrodactylidae) and species of Loricariidae (Actinopterygii, Siluriformes). Vie Et Milieu, 67, 91-102.

Team, R.C. (2020). R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria: Available at: https://www. R-project. org/. Last accessed 10 november 2021.

Reed, D.L., Light, J.E., Allen, J.M. & Kirchman, J.J. (2007). Pair of lice lost or parasites regained: the evolutionary history of anthropoid primate lice. Bmc Biology, 5, 1-11.

Revell, L.J. (2012). phytools: an R package for phylogenetic comparative biology (and other things). Methods in ecology and evolution, 3, 217-223.

Team, R. (2020). RStudio: Integrated Development for R. RStudio, PBC, Boston, MA. Available at: https://www.rstudio.com/. Last accessed 10 november 2021.

Streicker, D.G., Turmelle, A.S., Vonhof, M.J., Kuzmin, I.V., McCracken, G.F. & Rupprecht, C.E. (2010). Host phylogeny constrains cross-species emergence and establishment of rabies virus in bats. Science, 329, 676-679.

Willkens, Y., Furtado, A.P., Dos Santos, J.N. & de Vasconcelos Melo, F.T. (2021). Do host habitat use and cospeciation matter in the evolution of Oswaldocruzia (Nematoda, Molineidae) from neotropical amphibians? Journal of Helminthology, 95, e33.

Yule, U.G. (1925). A mathematical theory of evolution, based on the conclusions of Dr. JC Willis, FRS. Philosophical Transactions of the Royal Society of London Series B, 213, 21-87.

bioRxiv preprint doi: https://doi.org/10.1101/2021.11.27.470149; this version posted November 28, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

bioRxiv preprint doi: https://doi.org/10.1101/2021.11.27.470149; this version posted November 28, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Tables

Table 1. Description of the host sample size and parasite richness for each empirical study, of which host phylogenies were used as model parameters and host-parasite association to validate the simulations. All parasite groups are monoxenic, and the transmission in ectoparasites includes the larval and adult stages, and endoparasites' transmission includes only the larval. Legend: ID = Empirical study.

ID	Host group	Host richness	Parasites group	Parasite richness	Parasitism type	Spatial scale	Reference
1	Bird	11	Feather mites (*Trouessartia* spp.)	11	ectoparasites	regional	Donã et al. 2017
2	Mammals	6	Lice (*Pediculus* spp. and *Pthirus* spp.)	7	ectoparasites	regional	Reed et al. 2007
3	Wildlife	9	Arthropods*	8	ectoparasites	regional	Becker et al. 2018
4	Rodents	129	Fleas*	202	ectoparasites	regional	Krasnov et al. 2016
5	Rodents	11	Fleas*	19	ectoparasites	local	Krasnov et al. 2016
6	Fish	8	Platyhelminthes (Gyrodactylidae)	16	ectoparasites	local	Patella et al. 2017
7	Frogs	15	Polystomes (Polystomatidae)	13	endoparasites	regional	Badets et al. 2011
8	Frogs	31	Nematodes (*Rhabdias* spp.)	18	endoparasites	regional	Müller et al. 2018

bioRxiv preprint doi: https://doi.org/10.1101/2021.11.27.470149; this version posted November 28, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

9	Frogs	7	Nematodes (*Oswaldocruzia* spp.)	5	endoparasites	local	Willkens et al. 2021

*include different parasite groups.

bioRxiv preprint doi: https://doi.org/10.1101/2021.11.27.470149; this version posted November 28, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Figures

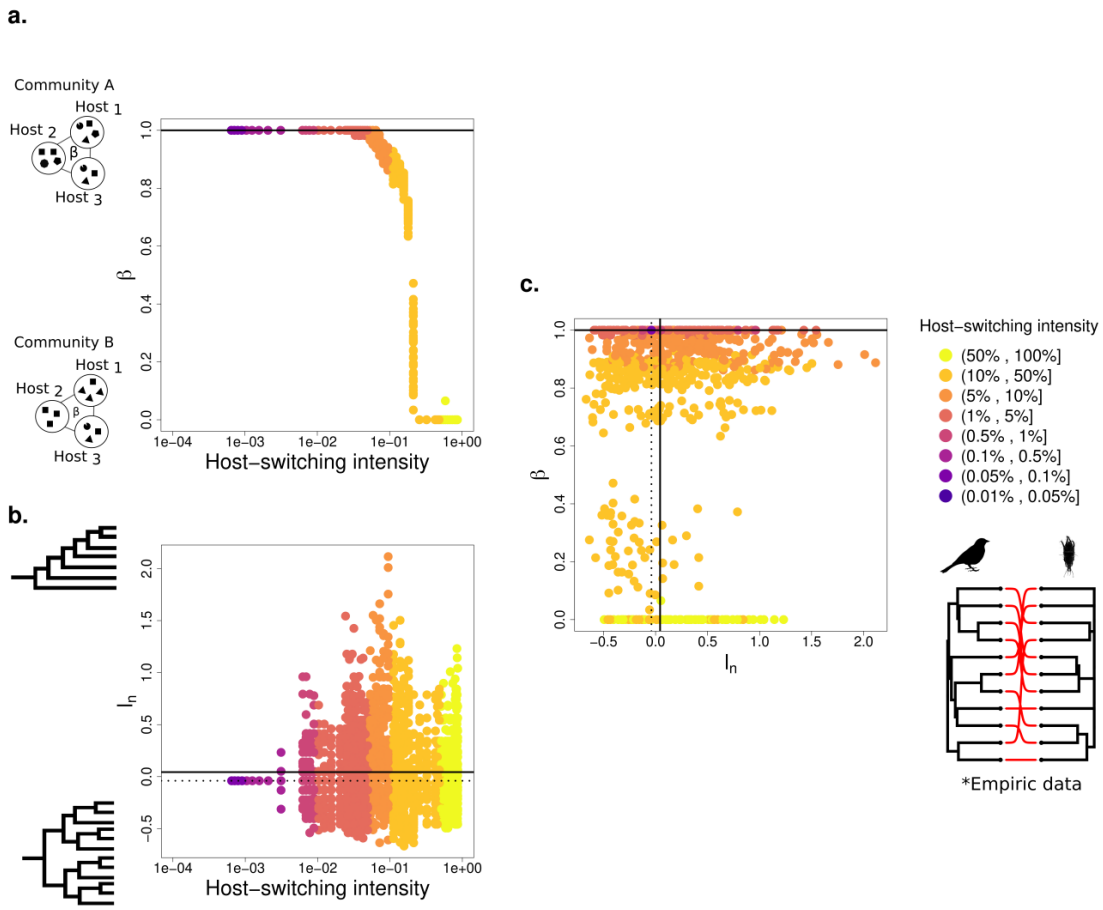

Figure 1. Influence of host-switching on the eco-evolutionary patterns of simulated parasites for feather mites associated with birds (see Table 1 for details). Here we demonstrated the relationship between: **a**. Host-switching intensity and variation in the composition of parasite species (β) between host species; **b**. Host-switching intensity and parasite normalized Sackin index (I_n); **c**. Relationship between β, I_n, and the host-switching intensity. The lines refer to empirical information of parasite (continuous) and host (dotted). The colored dots are redundant with the x-axis scale of graphs (a) and (b), but intend to guide the interpretation of (c). A total of 50 runs were performed with 250 individuals of carrying capacity, for each configuration of the parameters of host-switching intensity.

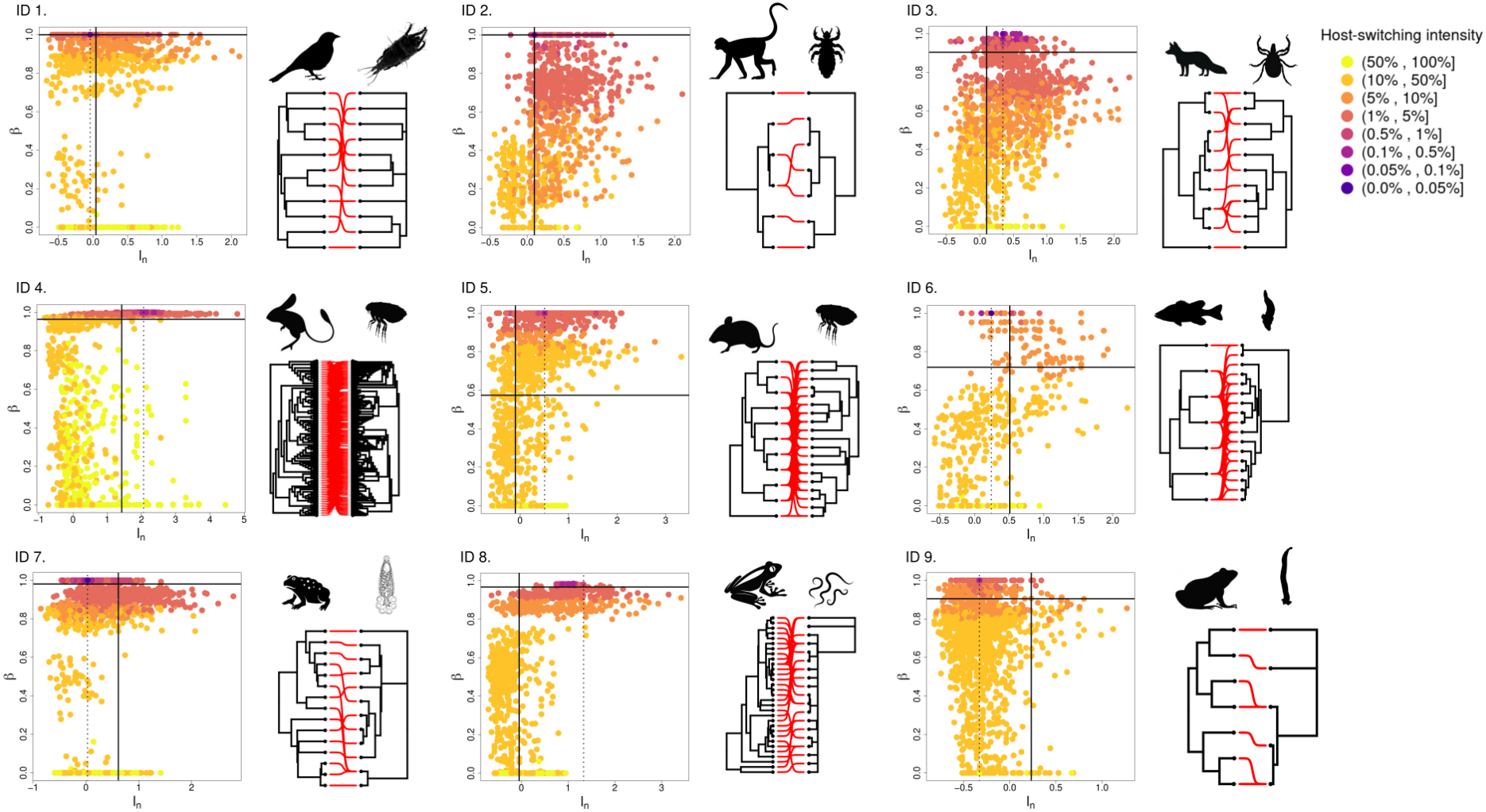

Figure 2. The relationship between variation in the composition, normalized Sackin index of parasite species and host-switching intensity for nine empirical cases: the variation in parasites' composition, measured by the metric beta diversity (β) on the y-axis and the normalized Sackin index (I_n) on the x-axis. Each ID represents an empirical case. The lines refer to empirical

information of parasite (continuous) and host (dotted). Color scales represent each percentage interval of host-switching intensity. A total of 50 runs were performed with 250 individuals of carrying capacity, for each configuration of the parameters of host-switching intensity.

bioRxiv preprint doi: https://doi.org/10.1101/2021.11.27.470149; this version posted November 28, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

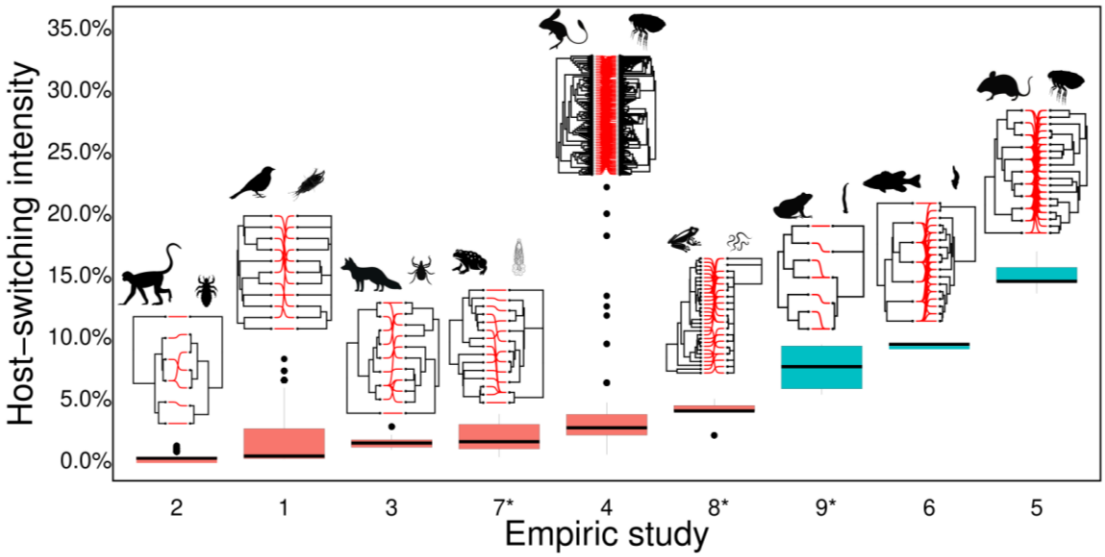

Figure 3. Relation of the host-switching intensity among empirical cases considering cases that correspond to ±5% confidence interval in relation to the metrics variation (beta diversity and the normalized Sackin index simulated and empirical). The boxplots show the simulation distributions for each empirical case. Regional scale cases are represented by salmon color, and local scale cases by blue. The number in axis x represents the empirical cases: ID. 1 - Birds and feather mites. ID. 2 - Mammals and lice. ID. 3 - Wildlife and ectoparasites. ID. 4 and 5 - Rodents and fleas. ID. 6 - Fish and Platyhelminthes (Gyrodactylidae). ID. 7 - Frogs and Polystomes (Polystomatidae). ID. 8 - Frogs and Nematodes (*Rhabdias* spp.). ID. 9 - Frogs and Nematodes (*Oswaldocruzia* spp.). The asterisks (*) represent cases of endoparasites.