When is cophylogeny evidence of coevolution?

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**Conceptual advances in the field of antagonistic coevolution resulted in an increased understanding of how hosts and parasites have a reciprocal impact on their ecology and evolution. While it is known that coevolution can trigger diversification in both the host and its parasite, it is not clear under which set of conditions coevolution will result in mirorring phylogenies. By reviewing the literature related to host-parasite diversification and antagonistic coevolution, I highlight that coevolution is neither necessary nor sufficient in order to establish a co-phylogenetic pattern. The consequences of this fact for the interpretation of the presence or absence of a co-phylogenetic pattern are discussed.**

# Introduction

Since the idea of coevolution as a relevant concept for the study of evolutionary ecology of communities was introduced by Ehrlich and Raven (1964), there has been a vast literature around this concept. The first formal definition of coevolution can be attributed to Janzen (1980): coevolution is a change of traits in a first population as a response to the trait value of a second population, *followed by* a change of trait in the second population in response to the new trait value in the first (different modalities of trait dynamics have been described since then, Gandon et al. 2008). Much emphasis is put on the fact that the existence of an interaction *is not* indicative that the species have coevolved (it can reflect a recent host acquisition, for example). Based on this, Janzen recommends a lot of cautiousness when using the word *coevolution*, and it is worth asking if more than 45 years later, we are being cautious enough.

It is a widely appreciated fact that some symbiontic or interacting systems display a co-phylogenetic pattern. In these situation, (1) the phylogeny of one group of species mirrors the phylogeny of the other group, and (2) species from one group tend to interact with species occupying a position similar to their own on the opposite tree (Fahrenholz 1913). Although exemples of pairs of trees conforming exactly to this rule are scarce, a significant cophylogenetic structure was reported for a variety of systems (some of which are revied by Nieberding, Jousselin, and Desdevises 2010), including monogeneans parasites of Mediterranean sparids (Desdevises et al. 2002) and African cichlids (Mendlova et al. 2012), aphids and their bacteria (Jousselin, Desdevises, and Coeur d’acier 2009), algae and prasinoviridae (Clerissi, Desdevises, and Grimsley 2012), and mimetic heliconid butterflies (Hoyal Cuthill and Charleston 2012). In other instances, phylogenetic analysis failed to demonstrate congruence of the two trees, such as in millipedes and mites (Swafford and Bond 2010). The accumulating evidences that species interactions (notably antagonistic ones, such as hosts-parasites) often resulted in partners sharing a phylogenetic structure was instrumental in developing the notion of *tangled trees* [@Page1994;@Page2003]. It posits that because hosts and parasites species are engaged in intimate interactions with one another, and often have a reciprocal effect on one another fitnesses, we expect that their evolutionary history will show some degree of similarity. A the macro-evolutionary scale, this can result in the host phylogeny and the parasite phylogeny looking alike. In a significant number of these studies, the significance of the cophylogenetic pattern is equated to the likelihood that the host-symbiont system considered is coevolved. Indeed, this trend is clear when looking at the bibliometry (Fig. **xx**).

Historically, looking for correspondences in the phylogenetic history of hosts and parasites to infer a coevolutionary history stems from two central ideas:

1. Both partners (the parasite and its host) represent a strong selective force for one another, given that their interaction has important consequences for their fitness and life-traits (Crofton 1971). They should hence influence each other evolutionary histories, to the point where evolutionary events in one of the partners (the host or the parasite) should trigger an evolutionary event in the other one.
2. One of the species is using the other as its environment, and as such, we should expect it to track this environment in the phylogenetic space, much in the same way that plants and animals track their environmental niche in space. A consequence of this would be that the phylogenetic tree of the exploiting species will mimic its of the exploited species, if only because host speciation will result in "allopatric" speciation in the parasite (Le Gac and Giraud 2004).

The current theoretical framework surrounding the notion of coevolution (Thompson 1994; Thompson 2005) relies on correlation between coevolved traits (Nuismer, Gomulkiewicz, and Ridenhour 2010), and correlations between traits values and fitness (Gomulkiewicz et al. 2000; Gomulkiewicz et al. 2007), which results in reciprocal selection. Although it makes predictions on the diversification of coevolving lineages (Yoder and Nuismer 2010), it is an inherently micro-evolutionary phenomenon. Yet, Thompson (1999) states that coevolution can bridge the gap between micro and macro-evolutionary scales, specifically by focusing on the relationships between traits values and diversification patterns. Phylogenetic tracking (parasites speciate in response to host speciation) can happen without reciprocal selection (several examples are given in the second part). On the contrary, novel hosts with trait values allowing them to escape their parasites should be advantaged. In this situation, there will be no co- diversification, and we predict a loss of the phylogenetic similarity between hosts and parasites. In this perspective, there are a large number of situations in which (i) co-phylogenetic structure can happen without coevolutionary dynamics (*i.e.* no reciprocal selection), and (ii) reciprocal selection will result in the loss of the co-phylogenetic structure.

More recently, the interactions between coevolutionary processes and phylogenetic structre (including trait conservatism and the phylogenetic determinism of species interactions) received an increased amount of attention in the emerging field of community phylogenetics. Cavender-Bares et al. (2009) showed that the phylogenetic structure of victims species can be significantly altered by enemies. Specifically, two factors are important in determining the shape of the current victim phylogenetic structure: the conservation (or convergence) of defenses, and the generality of enemies. Combination of these two factors can alter both the structure of the victim phylogeny, and the extent to which (defense) traits are conserved through it. @mouquet\_ecophylogenetics\_2012 emphasized that phylogenetic information is critical to understand the current structure of interaction networks, as long as we are able to understand (i) the current structure and evolutionary history of traits, and (ii) how this trait structure relates to species interaction.

With these elements in hand, it appears that understanding the relationship between the co-evolutionary process and the phylogenetic structure of host- parasite assemblages is an important research perspective. The literature mentioned in this introduction suggest that (i) a co-phylogenetic structure can emerge without co-evolutionary dynamics, and (ii) coevolutionary dyanmics can impede the establishment of a co-phylogenetic structure. In this contribution, I review empirical and theoretical studies to further clarify the interactions between the two. I challenge the idea that detecting a co- phylogenetic structure allows concluding that coevolution is occuring. I do so by showing that coevolution is neither necessary (co-phylogenetic structure can emerge outside of coevolving interactions), nor sufficient (coevolution can lead to non-matching phylogenies), to establish a cophylogenetic pattern. I briefly discuss the consequences of these facts for the methodology on co- phylogenies. Finally, I explore the role of several coevolutionary scenarios in preventing the establishment of a co-phylogenetic structure, and show that they have predictable consequences on the observed co-phylogeny. I conclude by recommending that we do away with the idea that co-phylogeny implies coevolution (and that conversely, the lack of a co-phylogeny implies no co- evolution), as it can severely undermine our ability to understand the evolution of defense mechanisms in coevolved interactions.

# Coevolution is neither necessary nor sufficient

In this section, I propose that cospeciation and coevolution should be considered as two distinct processes. One (cospeciation) can arise as a consequence of the other, but neither is coevolution necessary, nor sufficient, in triggering the establishment of a co-phylogenetic pattern. I illustrate these aspects through various empirical examples. In the first part, I review results form phylogeographic analyses, showing that the phylogeographic history of the host can be a major driver of the parasite phylogenetic structure. This shows that co-phylogeny can emerge even when there is no evolutionary interaction between the host and the parasite. In the second part, I show that even in the presence of coevolution, other factors can blur the co-phylogenetic pattern. Taken together, these elements strongly indicate that equating the presence of a co-phylogenetic pattern to coevolutionary history (or the other way around) is profoundly misleading.

## Coevolution is not necessary: cospeciation without coevolution

The importance of spatial processes in the establishment of a co-phylogenetic pattern has been recognized for a long time. Phylogenetic reconstruction of amphibians and their parasites from the genus *Polystoma* (Bentz et al. 2006) established that co-speciation events were for a vast majority well explained by the acquisition of new host habitats at a large (continental) biogeographic scale. A similar situation was reported in a variety of other systems. The highly significant cophylogenetic structure of toucans and chewing lices is explained by biogeographic events (Weckstein 2004). Peterson, Pfister, and Bell (2010) show that fungal parasites of the southern beech from the genus *Cyttaria* show some degree of cophylenetic structure with their host, despite having a wide host range. However, most of the clear co-divergence events can be attributed to biogeographic events, most notably the breakup of Gondwana. In these examples, the host and parasite phylogeny display a good level of congruence, but the mechanism through which this congruence emerges has nothing to do with the coevolutionary process.

Looking into more details into the biology of these systems, it is possible to better understand the properties of host-parasites associations having or not a cophylogenetic structure. Dispersal-limited parasites with a narrow host- range should be expected to display a better phylogenetic congruence with their hosts. Generalists parasites, or those able to disperse over long distances, should have a distinct phylogeny from their hosts. This is particularly striking in the analyses of Jackson and Charleston (2004): viruses with (mostly) vertical transmission are more phylogenetically congruent with their hosts than are viruses with (mostly) horizontal transmission. It must also be noted that higher dispersal can allow the evolution of a wider host range, as a more heterogeneous population of hosts is encountered (Poisot et al. 2011), which will (as illustrated later on) decrease the likelihood that a cophylogenetic signal is detected.

In the most extreme case, a perfect co-phylogenetic pattern is expected when host speciation events are completely independent of the parasites. Each time two host populations speciate because of distance separation, if parasite dispersal is low, a parasite speciation event is expected to occur. Note that this makes no assumption about trait matching between the host and the parasite, and can occur even if the parasite has almost no fitness effect on its host. In this case, concluding that the perfect co-phylogenetic pattern indicates coevolution is deeply misleading. Note that this can also arise in environments wherein the reciprocal selection is weak (the so-called "coevolutionary cold-spots"); in these environments, there is no correlation between traits values and fitness, and even though the two species can co- evolve, no coevolutionary dynamics is established (*i.e.* the direction of trait change of one species with regard to the other species trait value appears random). In these environments, parasites can co-speciate with their hosts, but coevolution is not the mechanism driving the co-speciation.

## Coevolution is not sufficient: coevolving without cospeciating

For coevolution to result in a co-phylogenetic pattern, a number of conditions must be met. First, the pathogen must be able to trigger a speciation in its host. Second, the pathogen population must divide on the two incipient host populations, and undergo a speciation event. These two criteria allow the emergence of a co-phylogenetic structure. Third, there should be limited potential for either intra-host diversification, host acquisition (range expansion), or host switch. This ensures that the co-phylogenetic structure is maintained. There are documented examples of potentially coevolving systems showing no phylogenetic congruence (for a list, see Johnson and Clayton 2004). In this section, I review theoretical and empirical studies highlighting the mechanisms through which coevolving systems can fail to show a co-phylogenetic pattern.

Yoder and Nuismer (2010) models a variety of ecological situations (mutualism, parasitim, and different underlying trait matching scenarios) to find out when coevolution should lead to diversification. One of their most striking results is that, when the interaction relies on increasingly stringent trait matching, coevolution leads to a bimodal distribution of host traits, but to a unimodal distribution of parasite traits, although with a great variance. In other words, the parasite selection pressure triggers the emergence of two host quasi-species, but the parasite itself do not speciate, it only increases its phenotypic variance. Weitz, Hartman, and Levin (2005) reported similar results in a model of coevolutionary arm-races in a microbial system. Both these studies agree on the fact that many coevolutionary interactions may not promote diversification.

Single traits models as used by Yoder and Nuismer (2010) and Weitz, Hartman, and Levin (2005) are more conservative in their estimates of when speciation can occur. However, Gilman, Nuismer, and Jhwueng (2012) reached similar conclusions using a more realistic multidimensional trait space. As the number of traits (hence the complexity of the underlying physiological, behavioral, etc, processes involved in attack/defense) increased, the chance of the victim escaping its enemy became higher. From a mechanistic point of view, this result makes sense if defending against an enemy is easier than attacking a victim, or if the evolution of defense mechanisms is less constrained than the evolution of attack mechanisms. For example, a host can avoid a parasite through several non-mutually exclusive ways: behavioral adjustment, specific adaptations, or interactions with protective symbiont. For example, plants defend themselves against herbivores through biomechanics means (Whitney and Federle 2013), rendering them unpalatable, but also evolved specific signaling pathways to attract parasitoids to defend themselves (Wei et al. 2007).

Finally, recent empirical findings on bacteria-phage systems, specifically the system formed by *Pseudomonas fluorescens* and its phage, can shed some light on the fact that co-diversification is seldom the rule in coevolving systems. Poullain et al. (2008) investigated the evolution of host range of bacteriophages on bacterial hosts in evolving (the host do not evolve) and coevolving (both the host and the parasite evolve) interactions. Coevolution resulted in a higher generalism of phage, with a clear nested pattern of interactions. This same nested pattern was reported for field isolates of this (Poisot, Lounnas, and Hochberg 2013) and other (Koskella and Meaden 2013) systems. These systems are well known for displaying coevolutionary dynamics in their natural habitats (Gomez and Buckling 2011; Koskella et al. 2011).

# The impact of coevolution on the co-phylogenetic structure

As mentioned in the introduction, coevolution requires correlations between the traits of one partner and both its fitness and the fitness of the other partner, though correlation itself do not necessarily result in coevolution (Nuismer, Gomulkiewicz, and Ridenhour 2010). Co-speciation, which can be revealed by the existence of a co-phylogenetic pattern, emerges when an evolutionary event (*i.e.* speciation) in one partner results in speciation in the other partner. The initial speciation even can be induced spatial constraints, niche differentiation, or can be triggered by the interaction with the parasite. In the previous part, I reviewed studies showing that (i) a co-phylogenetic structure can emerge in the absence of coevolution, and (ii) coevolutionary dynamics are not necessarily expected to result in a co-phylogenetic pattern. In this part, I will review several events likely to happen during host- parasite coevolution, and how they will blur the co-phylogenetic pattern. Specifically, I show that these events have predictable consequences on the phylogenetic structure of hosts and parasites, and the distribution of interactions in the phylogeny. Accounting for these events will likely help refine our understanding of the interactions between coevolutionary dynamics and the emergence of a co-phylogenetic structure.

The emergence of perfectly matching phylogenies requires that each host speciation event is matched by a parasite speciation event (and reciprocally), while no other evolutionary events happen [@Page1994]. Any deviation from this situation will result in a decrease of the matching between the host and parasite phylogenies. Broadly speaking, one can describe four categories of evolutionary events decreasing the matching between phylogenies: intra-host speciation (independent speciation of the parasite), failure to cospeciate (independent speciation of the host, with one incipient species non infected by the parasite), host acquisition and host switch, and finally parasite extinction. In this part, I show how coevolution can, and under some circumstances, is expected to, result in the four previously described events, thus preventing the establishment of a cophylogenetic structure.

## Coevolution can trigger parasite speciation or extinction

quite easy

adaptive dynamics

poullain

Simmons, Holmes, and Stephenson (2010) demonstrated experimentally that the genetic diversity of Zucchini yellow mosaic virus is high during infections, which can help in establishing a bank of strains with the ability to overcome some aspects of host defense. Interestingly, although mutations within the plant had a short residence time (in the experiment, most mutations are only observed once) due to them being mostly deleterious, the genetic structure of the ZYMV within aphid vectors is high. Accumulation of the virus in aphids is likely to introduce a strong bottleneck, and thus to be responsible for the establishment of several viruses lineages in the host population.

A modelling study by A. Best et al. (2010) suggests that "true" cospeciation events can be rare. Through simulating the co-evolution of a host-pathogen system, they were able to find that although epidemiological feedbacks were able to generate diversity both in the host *and* the parasite, this apparent cospeciation often followed the same scenario. First, there is a divergence of the host population, in which case the parasite do not diverge, but tracks the ancestral lineage, with the possibility of infecting the incipient host. Second there is a divergence of the parasite in two strains, each tracking one of the new host strains. This would correspond to "delayed cospeciation". However, given enough time and bifurcation events, the outcome of this process is the maintenance of hosts with a continuum of resistance values, and of parasites with a continuum of infectivity values. This result helps understanding why some coevolved systems, such as bacteria-phage interactions, display a "nested" structure (Flores et al. 2011), with hard to infect hosts being infected only by the most infectious parasites, and conversely.

## Coevolution can trigger host-switch

A major aspect of co-phylogenetic structure is that hosts and parasites should keep a one-to-one association, *i.e.* a parasite should interact with an host matching its position on the other tree. Yet, there is accumulating evidence that host-switch (*i.e.* the use of a novel host over time), and more broadly host rang expansion (*i.e.* the ability to infect a novel, additional host) are likely outcomes of the coevolutionary process. When host-switch events are accounted for by co-phylogeny reconstruction software, it is most often under the form of the spontaneous acquisition of a new host. @hall\_bacteria- phage\_2010 present experimental results seriously challenging of this view. Over long-term coevolution, parasites should evolve toward a greater generalism. Under this perspective, the spontaneous acquisition of a novel host is less likely than the progressive broadening of the host range. This broadening is made possible by (i) a shift in the selection regime over time, favoring fluctuating dynamics (in which generalism is basically cost-free) instead of arm races (Hall et al. 2011), and by (ii) the fact that compensatory mutations accumulate over time, reducing the pleiotropic costs of the progressive broadening of the host range (Scanlan et al. 2011).

With regard to these results, the fact that generalist pathogens have a higher phenotypic and genetic variability makes more (evolutionary) sense. @kaci\_chaouch\_host\_2008 report that within the genus *Lamellodiscus*, generalist species have more variability than specialist species both in terms of morphology and genetics. A frequently proposed hypothesis is that generalists parasites are more variable to accomodate the heterogeneity of their different hosts (Desdevises, Morand, and Legendre 2002). However, all ecological variables being equal, this can also reflect the fact that these species are the outcome of a longer coevolutionary process. In the *Lamellodiscus* group at least, this is contradicted by the fact that generalist species tend to be derived, rather than ancestral (Desdevises, Morand, and Legendre 2002). Given the importance that is attributed to host acquisition events in separating ecological and historical effects on the evolution of specificty (Morand et al. 2002), and the disagreement between predictions derived from coevolutionary studies and the phylogenetic distribution of generalism, it seems that the evolution of larger host ranges is an important point to clarify the coevolutionary consequences on phylogenetic structures.

Several evidences, however, point to the fact that these events can result in matching phylogenies. Jackson and Charleston (2004) and de Vienne, Giraud, and Shykoff (2007) observed that, as long as parasite acquire new hosts which are phylogenetically related to their current ones, the chances that a co- phylogenetic structure is detected increases. This is especially true if the parasite evolves faster than the host, in which case the host phylogeny serves as a "template" that will guide the parasite diversification.

## Coevolution can trigger host diversification

Hosts are selected on their ability to avoid, escape, and resist their parasites. This led to an important literature on the selection for "enemy-free" spaces, *i.e.* environments (or combination of traits) in which the host is freed from the selective and demographic pressure of its enemies (Jeffries and Lawton 1984).

@bernays\_on\_1988

@atsatt\_lycaenid\_1981

@brown\_role\_1995 observed that when a new host plant emerges, gallmakers tend to select preferentially the ancestral one to lay their eggs. In this perspective, the fact that the new host is not exploited is not a "failure" to cospeciate, but rather reflects the fact that exploiting the new host will result in a loss of performance for the enemy.

The question of diversification through coevolution has been extensively studied using microbial systems in experimental evolution. Buckling and Rainey (2002) used *Pseudomonas fluorescens* SBW25 and a lytic phage to understand the consequence of coevolution with parasites on host speciation. The SBW25 strain has the ability to speciate in three "morphotypes", each specialized on a narrow set of microhabitats within a test tube (specifically, the interface with air, the liquid medium in the middle of the tube, and the anoxygenic zone in the bottom, P. B. Rainey and Travisano 1998). Buckling and Rainey (2002) report that coevolution *decreased* the frequency of sympatric (*i.e.* within a test tube) speciations, but *increased* the frequency of allopatric (*i.e.* across test tubes) speciation. The conclusion of this study is that coevolution can increase host diversity at a *regional*, but does not consistently does so at a *local* scale. Brockhurst, Buckling, and Rainey (2005) further refined this result, using phages of the *Pseudomonas aeruginosa* bacterium. When diversification occured, resistant hosts specialized on different ecological phenotypes, suggesting that their new combination of traits freed then from the pathogen pressure.

M. Boots et al. (2012) report important theoretical results. In a one-host, one-parasite system, it is possible to observe a bifurcation of host traits (transmissibility and susceptibility), even though the parasite is *not* evolving at all. This happens when there is inheritable variation in both traits in the hosts. Specifically, diversity in hosts traits is favoured when the risk of a related individual transmitting the disease is high. Under these scenarios, the interactions between individuals with contrasted levels of (*e.g.*) resistance is not random: individuals with high resistance tend to interact between themselves, just as individuals with high susceptibility will do. This result shows that even when speciation of a paratized host occurs as a reponse to parasitism, this can happen without any sort of coevolutionary dynamics.

## Coevolution can trigger parasite extinction

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# Conclusions

The literature reviewed here point to an interesting problem: the relationship between the coevolutionary process, and the phylogenetic structure of hosts- parasites associations, is expected to vary with scales. At large taxonomic or temporal scales (*e.g.* across the species in a genus, or genus in a larger taxa), non-coevolutionary factors are expected to favor the emergence of a co- phylogenetic structure. Such is the case in the several systems mentioned, for which co-speciation events reflected large-scale biogeographic events. Conversely, and at a finer taxonomic or temporal scale (*e.g.* closely related species within a genus), the output of the coevolutionary process is expected to be a deviation from co-divergence, with hosts and parasites phylogenetic structures looking different. In short, at a "macro" scale, we expect the phylogenies of hosts and their parasites to look similar, although the cause of the similarity is not the coevolutionary process. At a "micro" scale however, there is no reason to expect, except under particularly restricted scenarios, that the coevolutionary process will result in matching phylogenies. This calls for more attention to the scale, both temporal, spatial, and taxonomic, at which the concept of coevolution is applied.

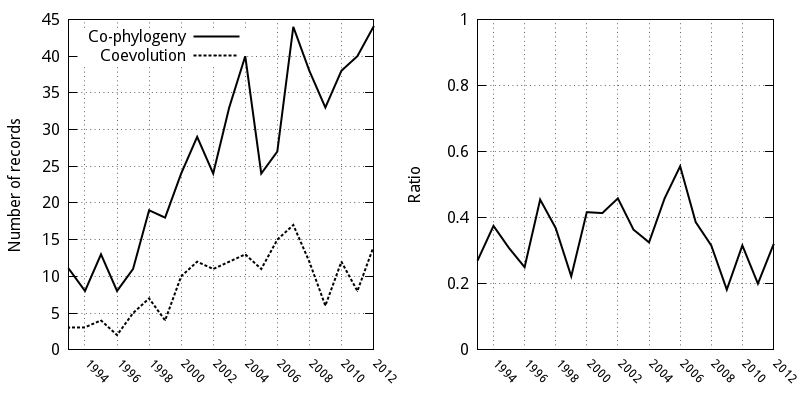
heterogeneity -- papiers lamello yves, moi, kaci-chaouch

However, there is a more pressing, and potentially problematic issue. Assuming that the existence of a co-phylogenetic structure indicates a coevolutionary past can hinder our ability to understand the evolution of host defense mechanisms. Early in the study of coevolution, **janzen** pointed out that current defense mechanisms most likely evolved in response to past enemies. In the field of bacteria-phage interactions, this proposition received some empirical support. CRISPRs, short genomic sequences of bacteria used for defense against contemporary phages, are most likely fragments of the genome of phage exploiting the ancestral bacteria **WEITZ**. The use of CRISPRs in defense was dubbed the *ghost of coevolution past* **VALE**, and illutrates that the contemporary defense mechanisms may not be a response to the contemporary enemies.

assuming that cophylo = coevo can hinder our understanding of how defense evolve: janzen (evolved IN THE PAST), cavender-bares

**FINAL POINT**: need to better integrate the spatial/temporal turnover (Alvarez et al. 2010)

# Figures



Bibliometric analysis of the cophylogeny-coevolution association. Left: Number of articles published each year (data from Web of Knowledge) with cospeciation, codivergence, or cophylogeny in the text (plain line), and subset of these articles also mentioning coevolution (dashed line). Right: proportion of the papers about cophylogeny, cospeciation or codivergence mentioning coevolution. This ratio has been stable (around 0.34) since the 1990s.

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