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A Field Synopsis, Systematic Review, and Meta-analyses of Cophylogenetic Studies: What Is Affecting Congruence between Phylogenies?

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Abstract

We conducted a field synopsis and systematic meta-analysis of studies that carried out cophylogenetic analyses using algorithms and available software. We evaluated the influence of three factors—namely, cophylogenetic method, association, and ecosystem type—on the outcome of the analyses, that is, the degree of congruence between phylogenies of interacting species.

The published papers were identified using 4 different databases and 13 keywords; we included all studies for which statistical approaches to compare phylogenies (cophylogenetic analyses) of interacting lineages were used. After the initial screening, 296 studies were selected to extract response variable (outcome of the cophylogenetic analyses, i.e., congruent, incongruent, or both) and coded information of the three selected factors (method of analyses, association, and ecosystem type). The final dataset included 485 entries. The data were analyzed using the chi-square test and regression techniques.

We provided evidence for the outcome to be strongly dependent on the method; in particular, we are confident in expecting that phylogenies in mutualistic associations are congruent when using global-fit methods and in parasitic associations are incongruent when using event-based methods. Using a mixed-model approach, the most parsimonious model includes a non-nested structure of two factors (method and association), with a higher probability for parasites, herbivores, and pollinators to provide incongruent results.

We discuss the use of an alternative theoretical framework, the Stockholm paradigm (SP), to reanalyze published raw data, and the integration of the cophylogenetic analyses into a workbench (DAMA protocol, the policy extension of SP) aimed to anticipate emerging infectious diseases.

Keywords: cophylogeny, codiversification, DAMA protocol, herbivory, host, pathogen, pollinator, Stockholm paradigm

Introduction

Coevolution, cospeciation, and codivergence, concepts often wrongly used interchangeably, embrace mechanisms that are thought to be driving much of the diversity in the tree of life (Hembry et al., 2014; Laine, 2009; Raguso, 2021). Since the founding idea by Darwin about the factors that generate diversity—"namely, the nature of the organism and the nature of the conditions. The former seems be much more the important" (Darwin, 1872)—a relentlessly increasing number of papers have tried to build theories and operational framework for the assessment of the processes that shape the associations among interacting species. The idea of cospeciation seems to have originated in the early twentieth century (Fahrenholz, 1913; Kellogg, 1913) with a seminal intuition about parasite phylogenies often mirroring host phylogenies. Using parasitic associations as study models, more than half a century later the term *cospeciation* was defined by Brooks as "cladogenesis of an ancestral parasite species as a result of, or concomitant with, host cladogenesis" (1979). Interestingly, in his original work, Brooks provided an interpretation of the concept of coevolution by concatenating two main processes, co-accommodation and cospeciation, the former being "the mutual adaptation of a given parasite species and its host(s) through time [. . .] co-accommodation refers to the relationship between a parasite species and its host during the period in which the parasite exhibits no cladogenesis" (Brooks, 1979). Concurrently, the idea of coevolution stemmed from the studies by Ehrlich and Raven (1964) on plant-insect herbivore interactions that used a primordial method for coevolutionary studies using phylogenetic information. In doing so, they provided evidence for insect-plant associations being shaped by similarities in plant chemical cues that "do not necessarily indicate the plants' overall phenetic or phylogenetic relationships." A more articulated, formal definition of coevolution arrived later with Janzen (1980) as "an evolutionary change in a trait of the individuals of a population, followed by an evolutionary response by the second population to the change in the first" and further developed by Thompson (1982, 1994). Subsequently, the term cospeciation has been revised repeatedly to expand its application to various types of associations, changing its interpretation to support specific testing models, which have included several other processes (e.g., host switching, independent speciation or duplication, extinction, failure to diverge, or missing the boat). Among them, some examples include:

> Cospeciation is the joint speciation of two or more lineages that are ecologically associated, the paradigm example being a host and its parasite. (Page, 2003)

> Process whereby a symbiont speciates at the same time as another species (this may result from vicarious events or from narrow host specificity). This is a pattern and does not assume causal relationships. (de Vienne et al., 2013, glossary)

> The process in which a lineage speciates as a result of another speciation event: more specific than codivergence, it is concerned only with species. (Charleston, 2016, glossary)

Along with the increasing controversy about how to define and concatenate all these concepts and processes in a single unified theory, various methods emerged to test which of the processes play the major role in shaping interacting communities. The most popular approach is to use cophylogenetic analyses—that is, the comparison of phylogenies of interacting lineages to uncover patterns of mutual descent with or without mutual modification or mutual speciation (D.R. Brooks, pers. comm.). In this area of comparative phylogenetics, the main aim is to test the congruence among phylogenies and the significance of the cophylogenetic structure. Brooks provided the first formal method to quantify the degree of cospeciation and co-accommodation (Brooks, 1979, 1981, 1985, 1988, 1990). Nevertheless, simultaneous cospeciation does not necessarily imply dependency and mutuality of the modifications and speciation. Unwarranted assumptions claiming that the congruence between phylogenies and the time estimates may be conclusive for the actual cospeciation reconstruction (i.e., cladogenesis of an ancestral species because of the cladogenesis of another interacting species) among taxa were often inherited without reflection (de Vienne et al., 2013). Even in some cases for which cospeciation may seem likely (such as vertically transmitted symbionts and their hosts), prior assumptions may unnecessarily cloud the conclusions of cophylogenetic studies. These assumptions support a causal inference, and few examples of methods based on deductive reasoning are available (e.g., Phylogenetic Analysis for Comparing Trees—PACT algorithm, Wojcicki and Brooks, 2004, 2005). This biased assumption builds upon the reasoning that the pathogen phylogeny mirrors host phylogeny. As a result, pathogens will always follow the evolutionary history of their hosts—that is, they will speciate as a consequence of host cladogenesis (or causative cladogenesis), and they will go extinct when they are not be able to adapt to their host, or they will duplicate sympatrically into the same host. In this scenario, host switches are rare, and the pathogen tends to be specialized on a single host species. A major consequence was the emergence of an unrealistic optimism about the very low likelihood that a pathogen would suddenly acquire a new host, as cospeciation, revealed by cophylogeny, is the dominant process. This process would represent an evolutionary firewall that would make emerging infectious diseases (EIDs) rare events; however, an increasing body of literature is providing evidence for host switching being as probable as other processes with no extra costs (Brooks et al., 2019; Boeger et al., 2022; Trivellone et al., 2022).

Previous cophylogenetic methods are grouped in two main categories: (1) global-fit and (2) event-based. Global-fit methods quantify the degree of congruence between phylogenies and significance of the overall associations or of each single link. These methods are based on statistical tests and do not infer about the importance of different evolutionary processes possibly involved and revealed by congruent or incongruent phylogenies. Event-based methods measure the fit between phylogenies and define the likelihood for numbers of single evolutionary events that may have caused the observed associations. These methods in general deliver the most probable reconstruction of the cophylogenetic history of the interacting lineages. All methods in both categories have computational or theoretical limits, and researchers often apply several of them to the same data set to take advantage of desirable characteristics of each.

Recently, a plethora of revisionary studies provided comprehensive discussion on terminology and theoretical approaches underlying the cophylogenetic analyses (Hoberg and Brooks, 2008, 2015; Suchan and Alvarez, 2015; Charleston, 2016; Hembry and Althoff, 2016; Marquis et al., 2016; Kariñho Betancourt, 2018; Doña and Johnson, 2019; Harmon et al., 2019; Morris and Moury, 2019; Maron et al., 2019; Sagoff, 2019; Zohdy et al., 2019; Blasco-Costa et al., 2021; Medina et al., 2022). Other papers provided overviews of statistical frameworks to test for coevolutionary diversification or available cophylogenetic methods (Brooks, 2003; Charleston, 2003; de Vienne et al., 2013; Althoff et al., 2014; Charleston and Libeskind-Hadas, 2014; Poisot, 2015; Filipiak et al., 2016; Martínez-Aquino, 2016; Groussin et al., 2020; Hernández-Hernández et al., 2021). Historically rooted and consistent with specialization on single taxa, several reviews evaluated overall patterns of codiversification, cospeciation, and coevolution of various groups of organisms representing specific association types, grouped as parasitic, mutualistic, and commensal (Clayton et al., 2004; Jackson, 2004; Aliouat-Denis et al., 2008; Mattiucci and Nascetti, 2008; Araújo and Hughes, 2016; Arbuckle et al., 2017; Anderson and de Jager, 2020; Anholt, 2020).

In the present review, we evaluated all previous papers that compared phylogenies, concurrent diversification, and mutual adjustment of interacting lineages. We performed an updated field synopsis for the evolution of cophylogenetic studies applied to symbiotic (*sensu lato*) associations. We investigated the influence of three factors, including **cophylogenetic method**, **association**, and **ecosystem type**, on the outcome of the statistical cophylogenetic analyses. To achieve this objective, we addressed the following questions:

(Q1) How has the usage of words such as "cophylogeny" and/or "codiversification" and quantitative cophylogenetic analyses of interacting lineages changed over time?

(Q2) What is the proportion of studies that yield congruent versus incongruent outcomes in cophylogenetic analyses with respect to the three factors of the present meta-analysis?

(Q3) Do cophylogenetic method, association, and ecosystem type significantly affect the outcome of cophylogenetic analyses?

Our hypotheses are mainly based on the field synopsis and are used in our meta-analysis as a baseline to compare alternative results (in particular for research question Q3). As the association type is concerned, parasitic association (Hartmann et al., 2019) and mutualistic or commensal associations (especially those that involve symbionts that are thought to be exclusively vertically transmitted, Bronstein et al., 2006; Groussin et al., 2020) show more congruent cophylogeny than expected by chance because the cospeciation events are thought to drive micro-evolutionary trajectories for these types of associations. A few alternative hypotheses were supported in the literature for parasitic associations, and evidence of incongruence was revised in Poulin (2021) (literature therewith). In addition, incongruence rather than congruence between phylogenies is expected to happen more often under a changing environment (Runghen et al., 2021), as also predicted by ecological fitting theory (Agosta, 2006; Agosta et al., 2010). In our meta-analysis, we considered herbivory as a special case for parasitic associations, a relationship that is hypothesized to show higher episodes of incongruences between phylogenies (as revised in Hoberg and Brooks, 2008). For pollination as a special example of mutualism, Hembry and Althoff

(2016) previously reported: "We find that most species-rich brood pollination mutualisms show significant phylogenetic congruence at high taxonomic scales, but there is limited evidence for the processes of both cospeciation and duplication, and there are no unambiguous examples known of strict-sense contemporaneous cospeciation." This finding is also in agreement with Lieuter et al. (2017).

We also hypothesized that global-fit methods may yield more congruent results than expected by chance because of the overuse during the last decades of distance-based cophylogenetic methods, which are prone to type I error (i.e., rejection of the H_0, independence between phylogenies, when it is true) (Balbuena et al., 2013). However, an alternative hypothesis is that event-based reconciliation methods may yield more congruent results because the assumption is that cospeciation is expected to be more likely than any other event, and the congruence is interpreted as evidence for cospeciation (Ronquist, 1995). We hypothesized that each main category has an idiosyncratic risk to provide either a congruent or an incongruent outcome. We further hypothesized that the ecosystem type has an influence on the outcome of the phylogenetic analyses regardless of the category of the method used because aquatic habitats are considered more stable compared to terrestrial habitats, and the interaction between lineages would be the major constraint with which to cope.

Based on the results, we suggest a reanalysis of published raw data sets using an alternative theoretical framework (i.e., the Stockholm paradigm [SP]) that will aid in shedding light on the fundamental biological mechanisms involved in coevolutionary processes. We also discuss how to integrate cophylogenetic analyses into the policy extension for SP—that is, DAMA (Document, Assess, Monitor, Act), which is a workbench for the implementation of strategies to anticipate EIDs.

Methods

To synthesize and evaluate the influence of three main factors on congruence between phylogenies of interacting lineages estimated in the available literature, we used a systematic review approach followed by a meta-analysis. We focused our field synopsis on a systematic and quantitative global-level overview of the current state of knowledge from studies that used different statistical approaches to compare phylogenies of two groups of organisms. We followed the established guidelines in Moher et al. (2009) to answer our three main questions: in particular we carried out a systematic search for prior studies and then we appraised and collected relevant coded data for the final statistical analyses. In Table 1, a list of the methods used in the selected studies is provided. Although our aim was not to revise the available methods, this overview largely reflects the revision of methods reported earlier in other reviews (e.g., de Vienne et al., 2013) and has been here further updated.

Search strategy

We carried out a literature search using four different databases: PubMed, ScienceDirect, Scopus, and Web of Science. The databases were searched on 12 February 2022. In order to eliminate the high ambiguity generated by some keywords used singularly and to include the maximum number of relevant studies, we used a defined set of single keywords and combinations of them. We selected 2 main keywords, "cophylogeny" and "codiversification," and 11 companion keywords were linked to them using the logical operator "AND" as follows:

"cophylogeny AND coevolution AND symbiosis"
"cophylogeny AND generalist"
"cophylogeny AND herbivore"
"cophylogeny AND host AND cladogram"
"cophylogeny AND host AND switching"
"cophylogeny AND pathogen"
"cophylogeny AND phytophagous"
"cophylogeny AND pollinator"
"cophylogeny AND specificity"
"cophylogeny AND symbiosis"
"codiversification AND coevolution AND symbiosis"
"codiversification AND generalist"
"codiversification AND herbivore"
"codiversification AND host AND cladogram"
"codiversification AND host AND switching"
"codiversification AND pathogen"
"codiversification AND phytophagous"
"codiversification AND pollinator"
"codiversification AND specificity"
"codiversification AND symbiosis"

Papers written in other languages were evaluated if an abstract in English was available. Additional studies from the gray literature recommended by experts were also considered.

Collection, screening, and eligibility

To appraise a paper's relevance to the three questions of our review, we first compiled a script written in R for importing and handling BibTeX files (using revtools v. 0.4.1 [Westgate, 2019] and rbibutils v. 2.2.8 [Boshnakov and Putman, 2022] R packages) downloaded during the database search (Figure 1, step 1).

Table 1. List of analytical methods and algorithms used for the cophylogenetic analyses in the 296 papers revised in this study. Ref., Reference; Cat., category of the cophylogenetic method used; Subcat., subcategory of the cophylogenetic method used.

Method[1]	#Pap[2]	Ref.	Cat.	Subcat.	Software	Ref.
Jane	138	Conow et al., 2010	Eb	Reconciliation	JANE	Libeskind-Hadas, 2019
ParaFit	114	Legendre et al., 2002	Gf	Distance-based	copycat	Meier-Kolthoff et al., 2007
					ape in R	Paradis and Schliep, 2019
					AxPARAFIT	Stamatakis et al., 2007
PACo	72	Balbuena et al., 2013	Gf	Distance-based	*paco* in R	Hutchinson et al., 2017
TreeMap	60	Page, 1994	Eb	Reconciliation	TreeMap (v. 1, 2, 3)	Charleston, 2012; Charleston and Page, 2002
CoRe-PA	22	Merkle et al., 2010	Eb	Reconciliation	CoRe-PA	SICSG, 2022a
Treefitter	12	Ronquist and Nylin, 1990	Eb	Cost-based	TreeFitter 1.3b1	Ronquist, 2002
Anc. Rec.	10	—	Gf		Mesquite	Maddison and Maddison,
2021						
					corHMM in R	Beaulieu, 2017
					SIMMAP	Bollback, 2006
					RASP	Yu et al., 2013, 2015
Mantel test	9	Mantel, 1967	Gf	Distance-based	Fstat 2.9.4	Goudet, 2002
					vegan in R	Oksanen et al., 2015
SH	7	Shimodaira and Hasegawa, 1999	Gf	Topology-based	PAUP*4.0beta	Swofford, 2001
					CONSEL ver 01.j	Shimodaira, 2002
BF	3	Jeffreys, 1961	Gf	Topology-based	MrBayes	Ronquist et al., 2012
Icong	3	de Vienne et al., 2007	Gf	Topology-based	—	—
Network analyses	3	Ulrich et al., 2009	Gf	Topology-based	ANINHADO, MODULAR	Guimarães, Jr. and Guimarães, 2006; Marquitti et al., 2014
					NetworkX, ForceAtlas2	Hagberg et al., 2008; Jacomy et al., 2014
eMPRess	3	Santichaivekin et al., 2021	Eb	Reconciliation	eMPRess	Santichaivekin et al., 2022
ABC	3	Baudet et al., 2015	Eb	Reconciliation	Coala 1.2.1, AmoCoala	Baudet, 2021; Sinaimeri et al., 2022
nPH85	2	Penny and Hendy, 1985	Gf	Distance-based	NELSI in R	Ho et al., 2015
AU	2	Shimodaira, 2002	Gf	Topology-based	CONSEL ver 01.j	Shimodaira, 2002
ILD	2	Farris et al., 1995	Gf	Distance-based	PAUP* v4.0beta	Swofford, 2001
GLMM	2	Hadfield et al., 2014	Gf		*MCMCglmm* in R	Hadfield, 2010
ALE	2	Szöllősi et al., 2013a	Eb	Reconciliation	ALE program	Szöllősi et al., 2013b
					ALEml version 0.5	Szöllosi, 2022
Tarzan	2	Merkle and Middendorf, 2005	Eb	Reconciliation	Tarzan	SICSG, 2022b
KH	2	Kishino and Hasegawa, 1989	Gf	Topology-based	PAUP* v4.0beta	Swofford, 2001
TaPas	2	Balbuena et al., 2020	Gf	Distance-based	*Rtapas* in R	Llaberia-Robledillo et al., 2022
Moran index	1	Borcard et al., 2011	Gf	Distance-based	*vegan* in R	Oksanen et al., 2015
CF	1	Minh et al., 2020	Gf	Topology-based	IQ-TREE	Minh et al., 2020
PACT	1	Wojcicki and Brooks, 2005, 2004	Eb[3]		—	
Dendroscope	1	Scornavacca et al., 2011	Eb	Reticulation	Dendroscope v. 1–v. 3	Huson et al., 2007; Huson and Scornavacca, 2012
Trip	1	Critchlow et al., 1996	Gf	Distance-based	Trip in Python	Kuhner and Yamato, 2015
RF	1	Robinson and Foulds, 1981	Gf	Distance-based	*phangorn* in R	Schliep, 2011
SOWH test	1	Goldman et al., 2000	Gf	Distance-based	PAUP*4.0beta	Swofford, 2001
D index	1	Poulin, 2011	Gf	Distance-based	—	
Hom	1	Hommola et al., 2009	Gf	Distance-based	—	

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[1] Acronyms for methods: PACo: Procrustean Approach to Cophylogeny; ALE: Amalgamated likelihood estimation; Anc. Rec.: Ancestral status Reconstruction; SH: Shimodaira-Hasegawa test; BF: Bayes Factor test; CoRe-PA: Cophylogeny Reconstruction; AU: Approximately unbiased test; CF: Concordance factors; Icong: Congruence Index; Trip: Triplet; Hom: Hommola permutation test; TaPas: Random Tanglegram Partitions; RF: Robinson-Foulds distances index; KH: Kishino-Hasegawa (KH) test

[2] #Pap: Number of publications using the method for cophylogenetic analyses revised in this study.

[3] Molecular clocks and fossil information need to be incorporated into the PACT algorithm, according to Lieberman (Lieberman, 2001, 2003a, 2003b).

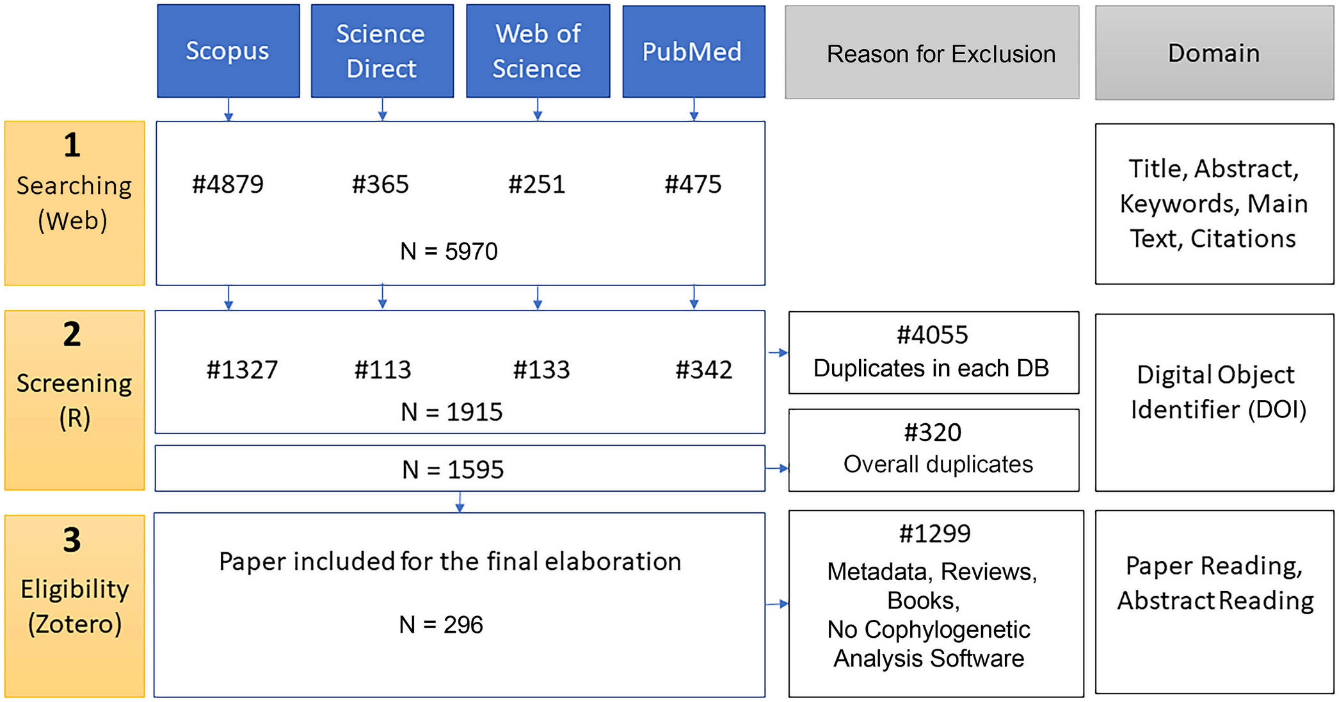

Figure 1. Three-step flow chart for the selection of publications to consider for the field synopsis, systematic review, and meta-analysis of this study.

During the initial screening, all the duplicates from the four databases were eliminated based on the Digital Object Identifier (DOI) (Figure 1, step 2). The performance of each database was summarized using the ggVennDiagram R-package v. 1.2.0 (Gao, 2021).

Initial evaluation was based on title and abstract, when available; however, for most of the published papers, examining the full text was necessary to retrieve relevant data. The criteria of inclusion (eligibility, Figure 1, step 3) were based on: (1) papers that used at least a pair of phylogenies (either molecular or morphological) to investigate the degree of congruence between groups of interacting lineages and (2) papers that either evaluated congruence or incongruence and/or attempted to reconcile phylogenies by using one or more of the cophylogenetic methods grouped in two main classes or categories (event-based and global-fit) based on statistical inference and formalized algorithms for which software or webtools are available.

The criteria of exclusion are summarized as follows: (1) monographs, syntheses, and literature reviews, not including original cophylogenetic studies, and (2) studies on methodological approaches that used either toy data, data from other papers (unless analyzed with different analytical approaches or software), or any other kind of simulation.

Data extraction and database creation

The selected published papers were scored according to three main explanatory variables (factors) related to the research questions: type of association (hereafter Association), type of ecosystem (Ecosystem), and type of method for cophylogenetic analysis (Method). Association is a categorical factor that includes five main levels: mutualistic (*mut*), commensal (*com*), parasitic (*par*), herbivory (*herb*), and pollination (*pol*). Mutualistic associations are those in which two different interacting species benefit from the relationship, commensal refers to one species benefitting while the other neither benefits nor is harmed, and parasitic occurs when one benefits and the other is harmed. While herbivory and pollination may be included, respectively, in the broader categories of parasitic and mutualistic/commensal, we kept them as separate levels to further explore the specific hypotheses of this study. To clarify these associations further, another level was created—*mixed*—to refer to association types that were defined by the authors as including more than one main level of the association type (e.g., organisms of one species that may be either parasitic or commensal with another species) or when the authors used a phylogeny for a broad group encompassing species from more than one type of association.

Ecosystem is a categorical factor with two levels: *terrestrial* and *aquatic*. Method is a categorical factor including an acronym for the cophylogenetic method used (Table 1). These methods were further grouped into two main levels: *event-based* and *global-fit*. Although Table 1 may not be an exhaustive list of all methods available to analyze cophylogeny, it includes the most popular algorithms and software used in the literature as of the year 2022. Moreover, our intent was not to evaluate the performance of each method but to analyze the contribution of the two main categories of methods on the outcome of the cophylogenetic analysis. For each factor, levels were assigned based on what the authors of the paper stated or on information retrieved from associated literature (i.e., from the reference list).

The response variable was scored as a categorical value based on the main **outcome** provided in the evaluated paper which resulted either from an analysis of overall fit (or fit of each single species-species association or link) between the two phylogenies and/or from either a reconciliation or cost-based method. Three outcomes were retrieved from the literature: the phylogenies were mainly congruent (*c*), mainly incongruent (*i*), or partially congruent and incongruent (*ic*). According to the literature evaluated, the last outcome is mainly driven by the specific methods of analysis used; for example, if a global-fit method suggests overall congruence between phylogenies, and the whole contribution is driven by few links, then some authors prefer to interpret the outcome as both congruent and incongruent.

When authors used more than one cophylogenetic method to analyze the phylogenies, we recorded the corresponding outcome for each analysis. The final dataset includes DOI, publication year, Method, Association, Ecosystem, and Outcome.

Statistical analyses

Field synopsis

To obtain an overview of the state of knowledge reflected by studies that addressed the topic of cophylogeny and codiversification (Q1), we considered the studies selected in the initial screening (N = 1,595, Figure 1, step 2). Using a paired t-test, we compared the sample means of two groups of studies: those that did not satisfy the eligibility criteria (i.e., discarded studies, N = 1,299) and studies retained for the meta-analyses which applied a quantitative cophylogenetic analysis (i.e., selected studies, N = 296). To evaluate the usage of cophylogenetic analyses over time, a linear regression was applied to publications that used cophylogenetic analyses expressed as a function of years. This was written as: Number of publications = $b_0 + b_1 \times$ Publication year, where b_0 is the intercept and b_1 is the slope.

Systematic review and meta-analyses

To study the relationship between the outcome of the analyses and each factor (Q2), we used a goodness-of-fit chi-square test and the Bayes Factor (Jeffreys, 1961) using the function "ggbarstats" from the ggstatsplot R-package v. 0.9.1 (Patil, 2021). For both tests, the null hypothesis is that two compared categorical variables are independent (H_0). The three categorical variables—outcome, cophylogenetic method, and association type—were first arranged in a structured contingency table using the function "structable" from the vcd R-package v. 1.4-9 (Meyer et al., 2006). Dependencies among variables were explored using contingency table frequencies and log-linear models as explained by Zeileis et al. (2007). To visualize expected frequencies, we used the "mosaic" function from the vcd R-package, which constructs a Cohen-Friendly association plot using a shading technique of the mosaic tiles using the Pearson residuals according to Friendly (1994).

To answer Q3, we fitted a generalized linear mixed model (GLMM) and specified a binomial error distribution and a logit-link function. We estimated the probability of receiving an incongruent (0) or congruent (1) outcome as a function of three predictors: cophylogenetic method, association, and ecosystem type. Our predictors were factors with two levels for the Method (*event-based* and *global-fit*), two levels for Ecosystem (*terrestrial* and *aquatic*), and six levels for Association (*mut*, *com*, *par*, *herb*, *pol*, *mixed*). Moreover, we included DOI (i.e., the study ID) as a nested random effect (a.k.a. mixed model, which allows the intercept to vary with DOI) to consider the nonindependence between observations within the same study that applied more than one method on the same dataset. In this way we consider the possible bias introduced by the tendency of the same dataset analyzed with different methods to provide the same result (pseudoreplication) (Hurlbert, 1984).

We fitted a total of six GLMMs: the full model, including all three predictors and their interactions, and five parsimonious models (Table 2). Thus, we accommodated cases in which inclusion of interactions among predictors and less powerful variables provided limited improvement in model fit.

In Models 1 to 5, we specified *global-fit*, *herb*, and *aquatic* as baseline, and the other levels of the factors were compared to this reference; in Model 6, we specified *global-fit* and *herb* only. We ranked our models using the second-order Akaike Information Criterion (AIC) scores, and the

Table 2. Candidate models for generalized linear mixed model (GLMM) analyses

Full model	Model 1 = Method * Association * Ecosystem + (1|DOI)
Partial interaction	Model 2 = Method + Association * Ecosystem + (1|DOI)
Partial interaction	Model 3 = Method * Association + Ecosystem + (1|DOI)
Partial interaction	Model 4 = Method * Ecosystem + Association + (1|DOI)
Additive model	Model 5 = Method + Association + Ecosystem + (1|DOI)
Simpler model	Model 6 = Method * Association + (1|DOI)

Note: * = interaction and additive effect between predictors, + = additive effect only, 1| = inclusion of random effect

final model with the lower value of AIC was selected. The AIC value indicates a more parsimonious model (Burnham and Anderson, 2002). The GLMM was fitted using "glmer"-function from the lme4 R-package v. 1.1-27.1 (Bates et al., 2015). Finally, we inspected the distribution of simulated model residuals using the DHARMa R-package v. 0.4.5 (Hartig, 2022). All statistical analyses were conducted using R software v. 4.1.2 (R Core Team, 2019).

Results

Field Synopsis

Overall, 5,970 published papers were selected using four different scientific literature databases that detected keywords and combinations of them in the title, abstract, keywords, main text, or reference list (Figure 1, step 1). After the initial search, the entire collection of BibTeX files was imported into R for evaluation of the relative performance of each database and to prescreen the studies (Figure 1, step 2). The four databases yielded 4,879 (Scopus), 365 (ScienceDirect), 251 (Web of Science), and 475 (PubMed) non-unique hits. Duplicates were eliminated based on the DOI unique number, yielding 1,327 (Scopus), 113 (Science Direct), 133 (Web of Science), and 342 (PubMed) citations. Scopus detected the highest number of unique citations (1,112, 70% of the total), PubMed found 203 (13%), ScienceDirect 62 (4%), and Web of Science 3 (0.2%) (Figure 2). The highest overlap was among PubMed, Scopus, and Web of Science (4% of shared published papers), between Pubmed and Scopus (4%), and Scopus and Web of Science (3%).

A total of 1,595 published papers were retained for the final step (Figure 1). The screened BibTeX collection was imported into Zotero, and eligibility was evaluated (see criteria defined in the section "Collection, screening, and eligibility" in Methods) by reading the entire published paper or occasionally the abstract (Figure 1, step 3). About 81% (1,299) of the published papers were discarded, mainly because they did not include a formal cophylogenetic analysis (scored as "no cophylogeny"); some that investigated the congruence between the phylogenies of the associates by plotting the taxon name of the host into the phylogeny of the consumer and vice versa were also discarded. After eligibility screening, we included and extracted data from 296 papers published from 1997 to 2022 (for the last year only the first two months), reporting cophylogenetic analyses that test significance of the congruence between phylogenies of interacting lineages and/or estimates of coevolutionary events.

(Q1) How has the usage of words such as "cophylogeny" and/or "codiversification" and quantitative cophylogenetic analyses of interacting lineages changed over time?

The usage of the words *cophylogeny* and *codiversification*, used to query the databases, ranged from 1997 to 2022. After the selection of published papers that used statistical analyses to study the cophylogeny of interacting lineages, the temporal range was narrowed by four years (2001–2022). In each, the proportion of published papers merely mentioning the two keywords rather than statistically analyzing cophylogeny or codiversification was significantly higher (t = 5.3907, df = 20, *p-value* < 0.001) (Figure 3A). For the selected published papers, usage of the keywords steadily increased over the years, showing a significant positive linear trend (*p-value* < 0.001, Figure 3B). The number of published papers released from 2001 to 2021 ranged from 1 to 35 papers per year.

Systematic review and meta-analyses

(Q2) What is the proportion of studies that yield congruent versus incongruent outcomes in cophylogenetic analyses with respect to the three factors of the present meta-analysis?

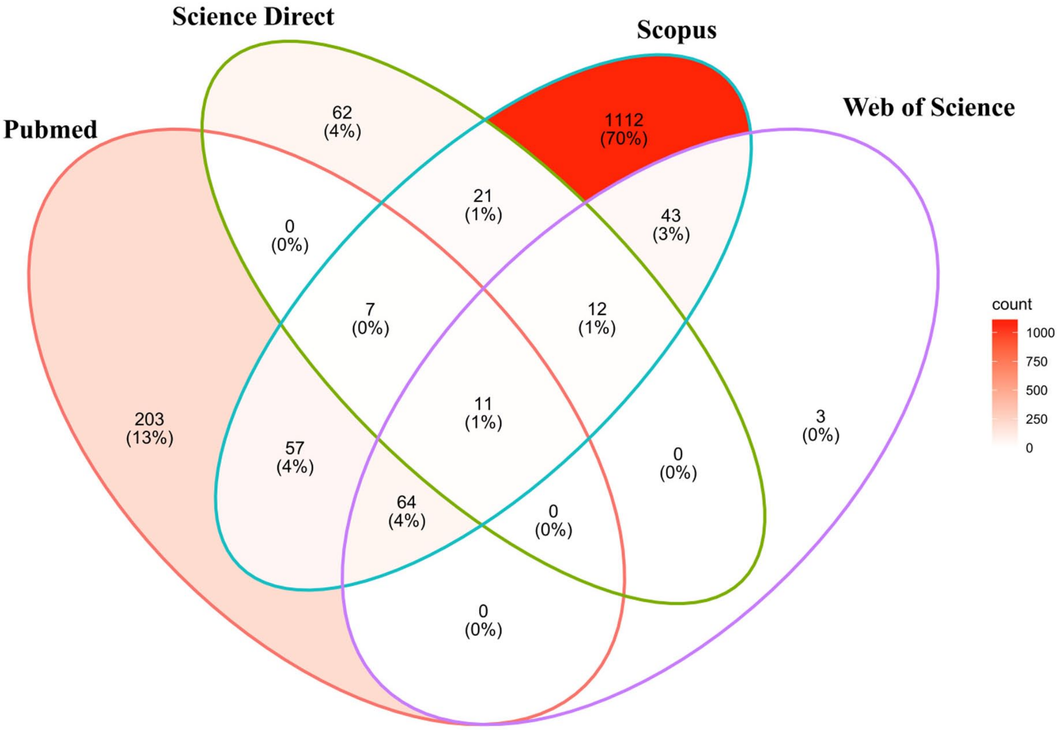

Figure 2. Venn diagram reporting the results of the literature search using four different databases: PubMed, ScienceDirect, Scopus, and Web of Science.

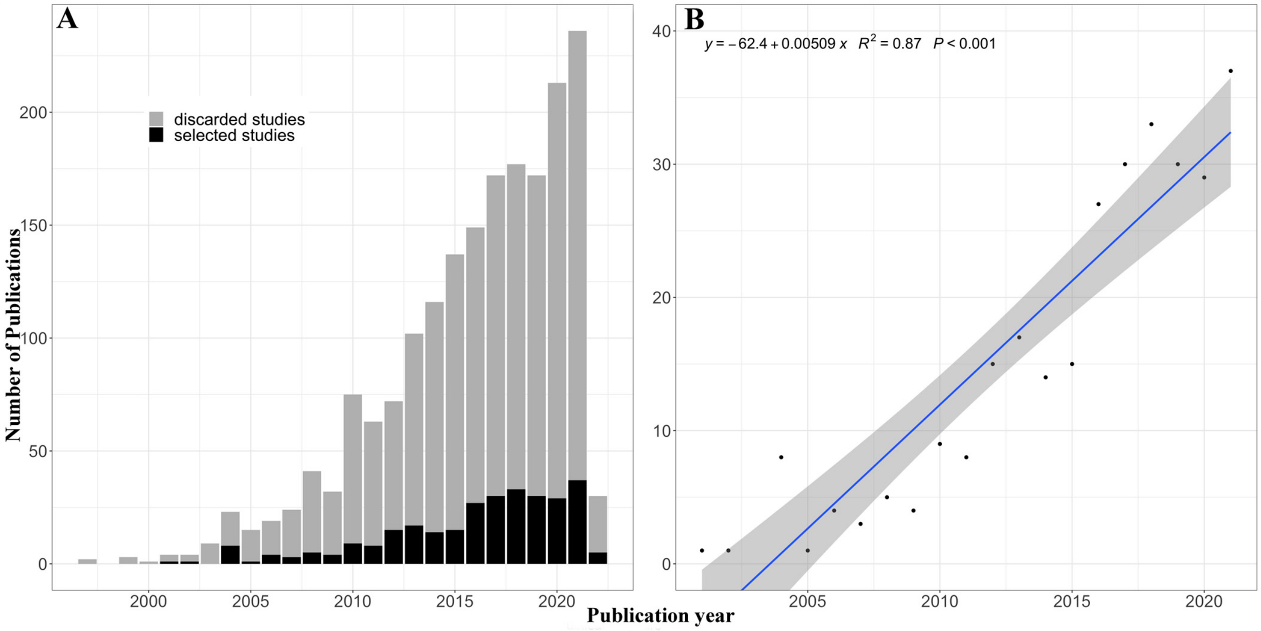

Figure 3. Number of published papers per year that include cophylogenetic studies of interacting lineages, selected using four scientific databases (Pubmed, ScienceDirect, Scopus, and Web of Science). **(A)** The proportion of studies that addressed the topics of cophylogeny, codiversification, and coevolution (discarded studies, gray bars) was compared with studies that carried out formal cophylogenetic analyses on real data (selected studies, black bars) over a time period of 25 years (from 1997 to 2022). **(B)** Linear increase (R^2 = 0.87) of the number of published papers that used one or more cophylogenetic methods to evaluate phylogenies of interacting lineages (from 2001 to 2022).

Table 3. Overview of the number of studies that carried out cophylogenetic analyses of interacting species. The proportion of the three outcomes (*c* = congruence, *i* = incongruence, *ic* = both) is reported in relation to Method, Association, and Ecosystem. Percentages for each outcome are based on the total row marginals.

		Outcome			
		c	***i***	***ic***	**Total**
Method	*Event based*	117 (48%)	94 (39%)	33 (14%)	**244**
	Global fit	153 (63%)	71 (29%)	17 (7%)	**241**
Association[1]	*com*	6 (86%)	1 (14%)	0 (0%)	**7**
	herb	2 (18%)	9 (82%)	0 (0%)	**11**
	mixed	8 (50%)	6 (38%)	2 (12%)	**16**
	mut	99 (67%)	39 (26%)	10 (7%)	**148**
	par	148 (52%)	101 (36%)	33 (12%)	**281**
	pol	7 (33%)	9 (43%)	5 (24%)	**21**
Ecosystem	*aquatic*	40 (56%)	20 (28%)	11 (16%)	**71**
	terrestrial	230 (56%)	145 (35%)	39 (9%)	**413**
				Total	**485**

[1] Abbreviations for the type of associations: *com*, commensal; *herb*, herbivory; *mixed*, a combination of more than two of the other levels; *mut*, mutualistic; *par*, parasitic; *pol*, pollination

The final dataset includes five columns: three factors (cophylogenetic method, association, and ecosystem type), the dependent variable (outcome), and the random variable (DOI). As a total, 484 entries were recorded, which indicates that on average each study applied at least two methods to analyze cophylogeny. For each of the three factors, Table 3 shows the proportion of studies yielding congruent, incongruent, or both outcomes. Overall, a higher number of studies reported congruent phylogenies (56%) compared to incongruent (34%), and only 10% of the studies reported both outcomes for the same analyses. The higher number of the reviewed studies investigated parasitic associations (58%); among them 52% yielded congruent results and 36% incongruent. The 31% of the studies that focused on mutualistic associations yielded a higher proportion of congruent results (66%) compared to incongruent (26%). Commensal associations showed a similar trend with all studies but one yielding congruent results. The two special cases of parasitic and mutualistic associations, herbivory and pollination, yielded predominantly incongruent results: 81% and 42%, respectively. The large majority of the reviewed studies focused on terrestrial ecosystems (85%). Nonetheless, congruent results were obtained in about half of the analyses carried out for each Ecosystem type.

The probability of independence between the Outcome of the analysis and both Method and Association is lower than expected (*p-value* < 0.001)—that is, there is a high probability that the outcome significantly depends on the method of analyses used and the type of association. On the other hand, the probability of independence is higher than expected for Ecosystem type (*p-value* = 0.22) but not significant (Table 4). The Cramér's V value measures the degree of association between categorical variables and varies from 0 to 1. Our results indicated a weak relationship of the outcome with both Method and Association type, with Cramér's V values of 0.15 and 0.14, respectively. The relationship between Outcome and Ecosystem was negligible (0.05). The Bayes Factor (log(BF)) tests were both null (H_0 = the variables are independent) and alternative hypotheses (H_1) and values greater than 2.30 indicate strong evidence for H_0, whereas values lower than –2.30 strongly support H_1. The outcome of cophylogenetic analyses is strongly dependent on the Method used. Similarly, the Bayesian Cramér's V effect sizes (Cramér's V posterior, Table 4) yielded the same result of the Cramér's V values.

The p-values of single comparisons between the outcomes and each level of each factor are reported in Figure 4 (A–C).

To further analyze the independence between the outcome and our factors (H_0), we used a mosaic plot and inferred the departure of each cell from H_0 using Pearson standardized residuals (Figure 5). When including the Method and Association as nested factors, mutualistic associations analyzed with global-fit methods yielded more congruent results than expected by chance, whereas

Table 4. Summary statistics of the statistical relationship between the outcome (*c* = congruence, *i* = incongruence, *ic* = both) of cophylogenetic analyses (as response variable X) and three categorical variables (Method, Association, and Ecosystem) as explanatory variables (Var Y)

Var Y	χ^2 Pearson	p-value	Cramér's V	log(BF)[1]	Cramér's V posterior [95% HDI][2]
Method	12.85	< 0.001	0.15	–2.62	0.16 [0.09–0.25]
Association	29.38	< 0.001	0.14	5.82	0.18 [0.13–0.25]
Ecosystem	3.01	0.22	0.05	2.98	0.09 [0.02–0.18]

[1] log(Bayes Factor)

[2] HDI = Highest Density Intervals

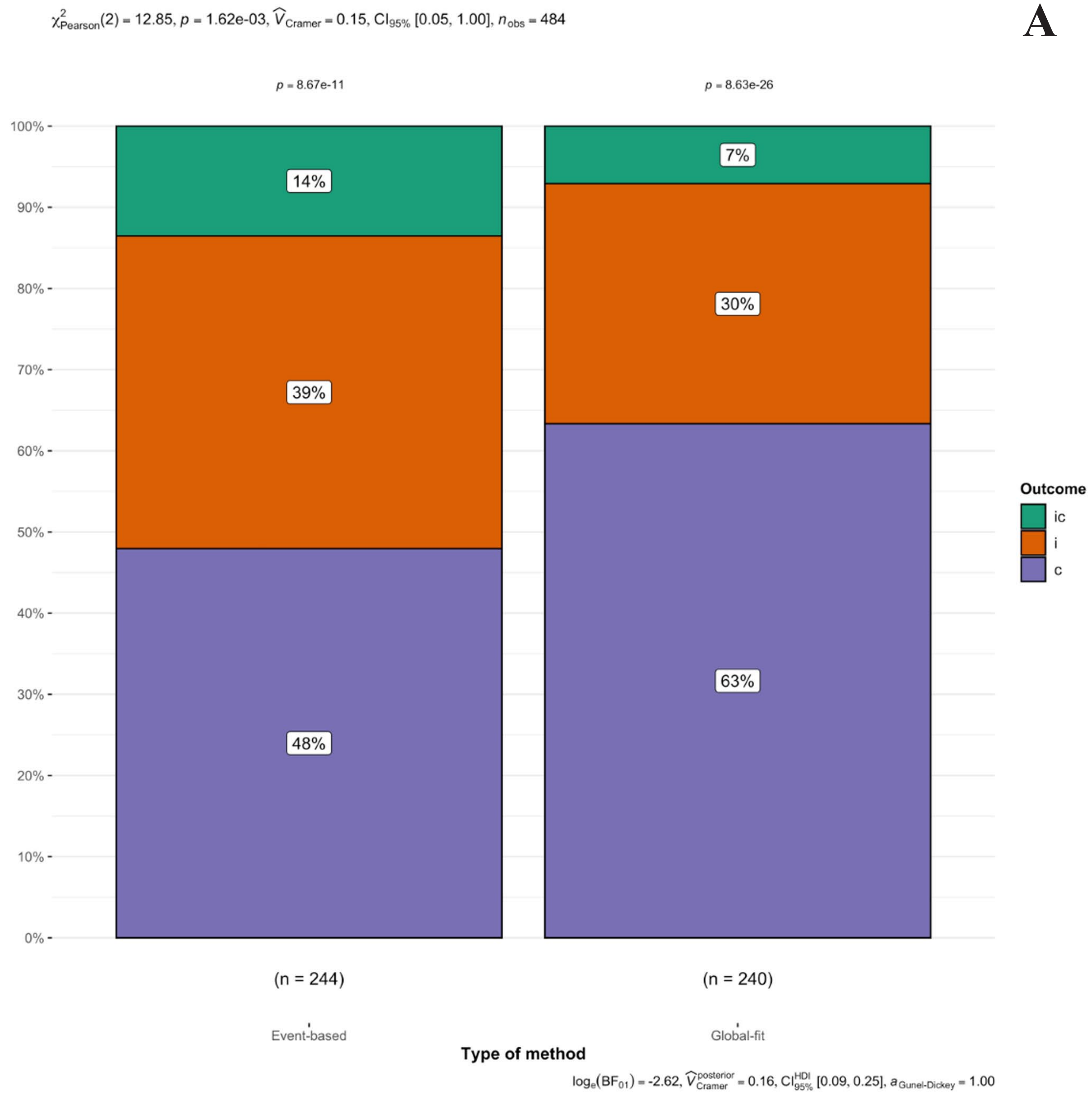

Figure 4. Mosaic plot comparing the distribution of different outcomes of cophylogenetic analyses (congruent, blue; incongruent, orange; and both, green) across **(A)** two method types, **(B)** two ecosystem types, and **(C)** six groups of association types, labeled by percentages.

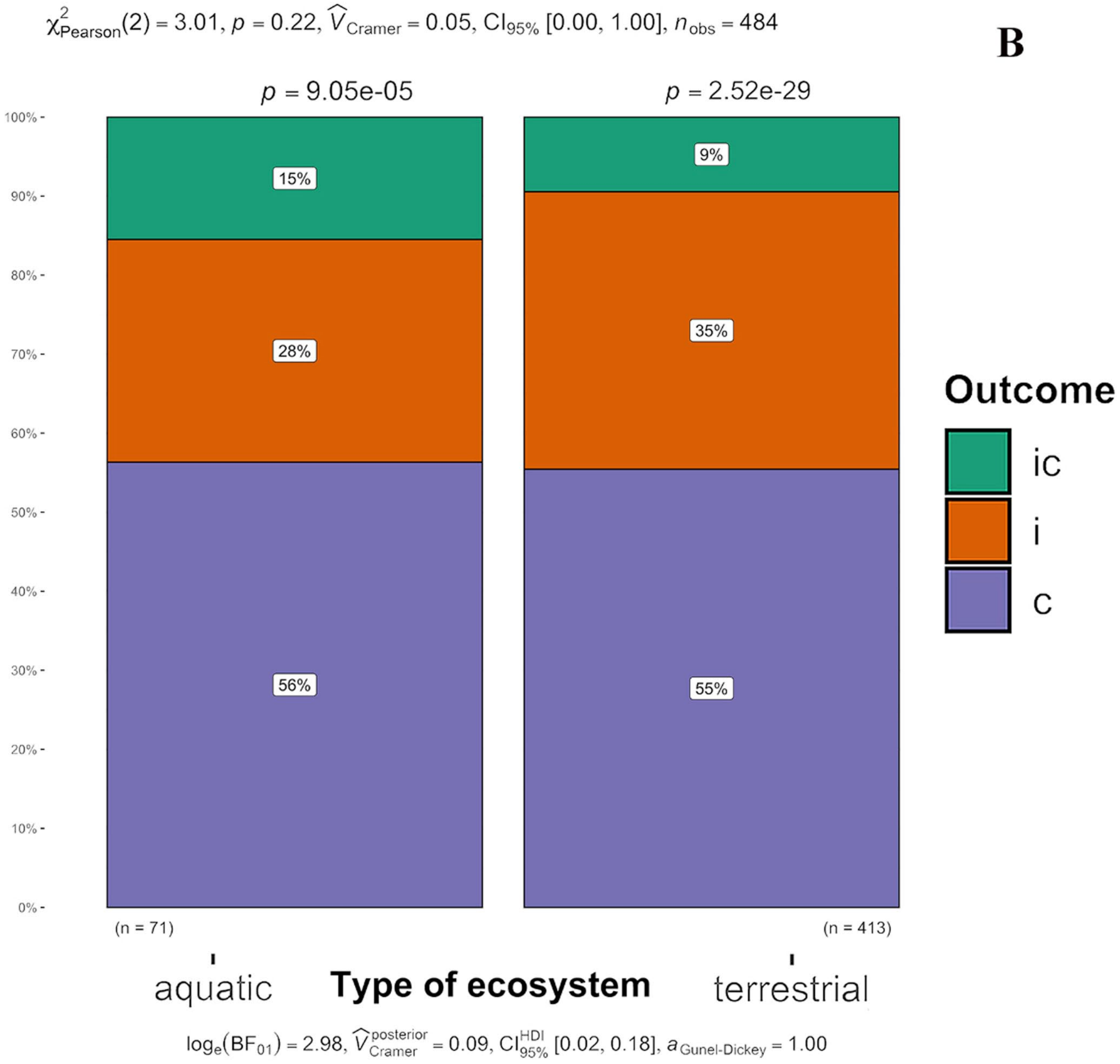

Figure 4(B).

herbivory yielded more incongruent results (blue-shaded area, Pearson residuals > 2). Using event-based methods, parasitic associations yielded more incongruent results or mixed results than expected. The area of each box also gives an indication of its proportion to the whole, relative to the same row. In other words, we can confidently expect that parasitic associations will be incongruent and mutualistic associations will be congruent. All the white boxes indicate independence between the Outcome and the specific level of the two factors (Figure 5).

The same analysis was carried out using pollination, commensal, and mixed types of Associations, and all Pearson residuals fell between 2 and –2, indicating independence between variables (Figure 6).

(Q3) Do method, association, and ecosystem type significantly affect the outcome of cophylogenetic analyses?

All models were built using a binomial GLMM by eliminating 50 out of 485 entries of the collected metadata, which

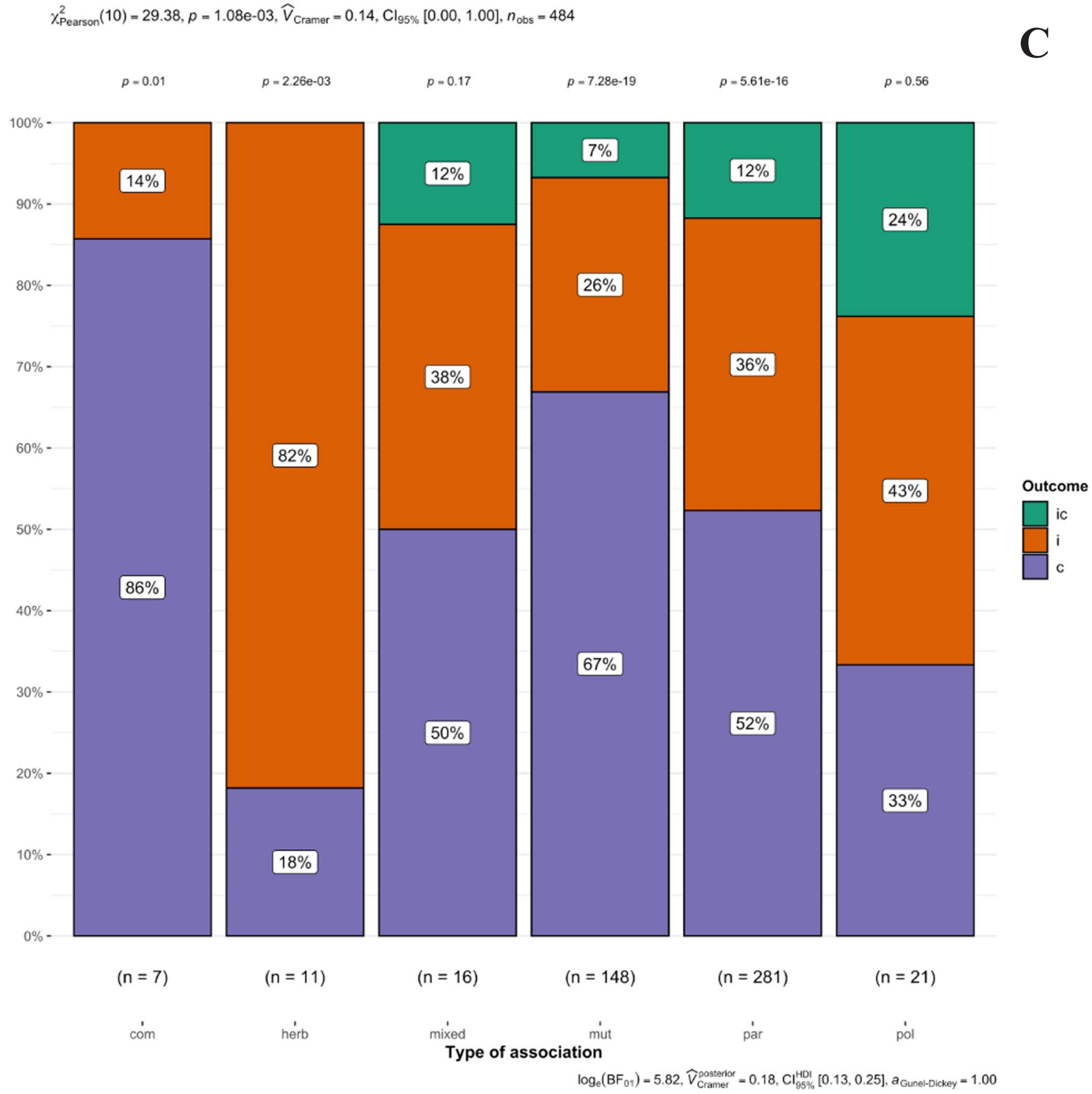

Figure 4(C).

included the *ic* outcome. Among the discarded entries, only 7 studies that used more than one method yielded the same mixed outcome.

Among the six candidate models tested, we selected the most parsimonious model (AIC = 512.1, Model 6 in Table 2) with additive main effects of Method and Association and without interaction (simpler model). The results of the other models are reported in Table 5.

We found that the type of Method and Association significantly influence the outcome of cophylogenetic analyses (Table 6). The coefficient estimates of the linear predictor for the final model may be interpreted as follows: Intercept + M(Event-based) + A(com) + A(par) + A(mut) + A(mixed) + A(pol). Two levels, one from each factor, M(Global-fit) and A(herb) are listed as Intercept. The continuous values of the linear predictor are transformed to the range between 0

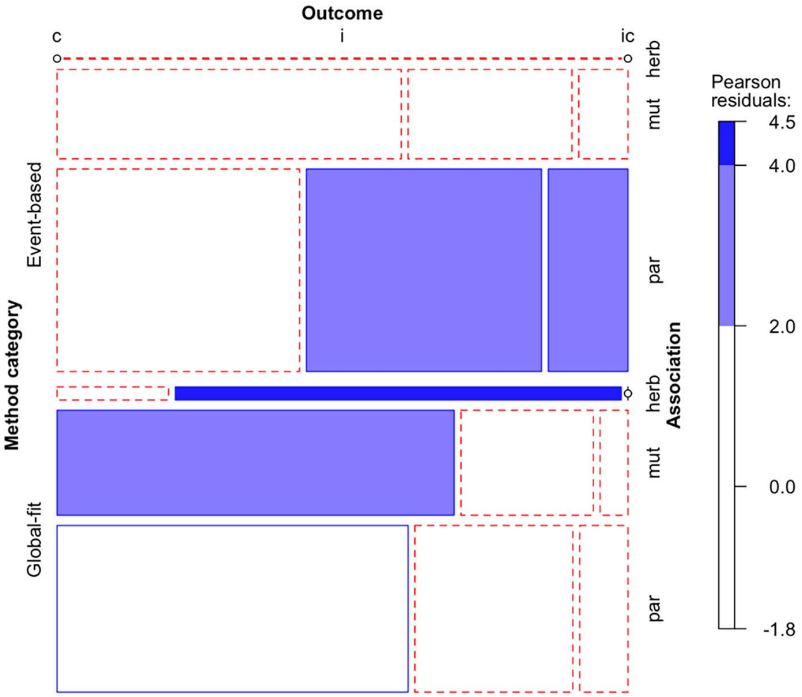

Figure 5. Mosaic plot showing the frequency of the three possible outcomes of the cophylogenetic analyses (c, congruent; i, incongruent; ic, both) when using a specific method category for the analyses and for three different association types (par, parasitic; mut, mutualistic; herb, herbivory).

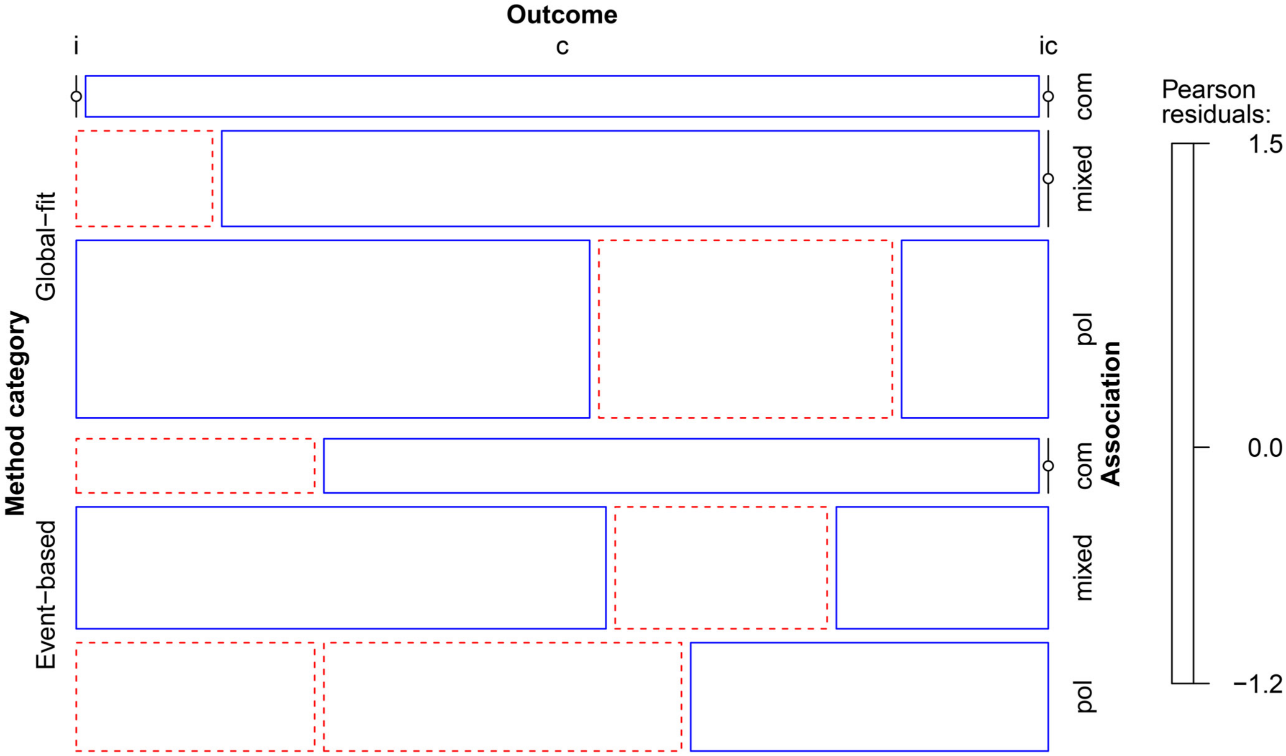

Figure 6. Mosaic plot showing the frequency of the three possible outcomes of the cophylogenetic analyses (c, congruent; i, incongruent; ic, both) when using a specific method category for the analyses and for three different association types (par, parasitic; mut, mutualistic; herb, herbivory).

Table 5. Summary statistics of coefficients of five candidate models analyzed with a binomial GLMM with outcome of cophylogenetic analyses (incongruent, congruent) as a function of three factors (Method, Association, and Ecosystem), depending on the model. Coefficient estimates are on logit (log-odds) scale. Levels for Method: *event-based* and *global-fit*; Association: *com* (commensal), *mixed*, *mut* (mutualistic), *par* (parasitic), *pol* (pollination), *herb* (herbivory); Ecosystem: *terrestrial* and *acquatic*. The following levels are included in the intercept of each model: *global-fit*, *herb*, and *acquatic*. Models 1, 2, and 3 failed to converge.

Model 1 (AIC = 515.8)	**Estimate**	**Std. Error**	**z value**	**Pr(>|z|)**
(Intercept)	–2.19	2.90	–0.75	0.4514
Event-based	–16.53	33737.50	0.00	0.9996
com	22.48214	6036.06	0.004	0.9970
mixed	26.56	2871.04	0.009	0.9926
mut	2.04	3.67	0.557	0.5774
par	5.93	2.53	2.336	0.0195*
pol	1.93	2.99	0.646	0.5186
terrestrial	–2.08	1.52	–1.369	0.1710
Event-based : com	1.42	34273.21	0.000	1.0000
Event-based : mixed	8.07	33737.50	0.000	0.9998
Event-based : mut	16.53	33737.50	0.000	0.9996
Event-based : par	14.87	33737.50	0.000	0.9996
Event-based : pol	18.31	33737.50	0.001	0.9996
Event-based : terrestrial	–0.04	1.34	–0.036	0.9711
mixed : terrestrial	–17.84	2871.03	–0.006	0.9950
mut : terrestrial	6.11	2.83	2.156	0.0311*
Event-based:mut:terrestrial	–0.57	3.17	–0.182	0.8559

Model 2 (AIC = 511.2)	**Estimate**	**Std. Error**	**z value**	**Pr(>|z|)**
(Intercept)	–2.00	1.80	–1.11	0.26529
Event-based	–1.30	0.42	–3.06	0.00216**
com	8.09	3.20	2.52	0.01165*
mixed	18.16	323.82	0.05	0.95525
mut	2.50	2.52	0.98	0.32245
par	5.00	1.84	2.70	0.00676**
pol	2.76	2.02	1.36	0.17176
terrestrial	–1.71	1.13	–1.50	0.13216
mixed : terrestrial	–13.17	323.82	–0.04	0.96754
mut : terrestrial	4.76	2.44	1.95	0.05109

Model 3 (AIC = 515.8)	**Estimate**	**Std. Error**	**z value**	**Pr(>|z|)**
(Intercept)	–3.45	2.66	–1.29	0.1956
Event-based	–15.64	21165.82	–0.00	0.9994
com	20.82	2635.33	0.00	0.9937
mixed	8.90	4.13	2.15	0.0312*
mut	7.82	2.58	3.02	0.0025**
par	6.15	2.53	2.42	0.0152*
pol	1.93	3.00	0.64	0.5191
terrestrial	–0.81	0.99	–0.82	0.4122
Event-based : com	2.15	21329.25	0.00	0.9999
Event-based : mixed	8.45	21165.82	0.00	0.9997
Event-based : mut	15.05	21165.82	0.00	0.9994
Event-based : par	13.96	21165.82	0.00	0.9995
Event-based : pol	17.38	21165.82	0.00	0.9993

Model 4 (AIC = 515.6)	**Estimate**	**Std. Error**	**z value**	**Pr(>|z|)**
(Intercept)	–3.28	1.94	–1.68	0.09172
Event-based	–1.13	0.95	–1.18	0.23572
terrestrial	–0.51	1.07	–0.48	0.63132
com	8.27	3.28	2.51	0.01184*
mixed	5.69	2.61	2.17	0.02962*
mut	7.12	2.31	3.07	0.00211**
par	5.31	1.93	2.74	0.00600**
pol	2.79	2.06	1.35	0.17515
Event-based : terrestrial	–0.18	1.05	–0.17	0.86009

Model 5 (AIC = 513.6)	**Estimate**	**Std. Error**	**z value**	**Pr(>|z|)**
(Intercept)	–3.17	1.82	–1.73	0.08275
Event-based	–1.28	0.42	–3.03	0.00238**
com	8.21	3.25	2.52	0.01154*
mixed	5.66	2.59	2.18	0.02915*
mut	7.07	2.28	3.09	0.00196**
par	5.27	1.91	2.76	0.00576**
pol	2.78	2.05	1.35	0.17529
terrestrial	–0.61	0.91	–0.67	0.49940

Note: * < 0.05; ** < 0.01

Table 6. Summary statistics of coefficients of fixed effects from a binomial generalized linear mixed model (GLMM) with outcome of cophylogenetic analyses (incongruent, congruent) as a function of method and association. Coefficient estimates are on logit (log-odds) scale.

Model 6	**Estimate**	**Std. Error**	**z value**	**Pr(>|z|)**
(Intercept)	–3.79	1.65	–2.29	0.022*
Method—*Event-based*	–1.28	0.42	–3.03	0.003**
Association—*com*	8.23	3.25	2.53	0.011*
Association—*mixed*	5.72	2.59	2.20	0.027*
Association—*mut*	7.15	2.29	3.12	0.002**
Association—*par*	5.38	1.91	2.81	0.005**
Association—*pol*	2.78	2.05	1.35	0.176

Note: * < 0.05; ** < 0.01

and 1 using the inverse logit, where 1 is the probability of obtaining a congruent outcome.

Overall, we found a slightly higher probability of global-fit methods to yield congruent results compared to event-based independently of type of association under study. The associations with the highest probability of a congruent outcome were commensal (*com*) and mutualistic (*mut*). On the other hand, the probability of obtaining incongruence between phylogenies is higher for plant-pollinator associations (*pol*) than plant-herbivore associations (*herb*) (Figure 7).

Discussion

A previous attempt to review studies reporting cophylogenetic analyses was provided by de Vienne et al. (2013). In this study, the authors reviewed 103 published papers retrieved from the ISI Web of Knowledge with the main aim to evaluate convincing cases of cospeciation by attributing a qualitative score (1–5) that summarized their evaluation varying from convincing case of cospeciation (1) to unclear results (5). Their conclusion is that cases of "true" cospeciation are rare (7%) and that cophylogenetic methods overestimate the occurrence of such events. Although we strongly agree with these authors regarding the different biases introduced by available statistical approaches and by overused assumptions, in our review we wanted to provide a systematic meta-analysis of the main results in order to quantify the outcomes and provide a more objective evaluation.

To our knowledge, this is the first systematic review of cophylogenetic studies using four different search databases and the first quantitative meta-analysis to test the most popular assumption in the literature (usually used as H_0, congruence between phylogenies) against alternatives (H_1, incongruences).

Our systematic search confirmed that Scopus provides about 84% more coverage than PubMed, ScienceDirect, and Web of Science, which is a percentage four times higher than that reported in another revisionary study on biomedical sciences (Falagas et al., 2008). This discrepancy is possibly due to the multidisciplinary nature of our research topic and the keywords used, as pointed out by Al-Ryalat et al. (2019).

An interesting result emerging from our systematic review of cophylogenetic analyses of interacting lineages is that only about one-fifth of the reviewed published papers attempted to disentangle the processes driving codiversification statistically, regardless of the strategy or algorithm used. Most of the published papers (~80%) focused on a specific lineage and discussed the potential role of biotic interactions driving the diversification of each single taxa, with no attempt to compare phylogenies. From a review of previous summary studies on this topic (e.g., Brooks, 1979; Janzen, 1980; Page, 2003; Poisot, 2015; de Vienne et al., 2013; Charleston, 2016; Martínez-Aquino, 2016), it became evident that the concepts used as keywords in our search (such as codiversification and coevolution) or related words (e.g., cospeciation) are defined differently or used interchangeably as also pointed out earlier (Charleston and Perkins, 2006). This may create confusion and has hindered the implementation and validation of a unified statistical approach or the application of these methods of analysis to specific Association types (e.g., commensal associations).

Although they are becoming more popular, cophylogenetic studies of interacting lineages are proportionally fewer than studies that do not compare phylogenies and merely mention concepts such as coevolution (Figure 3A). In a similar synoptic study, Poisot (2015) showed that

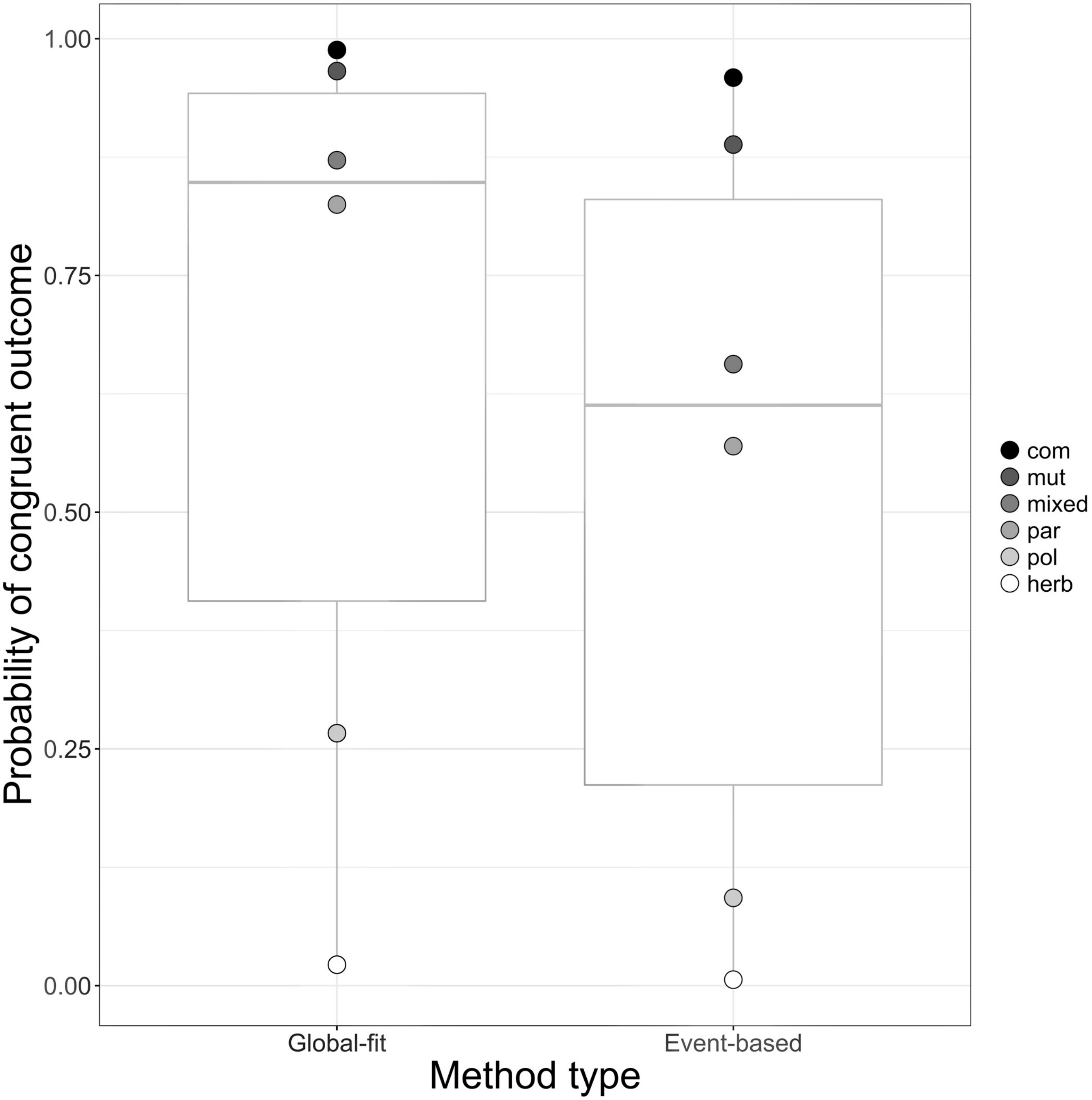

Figure 7. Predicted probabilities of congruent outcomes as a function of association and method.

between 1997 and 2012 the ratio between the number of studies addressing cophylogeny analyses and those mentioning coevolution was stable around 0.34. Our review extends this earlier analysis by adding 10 more years of data and shows an increase of the ratio by more than 5 times. This indicates an increasing tendency by researchers to use qualitative methods rather than phylogenetic or cophylogenetic analyses to infer/assume coevolution between/among interacting lineages and to operate over short (ecological), nonevolutionary timescales.

The likelihood of obtaining a specific outcome using available cophylogenetic analyses has been tested here by evaluating three main factors: two inherent to the biological system investigated (Association and Ecosystem types) and one pertaining to the statistical method applied. Overall, we retrieved only a few studies (seven published papers) that analyzed commensal associations to uncover the strength of the cophylogenetic associations. A previous review reported that despite commensalism being frequently mentioned in the ecological literature, it has been little studied because of limited understanding of commensal associations (e.g., inconsistent and divergent definitions of the term leading to miscataloging of the associations and lack of empirical evidence) (Mathis and Bronstein, 2020). We speculate that the lack of cophylogenetic studies on commensal associations may be due to the misleading assumption that if no harm or benefit occurs between interacting lineages, then there will be no driving force for cospeciation to happen. On the other hand, we believe that expanding the analyses of cophylogeny to classical commensal study cases may allow explicit tests of the assumption that cospeciation is the only process that leads to congruent phylogenies. This erroneous outcome, recently referred as "apparent cospeciation" (Blasco-Costa et al., 2021), has been discussed extensively in other reviews (de Vienne et al., 2013; Charleston, 2016). We also point out that the cophylogenetic structure and the reconstruction of the associations is largely affected by the possible change of the Association type over time, and none of the analytical methods formally take into account this aspect.

By calculating expected frequencies from contingency tables, we provided evidence for the Outcome to be strongly dependent on the Method, and this result is driven by mutualistic and herbivory associations for global-fit methods and parasitic associations for event-based methods. Our meta-analysis yielded a significant number of congruent outcomes among phylogenies of species in mutualistic associations supported by several authors in the reviewed literature (see hypotheses in the Introduction section). However, as suggested by de Vienne et al. (2013), among others, obtaining congruent phylogenies among interacting lineages is not a definitive indication for cospeciation. Indeed, our results also indicate that we cannot confidently expect that phylogenies in mutualistic associations will be congruent when using event-based methods. For host-parasite systems, our analysis showed a confident association to incongruent outcomes especially when using event-based approaches, these results support alternative hypotheses that would have parasites not mirroring the host phylogeny. For parasitic association, the assumption known as Fahrenholz's rule (Fahrenholz, 1913)—that is, the parasite's phylogeny mirrors the host's phylogeny—may have driven more than 50 years of misleading analyses of cophylogeny. For this reason, we expect phylogenetic incongruency among lineages to be much more common than those observed with the available methods.

We used a mixed-model approach, which provided evidence for a non-nested structure of the explanatory factors that singularly affect the outcome of specific associations while using two different categories of methods to study cophylogeny. This analysis supported a higher probability for parasites, herbivores, and pollinators to provide incongruent results when compared to their hosts' phylogenies. Although cospeciation is imposed as "Assumption 0" in most of the methods, other processes, such as host switching, that may lead to incongruence between phylogenies, have been extensively discussed (Hoberg et al., 1997; Brooks and McLennan, 2003). Using a discovery-based approach (i.e., with no a priori assumption), implemented in algorithms such as secondary BPA (Brooks and McLennan, 2003) and PACT (Wojcicki and Brooks, 2005), all processes are equally possible. These methods were applied to only a few parasitic associations—for example, the classic case of cospeciation between pocket gophers and lice, which has been reanalyzed using PACT, showing about half of the links between parasite and host are explained by speciation of the parasite after a host switch rather than cospeciation (Brooks et al., 2015).

To obtain a comprehensive understanding of the real effect of "Assumption 0" on the main outcome of cophylogenetic analyses, more datasets from different types of associations need to be tested using algorithms that do not assume one event to be more probable and costly than another or are not founded on the prevailing paradigm of maximum cospeciation.

An alternative paradigm, the Stockholm paradigm (SP), is formalized on the idea that symbionts do not have to evolve genetic novelties to be able to adapt to a new host, which means that mirroring the host's phylogeny is not the only option (Brooks et al., 2019). Given the opportunity, a symbiont may colonize a new host successfully with no morphological or genetic changes required (according to ecological-fitting theory), eventually resulting in incongruence between phylogenies. Reconstructing the cophylogenetic history of interacting lineages is not merely a reconciliation problem, it is an estimation of the most parsimonious events inferred using a deductive rather than inductive approach (e.g., PACT). A software package for PACT is in preparation (Trivellone, Panassiti, Boeger, and Brooks, in prep.) and will provide an easy-to-use tool to test more phylogenies of interacting lineages.

Moreover, uncovering the processes driving the interactions between lineages also has a broader impact beyond the advancement of knowledge. The episodes of incongruence between phylogenies may be interpreted as extinction, duplication where the parasite speciates while the host does not, or host switching. The SP postulates that many more incongruences than previously thought are expected due to host switching. Those incongruences define specific preexisting capacities of the symbiont to colonize a new host and are phylogenetically conserved. In particular for host-parasite associations, the SP also provides a policy extension (DAMA: Document, Assess, Monitor, Act) that is a workbench that translates the scientific outcomes in action (Brooks et al., 2021; Trivellone et al., 2022). Cophylogenetic analyses, using PACT or similar discovery-based approaches, represent the fundamental tool for the second step in DAMA (Assess). Once all the diversity has been reasonably documented (DAMA—Document), it will inform the phylogenies of interacting lineages, and the cophylogenetic analysis will aid in predicting the extension of the potential host range within an evaluation known as phylogenetic triage (i.e., uncover phylogenetically conservative traits that allow the parasite to colonize a new host). Another tool is available for this step in DAMA, a modeling platform that evaluates the dynamics of host switching through ecological fitting (for a review see Souza et al., 2022).

To conclude, in our review we highlighted that the method selected may affect the outcome of cophylogenetic analyses, depending on the assumptions applied to a specific type of interacting species used as a study model. Knowing how new associations emerge between pathogens and their hosts is critical for informing a global strategy to anticipate the risk of future disease outbreaks and EIDs. Future research should focus on evaluation of real raw metadata to establish whether deductive versus inductive methods affect the main outcome of the cophylogenetic analysis and the significance of congruence between phylogenies.

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Authors' contributions – The authors contributed equally to design the search strategy, perform the literature research, evaluate and analyze data, and write and edit the manuscript.

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