

The quasi-universality of nestedness in the structure of quantitative plant-parasite interactions

Benoît Moury, Jean-Marc Audergon, Sylvie Baudracco-Arnas, Safa Ben Krima, François Bertrand, Nathalie Boissot, Mireille Buisson, Valérie Caffier, Melissa Cantet, Sylvia Chanéac, et al.

▶ To cite this version:

Benoît Moury, Jean-Marc Audergon, Sylvie Baudracco-Arnas, Safa Ben Krima, François Bertrand, et al.. The quasi-universality of nestedness in the structure of quantitative plant-parasite interactions. 2021. hal-03169796

HAL Id: hal-03169796 https://hal.inrae.fr/hal-03169796

Preprint submitted on 23 Jun 2021

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial - NoDerivatives 4.0 International License

1 The quasi-universality of nestedness in the structure of quantitative plant-

2 parasite interactions

3

4 Moury Benoît¹, Audergon Jean-Marc², Baudracco-Arnas Sylvie³, Ben Krima Safa⁴, Bertrand François⁵,

- 5 Boissot Nathalie², Buisson Mireille⁶, Caffier Valérie⁷, Cantet Mélissa²*, Chanéac Sylvia⁸, Constant
- 6 Carole⁹, Delmotte François¹⁰, Dogimont Catherine², Doumayrou Juliette^{1§}, Fabre Frédéric¹⁰, Fournet
- 7 Sylvain¹¹, Grimault Valérie¹², Jaunet Thierry¹³, Justafré Isabelle¹⁴, Lefebvre Véronique², Losdat Denis¹⁵,
- 8 Marcel Thierry⁴, Montarry Josselin¹¹, Morris Cindy E.¹, Omrani Mariem^{1,2}, Paineau Manon¹⁰, Perrot
- 9 Sophie¹², Pilet-Nayel Marie-Laure¹¹, Ruellan Youna²
- 10
- 11 ¹Pathologie Végétale, INRAE, 84140 Montfavet, France
- 12 ²GAFL, INRAE, 84140, Montfavet, France
- 13 ³Laboratoires ASL, 755 chemin de Meinajaries, 84140 Montfavet, France
- ⁴University of Paris-Saclay, INRAE, AgroParisTech, UMR BIOGER, 78850 Thiverval-Grignon, France
- ⁵Bayer Seeds SAS, Chemin de Roquemartine Mas Lamy, 13670, Saint-Andiol, France
- 16 ⁶GAUTIER SEMENCES, Route d'Avignon, 13630 Eyragues, France
- 17 ⁷Univ Angers, Institut Agro, INRAE, IRHS, SFR QUASAV, 49000 Angers, France
- ⁸TAKII FRANCE SAS, 660 Chemin de la Crau, 13630 EYRAGUES, France.
- ⁹Sakata Vegetables Europe, Domaine de Sablas, rue du moulin, 30620 Uchaud, France
- 20 ¹⁰SAVE, INRAE, Bordeaux Sciences Agro, ISVV, 33140 Villenave d'Ornon, France
- 21 ¹¹IGEPP, INRAE, Institut Agro, Univ. Rennes, 35653 Le Rheu, France
- 22 ¹²GEVES, 25 rue Georges Morel, CS 900024, 49071 Beaucouzé, France
- 23 ¹³HM.Clause, 1 chemin du Moulin des Ronzières, 49800 La Bohalle, France
- 24 ¹⁴Vilmorin, Mas Pazac, 30210 Ledenon, France
- 25 ¹⁵RIJK ZWAAN France, La Vernède, 30390 Aramon, France
- 26
- 27 *present address: Bayer Seeds SAS, Chemin de Roquemartine Mas Lamy, 13670, Saint-Andiol, France
- 28 [§]present address : Syngenta Seeds B.V., Westeinde 62, P.O. box 2, Enkhuizen 1600 AA, The

29 Netherlands

31 Abstract

32 Understanding the relationships between host range and pathogenicity for parasites, and between 33 the efficiency and scope of immunity for hosts are essential to implement efficient disease control 34 strategies. In the case of plant parasites, most studies have focused on describing qualitative 35 interactions and a variety of genetic and evolutionary models has been proposed in this context. 36 Although plant quantitative resistance benefits from advantages in terms of durability, we presently 37 lack models that account for quantitative interactions between plants and their parasites and the 38 evolution of these interactions. Nestedness and modularity are important features to unravel the overall structure of host-parasite interaction matrices. Here, we analysed these two features on 32 39 40 matrices of quantitative pathogenicity trait data gathered from 15 plant-parasite pathosystems 41 consisting of either annual or perennial plants along with fungi or oomycetes, bacteria, nematodes, 42 insects and viruses. The performance of several nestedness and modularity algorithms was evaluated 43 through a simulation approach, which helped interpretation of the results. We observed significant 44 modularity in only six of the 32 matrices, with two or three modules detected. For three of these 45 matrices, modules could be related to resistance quantitative trait loci present in the host. In contrast, we found high and significant nestedness in 30 of the 32 matrices. Nestedness was linked to 46 47 other properties of plant-parasite interactions. First, pathogenicity trait values were explained in 48 majority by a parasite strain effect and a plant accession effect, with no parasite-plant interaction 49 term. Second, correlations between the efficiency and scope of the resistance of plant genotypes, and between the host range breadth and pathogenicity level of parasite strains were overall positive. 50 51 This latter result questions the efficiency of strategies based on the deployment of several 52 genetically-differentiated cultivars of a given crop species in the case of quantitative plant immunity. 53

54 Keywords

55 Plant resistance, pathogenicity, plant parasite, bipartite network, nestedness, modularity

57 Introduction

58 The effectiveness of strategies of disease control based on host immunity depends on the underlying 59 capabilities of hosts to resist infection, of parasites to overcome this resistance and on the potential 60 of these traits to evolve. Parasites and hosts can be specialists or generalists in, respectively, their capacity to infect and their immunity. Confronting multiple genotypes of a parasite with multiple 61 62 genotypes of a host reveals their interaction patterns, *i.e.* the magnitude and arrangement of their 63 mutual specialization or generalism, which gives insights into the underlying genetic bases of these 64 characters and allows implementing strategies of disease management based on host diversification. 65 Importantly, the word "interaction" has different meanings in this context. In ecology, interactions 66 between hosts and parasites are the effects that each of these two categories of living organisms

67 have on each other. These host-parasite interactions can involve molecular interactions, which are

68 attractive or repulsive forces between molecules, for example between parasite elicitors or effectors

69 and host receptors. Finally, quantitative pathogenicity traits can be analysed thanks to statistical

70 models that include, or not, a significant interaction between variables representing hosts and

71 parasites. In the latter acception, "interaction" means that the model departs significantly from a

purely additive model, including only a parasite effect and a host effect. Statistical interactions are

used in the context of quantitative data and linear regression models, but not for qualitative binarydata.

75 The structure of any host-parasite interaction can be represented as a matrix where columns 76 correspond to host genotypes (either inbred lines, clones or F_1 hybrids) and rows to parasite strains 77 (either isolates, clones or populations depending on the considered parasite). Each cell in the matrix 78 indicates the result of the pairwise confrontation between the corresponding host genotype and 79 parasite strain. Qualitative interactions generate binary matrices with 1 and 0 grades, which 80 correspond to successful and unsuccessful infections. Nestedness and modularity are two 81 quantitative properties that reveal non-random distributions of 1 and 0 grades in such matrices (Weitz et al. 2013). Nestedness measures the tendency of the hosts of a parasite to have a 82 hierarchical organization, where the set of hosts of a given parasite (a species or a genotype) is a 83 subset (respectively superset) of that of the parasites of broader (respectively narrower) host ranges. 84 85 Here, the breadth of the host range of a given parasite is defined as the percentage of host species 86 (or genotypes) that are infected by this parasite. The same tendency is observed for host immunity (Fig. 1A): the set of parasites that are controlled by the immunity of a given host is a subset 87 88 (respectively superset) of that of hosts with broader (respectively narrower) scopes of resistance. 89 Here, the scope of the resistance of a given host is defined as the percentage of parasite species (or 90 strains) that are targeted by this resistance.

91 Modularity measures the strength by which the matrix can be divided into several modules grouping 92 subsets of hosts and parasites characterized by successful infections, infections being rare for hosts 93 and parasites belonging to different modules (Fig. 1B). Depending on the genetic, evolutionary and 94 mechanistic patterns of host-parasite interactions, contrasted scores for nestedness and modularity 95 are expected.

96 Three main models of host-parasite interactions have been proposed for qualitative plant-parasite 97 interactions (Fig. 1C to F; see Thrall et al. 2016 for details). These models represent the mutual 98 specialization of hosts and parasites in terms of underlying molecular mechanisms, genetic 99 determinism and coevolution pattern. Each one generates a specific structural pattern in the 100 corresponding interaction matrix. Historically, the first model was the gene-for-gene (GFG) model 101 proposed to describe interactions between crop plants and their parasites, based on genetic studies 102 of flax and rust (Flor 1956). In this model, plant immunity is inducible and requires recognition of the 103 parasite by its host. Recognition occurs between a host receptor and a parasite elicitor, each of them 104 being encoded by a single gene. The loss or alteration of the elicitor in the parasite or the absence of 105 a cognate resistance allele in its host results in infection. Here, the word 'elicitor' is used in the broad 106 sense of a parasite component triggering plant defenses, and thus includes effectors and avirulence 107 factors (Bent and Mackey 2007). This model is coherent with dominant resistance that involves plant 108 proteins containing nucleotide-binding and leucine-rich-repeat domains as receptors, and that 109 mounts hypersensitive reactions (programmed cell death) upon recognition of various kinds of 110 parasite elicitors. In this system, a parasite strain may have universal infectivity, *i.e.* may be able to 111 infect all host genotypes, if it lacks all the elicitors that correspond to the host resistance factors. 112 Accordingly, the matrix has a global nested pattern, with partial or complete overlap of the host 113 ranges of the parasite strains and of the resistance spectra of the host genotypes (Fig. 1C,D). 114 Secondly, the matching-allele (MA) model was proposed to describe the self/non-self recognition 115 system of invertebrate immunity (Grosberg and Hart 2000). In that case, infectivity requires a specific 116 match between the host genotype and the parasite strain and, accordingly, universal infectivity is 117 impossible. The corresponding host-parasite matrix has a modular structure. Cross-infections are 118 frequent between hosts and parasites belonging to the same module but rare between hosts and parasites belonging to distinct modules. In extreme cases of specialization, modules can be as small 119 120 as a single host-parasite pair (Fig. 1E). Mechanistically, this model is coherent with recessive plant 121 resistance to viruses mediated by eukaryotic translation initiation factors (e.g. Sacristán and García-122 Arenal 2008) and with necrotrophic fungi which secrete elicitors of programmed cell death that 123 increase plant susceptibility by allowing the fungus to feed on dying cells (Peters et al. 2019). In the 124 context of plant necrotrophic parasites, this model is also confusingly named 'inverse gene-for-gene'

125 (Peters et al. 2019). Thirdly, the inverse-matching-allele (IMA) model was proposed to reflect the 126 adaptive immune system of vertebrates, where the host resists through recognition of the parasite 127 and infections occur when the parasite mismatches the host (Kidner and Moritz 2013; Thrall et al. 128 2016). The IMA model was defined in the context of multi-allelic series of resistance and 129 pathogenicity genes. Mechanistically very similar to the GFG model, it assumes that recognition between host and parasite genotypes is highly specific. The corresponding host-parasite matrix is 130 131 therefore similar to the matching-allele model but with 0 and 1 grades replaced by 1 and 0 grades, 132 respectively (Fig. 1F). Hence, a modular pattern is the expected result when immunity levels (instead 133 of the degree of pathogenicity) are indicated in the matrix. 134 The distinguishing feature of the genetic models described above is that they describe qualitative

135 binary interactions, where each host-parasite pair is characterized by its compatibility or noncompatibility. Models that describe quantitative host-parasite interactions are rare and their 136 137 adequacy to represent empirical data have not been extensively tested (Lambrechts 2010; Wang et 138 al. 2018). Analysis of quantitative plant immunity has mostly been confined to the framework of 139 quantitative genetics and QTL (quantitative trait loci) mapping. These methods usually assume that 140 resistance is determined by the additive effect of QTLs. More complex effects (dominance, epistasis) 141 are rarely considered (Gallois et al. 2018). Furthermore, there are few studies of quantitative 142 genetics and QTL mapping of parasite pathogenicity traits, especially in the case of plant parasites (Wang et al. 2018). Most importantly, these few analyses were conducted either with a set of hosts 143 144 confronted to a single parasite or with a set of parasites confronted to a single host. In any case, 145 there is a clear need for new models describing quantitative host-parasite interactions while properly 146 accounting for the variability of both partners (Lambrechts 2010; Bartoli and Roux 2017). Moreover, 147 previous work has shown that the outcome of analysis of matrix structure is markedly impacted when quantitative interactions are considered. Quantitative data are especially influencing the 148 149 significance of nestedness (Staniczenko et al. 2013).

150 These considerations motivated us to conduct a comprehensive analysis of the nestedness and 151 modularity of interaction matrices to deepen our knowledge in the specialization between plants and 152 diverse parasites using quantitative data. The objectives of this work are (i) to assess the 153 performance of available algorithms to identify nested and modular patterns in matrices of 154 quantitative data and (ii) to determine if these patterns are specific to each pathosystem or show a general trend. In addition, our work provides a new perspective and insight into appropriate genetic 155 156 and evolutionary models for representing quantitative plant-parasite interactions and for outcomes 157 for plant resistance management.

158

159 Results

160 We gathered 32 matrices corresponding to 15 plant-parasite pathosystems and containing quantitative pathogenicity trait values (Table 1; Fig. 2). Among the 13 parasite species included, most 161 were fungi or oomycetes (five and four, respectively), while bacteria, nematodes, insects and viruses 162 163 were represented only once. Only three pathosystems included perennial (tree) plants and all plant 164 species were temperate-climate crops (or crops adapted to both temperate and tropical climates). 165 Each pathosystem included a set of strains belonging to the same parasite species and a set of 166 accessions belonging to the same plant species with four exceptions, matrices 9, 18, 19 and 26, 167 where accessions belonged to several closely-related plant species. Among the matrices, the number of plant accessions varied from seven to 53 (median 12) and the number of parasite strains varied 168 169 from six to 98 (median 11.5). The number of matrix cells varied from 49 to 1470 (median 180). For 170 most pathosystems, we analyzed several matrices corresponding to either different pathogenicity 171 traits, different plant-parasite sets or different experiments. In order to meet the requirements of 172 methods that allow the estimation of nestedness and modularity of matrices, the pathogenicity traits 173 in each matrix were standardized into integer values ranging from 0 (minimal plant resistance and/or 174 maximal parasite pathogenicity) to 9 (maximal plant infection and/or minimal parasite 175 pathogenicity). We then tested for the occurrence of nestedness and modularity. For significance 176 assessment, the nestedness/modularity scores of the matrices derived from experimental data were 177 compared to those of simulated null-model matrices that are not expected to possess any nested or 178 modular pattern (Supplementary Methods 1). Nestedness (or modularity) is significant if the actual 179 matrix is more nested (or modular) than at least 95% of the matrices simulated under a given null 180 model (black numbers on grey background in Tables 2, 3 and 4). As there are many possible null 181 models and because their choice is crucial to conclude about the significance of nestedness or 182 modularity, we analyzed the performance of the different available nestedness/modularity 183 algorithms and of different null models by estimating their type I and type II error rates through a 184 simulation approach (Supplementary Methods 1; Tables S1 to S18).

185

186 Ubiquitous nestedness in quantitative plant-parasite interactions

187 First, we evaluated the performance of two algorithms, *WINE* and *wNODF* (Galeano et al. 2009;

188 Almeida-Neto and Ulrich 2011), to estimate the nestedness of the 32 matrices. Simulations revealed

that statistical significance with both null models C1 and R1 (or C2 and R2) provided the lowest false

190 positive rates for nestedness (Supplementary Methods 1; Tables S1 and S2). Under null models C1

and R1, matrices are generated column by column or row by row, respectively, and the cell numbers
are chosen randomly in order that (i) the marginal sums of cells and (ii) the numbers of zero-valued
cells are kept the same as in the actual matrix. To generate matrices under null models C2 and R2,

the cell values of the actual matrix are shuffled column by column or row by row, respectively.

195 With the WINE algorithm, nestedness values were quite high in general (from 0.46 to 1.04; mean

196 0.77 on a scale varying from 0 to ≈1). Thirty of the 32 matrices showed significant nestedness (p-

197 values \leq 0.05) with null models C1, R1, C2 and R2 (Table 2). Only matrices 21 and 32 were not

significantly nested with either null model C1, R1, C2 or R2.

199 With the wNODF algorithm, nestedness estimates varied from 6.1 to 75.4 (mean 38.2) on a scale 200 varying from 0 to 100 and nestedness was significant for only 19 of the 32 matrices with null models 201 C1, R1, C2 and R2 (Table 2). This lower number of matrices showing nestedness is consistent with the 202 lower statistical power of wNODF compared to WINE (Supplementary Methods 1). As both methods 203 are based on different principles, the correlation of their nestedness scores among the 32 matrices is 204 only moderate (Pearson's r = 0.37; p-value = 0.038). Importantly, unlike the WINE method, wNODF 205 cannot estimate the nestedness of matrices devoid of zero-valued cells and underestimates 206 nestedness when zero-valued cells are scarce. Indeed, most of the matrices significantly nested with 207 WINE but not significantly nested with wNODF contained few zero-valued cells, most of which being 208 distributed on a single row or column. Consequently, the discrepancy between results obtained by 209 WINE and WNODF may be a bias due to the lack or peculiar distribution of the zero-valued cells. Five 210 more matrices (numbers 13, 15, 20, 29 and 31) were significantly nested with wNODF if 1-valued 211 cells or 1- and 2-valued cells were transformed into 0-valued cells.

With *wNODF* (but not with *WINE*), several matrices were less nested than at least 95% of the
matrices simulated under one or several null models (white numbers on black background in Table

214 2), a property that we will name anti-nestedness. Matrix 14 was significantly anti-nested with null

215 models N, C1, R1 and R2. For six other matrices, significant anti-nestedness was detected with one or

a few null models, a bias attributable to the small number of 0-valued cells (matrices 12, 23 and 24)

which disappeared largely when 1- and 2-valued cells were transformed into 0-valued cells.

218 Overall, taking into account the limitations of the *wNODF* algorithm, our analysis revealed that the

219 huge majority of the matrices (30/32; 94%) were significantly nested.

220

221 Investigation of the biological significance of nestedness

222 Adequacy of an additive linear regression model for pathogenicity matrices

223 The high and significant nestedness observed among most of the analysed matrices suggests that an 224 additive model combining pathogenicity QTLs in the parasites and resistance QTLs in the hosts, with 225 no QTL x QTL interactions between hosts and parasites, would fit well with the data (Fig. 1G). We 226 evaluated the performance of the linear regression model: 'pathogenicity' ~ 'parasite strain' + 'plant 227 accession', with no interaction term, on the datasets. For each plant accession-pathogen strain pair, the mean pathogenicity value was considered for the 'pathogenicity' variable. The 'parasite strain' 228 229 and 'plant accession' effects were highly significant (p-value < 0.0012), except for matrices 21 and 32 230 which were the only ones not significantly nested according to the WINE method (Table 2). Omitting 231 these two matrices, the multiple coefficient of determination (R²) indicating model fit varied from 232 0.49 to 0.98 (mean 0.75) (Table 1), which lends support to the suggested genetic model. Moreover, the multiple R² values of the linear regression model were significantly correlated with the 233 234 nestedness scores obtained with the WINE algorithm (Pearson's r = 0.73; p-value = 2.6e-06) across 235 the 32 matrices. They were only marginally correlated with the nestedness scores of the wNODF 236 algorithm (r = 0.32; p-value = 0.07).

237

238 Evaluating potential trade-offs: Host range breadth *vs.* pathogenicity in parasites and scope *vs.*

239 efficiency of resistance in host plants

240 The ubiquitous nestedness detected suggests a positive correlation between the host range breadth, 241 *i.e.* the percentage of host accessions that a parasite can efficiently infect, and the pathogenicity 242 level of the parasite. Similarly, a positive correlation is expected between the scope of the resistance and the resistance efficiency of the plants. Given the continuous distribution of the quantitative 243 244 pathogenicity traits, we defined arbitrary pathogenicity thresholds to distinguish host and non-host 245 accessions for a given parasite strain, and to distinguish parasite strains included or not included in 246 the scope of the resistance of a given plant accession. Nine thresholds were defined, varying from 247 10% to 90% of the maximal pathogenicity value in the whole matrix by increments of 10%, and 248 allowed estimating the percentage of plant accessions included in the host range of each parasite 249 strain (*i.e.* the host range breadth) and the percentage of parasite strains included in the scope of 250 resistance of each plant accession. The mean Pearson's coefficient of correlation (r) between host 251 range breadth and pathogenicity varied from 0.20 to 0.38 across the different threshold values 252 (mean 0.31). Depending on the threshold, from 23.1% (6/26 matrices) to 40.6% (13/32) (mean 253 31.9%) of the matrices showed significantly positive r values, whereas from 0 (0/11) to 9.7% (3/31) 254 (mean 4.8%) of the matrices showed significantly negative r values (Fig. 3). Note that the coefficient 255 of correlation could not be calculated for several matrices for some of the thresholds because of the

lack of pathogenicity values above (for correlation between host range breadth and pathogenicity) or
below (for correlation between resistance scope and efficiency) that threshold.

258 The mean r between resistance scope and efficiency varied from 0.18 to 0.59 across the different

- threshold values (mean 0.39). Depending on the threshold, from 25.0% (6/24) to 46.9% (15/32)
- 260 (mean 35.8%) of the matrices showed significantly positive r values, whereas from 0 (0/32) to 9.4%

261 (3/32) (mean 2.9%) of the matrices showed significantly negative r values (Fig. 3).

262

263 Rare cases of modularity in quantitative plant-parasite interactions

264 We applied five algorithms to estimate the modularity of the 32 matrices (Newman and Girvan 2004;

Clauset et al. 2004; Newman 2006; Blondel et al. 2008; Traag and Bruggeman 2009; Supplementary

266 Methods 1). By maximizing a modularity score, these algorithms estimate the optimal number of

267 modules and the distribution of plant and parasite genotypes in the modules. Modularity scores

were low overall, with a maximum of 0.240 and a mean of 0.075, on a scale varying from 0 to 1

269 (Tables 3 and 4). The *fast greedy, louvain* and *leading eigenvector* methods provided highly similar

- 270 modularity scores among the 32 matrices, with Pearson's coefficients of correlation r > 0.91 (p-values
- 271 ≤ 1e-12). Scores of the *edge betweenness* method were highly correlated with the previous three
- 272 methods (0.58 < r < 0.74; p-values $\le 6e-04$) whereas scores of the *spinglass* method were moderately
- 273 correlated with the previous ones (0.39 < r < 0.61; p-values ≤ 0.027). Our analysis of the performance
- of these methods showed that the *spinglass* algorithm had a very low rate of false positive
- 275 modularity, whatever the null model (Supplementary Methods 1). In contrast, the fast greedy,

276 *louvain* and *edge betweenness* algorithms had high rates of false positive modularity with several null

- 277 models, except models S (where cell values of the actual matrix are shuffled, with no constraints on
- 278 row or column marginal sums), C2 and R2 (Tables S7-S9).

According to the *spinglass* method, six matrices (numbers 5, 6, 10, 11, 14 and 17b) were significantly

280 modular with a majority of null models (Table 3), though their modularity scores were low (≤ 0.102).

281 Depending on the matrix, *spinglass* defined an optimal number of two or three modules, which

provided the maximal modularity score (Table 3; Fig. 4). In addition, matrices 8 and 22 were only

significantly modular with one null model. Evidence of modularity with the *edge betweenness, fast*

284 greedy, louvain and leading eigenvector methods was scarce, significant modularity being usually

observed for one of the null models S, C2 or R2 only and not for all methods (Table 4).

286 With all modularity methods, several matrices were less modular than at least 95% of the matrices 287 simulated under one or several null models (white on black numbers in Tables 3 and 4), a property 288 that we will name anti-modularity. For spinglass, only matrix 7 was significantly anti-modular with 289 null models N, C1 and R1 (Table 3). The other methods detected significant anti-modularity in most 290 matrices with most null models but suffered high rates of false positive anti-modularity for many null 291 models (Supplementary Methods 1; Tables S11-S13). Considering only matrices that are significantly 292 anti-modular with both null models C2 and R2, which correspond to the lowest rates of false 293 positives (null model CR2 in Tables S11 to S13), 13 matrices were significant with at least two 294 methods and three (matrices 17, 28 and 29) were significant with the four methods (Table 4). Results 295 obtained with the other matrices varied according to algorithms and null models, showing both 296 significant modularity and anti-modularity, which could be due to low type I error performances of 297 the algorithms for detection of modularity and/or anti-modularity.

298

299 Investigation of the biological significance of modularity

300 We examined the relevance of the detected modules for the six matrices showing significant

301 modularity with most null models with *spinglass* (Table 2) by analysing whether the plant and

302 parasite genotypes belonging to each module shared common properties (common resistance gene

303 or QTL for plants; common pathogenicity factor for parasites; common origin for plants or parasites).

For matrix 5 (*Puccinia hordei*-barley), two modules were detected (Fig. 4). The first one grouped the five accessions with resistance QTLs *Rphq3* and *Rphq11*, showing delayed infection with most isolates of the second module, and one accession carrying QTLs *Rphq1*, *Rphq2* and *Rphq3*, showing delayed infection with almost all isolates (González et al. 2012). The second module contained four accessions with either no resistance QTL or QTL *Rphq18*, that were quickly infected by almost all isolates. The country of origin or date of collection of the isolates did not explain their distribution in the two modules (Marcel et al., 2008).

For matrix 6 (*Venturia inaequalis*-apple), three modules were detected. The first one grouped the eight accessions carrying QTL *T1* and the four *V. inaequalis* isolates collected on apple trees carrying *T1* (Laloi et al. 2017). The two other modules grouped (i) the remaining accessions that were either carrying no resistance QTL or QTLs F11 or F17 that have only a low effect on disease reduction and (ii) isolates collected on these accessions. One of these modules grouped a single isolate and a single accession. Infections were on average high within all modules and low between any pair of modules. Two modules were also detected for matrix 14 (*Zymoseptoria tritici*-bread wheat). These modules could be partially explained by the interaction between the resistance gene *Stb6* (Saintenac et al.

could be partially explained by the interaction between the resistance gene *Stb6* (Saintenac et al.

2018), that confers a high level of resistance in the absence of a hypersensitive response, and the

pathogen avirulence gene *AvrStb6* (Zhong et al. 2017). Six of the eight cultivars in the first module
carry *Stb6*, while at least six of the seven cultivars in the second module do not carry *Stb6*. Moreover,
the 44 fungal isolates structuring the first module are pathogenic on *Stb6* while the 54 isolates from
the second module are either pathogenic or not pathogenic on *Stb6*.

324 Concerning matrices 10, 11 (Podosphaera xanthii-melon) and 17b (Phytophthora capsici-pepper),

three modules were detected but there was no evidence of similarity in the genetic composition of

accessions, the presence of particular resistance genes or QTLs or the origin of isolates belonging to a

- 327 same module.
- 328

329 *Modularity of reverse matrices*

To test the occurrence of IMA patterns (Fig. 1F), we also analyzed the modularity of the 32 matrices

transformed such that a grade of 0 corresponds to the maximal plant susceptibility and grades 1 to 9

correspond to the range of increasing plant resistance (hereafter "reverse matrices"). Using the

spinglass algorithm, four matrices (numbers 10, 11, 14 and 15) showed significant but low modularity

(≤0.078) with either null models C1 and R1 or C2 and R2. Depending on the matrix, *spinglass* defined

an optimal number of two to five modules (Fig. 5).

The modules identified in reverse matrices 14 and 15 using the *spinglass* algorithm were biologically 336 337 more meaningfull than the two modules previously identified for matrix 14. Matrices 14 and 15 correspond to two different phenotypic traits measured in the same plant-parasite interactions (i.e. 338 339 necrosis and sporulation, respectively). Interestingly, modules identified in the two matrices were 340 similar but not identical since five modules were identified in matrix 14 and four modules were 341 identified in matrix 15. This may reflect differences in the genetic determinism of the two phenotypic 342 traits measured or differences in the mechanisms of various Stb resistance genes. For matrix 14, 343 three modules correspond to the presence of resistance genes Stb7 (one cultivar), Stb9 (three 344 cultivars) and Stb6 (four cultivars), one module to cultivars carrying various Stb genes (three 345 cultivars), and one module to susceptible (or partially resistant) cultivars (four cultivars). For matrix 346 15, the modules corresponding to the presence of Stb6 and Stb9 are also identified (with an 347 additional cultivar in the Stb6 module), the module corresponding to susceptible cultivars as well 348 (with two additional cultivars), and the cultivar Salamouni carrying *Stb13* and *Stb14* forms the fourth 349 module. As above, there was no evidence of similarity in the composition of accessions and isolates 350 belonging to the same module for reverse matrices 10 and 11.

Overall, considering both the initial and reverse matrices, our analysis revealed that only a minority
 of the matrices (7/32; 22%) were significantly modular.

353

354 Discussion

There is nothing more fundamental to the concepts in Plant Pathology as a science and to the 355 356 practical strategies used for managing plant health than the host range of a parasite and the scope of 357 resistance of a plant (Morris and Moury 2019). Based on the patterns in matrices of plant-parasite 358 interactions, we can conceive and test hypotheses about the molecular and evolutionary processes 359 that underlie plant-parasite interactions, develop robust diagnostic tools, design breeding programs 360 and strategies for deploying resistant cultivars, and construct models to anticipate disease 361 emergence. Given the complexity of the mechanisms involved in disease, it would be reasonable to 362 assume that the particularities of each pathosystem would be an impediment to identifying universal 363 principles that can guide these efforts. However, here we have used network-based analyses to 364 reveal the quasi-universal principle that the structure of quantitative matrices of plant-parasite 365 interactions is nested. Indeed, evidence of nestedness was found in 94% (30/32) of the matrices that 366 we analyzed and one of the two non-nested matrices (number 32) was one of the smallest ones, 367 which may have precluded the detection of a significantly nested pattern. Our results were based on 368 statistically robust analyses of quantitative assessments of compatible interactions between hosts 369 and parasites for large interaction matrices involving from 49 to 1470 (median 180) host-parasite 370 combinations. Quantitative data are key to the accuracy and genericity of these analytical methods. 371 Indeed, in a study of 52 published matrices containing data on plant-pollinator, plant-seed disperser 372 and parasitoid-host interactions, Staniczenko et al. (2013) found evidence of nestedness in only 3% 373 of matrices including quantitative data, whereas the same matrices considered in a binary manner 374 showed evidence of nestedness in 98% of cases.

375 Network theory has its origins in the study of social networks and in ecology of interacting organisms 376 (Patterson and Atmar 1986). Ecological networks are typically identified by counting in natura the 377 interactions between (or co-occurrence of) two sets of taxa. Evidence of nestedness was frequent for 378 all kinds of matrices, including interactions between hosts and symbionts, either mutualistic or 379 parasitic (Bascompte et al. 2003; Joppa et al. 2010; Dormann et al. 2017). A number of factors that 380 are external to the interacting organisms can affect properties of such ecological networks. For 381 example, nestedness increases with the abundance of taxa (Joppa et al. 2010; Staniczenko et al. 382 2013; Suweis et al. 2013; Valverde et al. 2018), with heterogeneous distribution of connections, *i.e.* of numbers of links between interacting taxa (Jonhson et al. 2013), with the occurrence of broad 383

384 connectivities (Feng and Takemoto 2014) and with spatially-limited interactions between taxa 385 (Valverde et al. 2017). These analytical methods were recently used to analyse host-symbiont 386 interactions resulting from cross-inoculation experiments, where every host taxon was inoculated 387 with every symbiont taxon, and the compatibility of each host-symbiont pair was reported in the 388 matrix (Flores et al. 2011; Flores et al. 2013; Weitz et al. 2013). The structural patterns of such 389 matrices, where all host-symbiont pairs are evaluated under the same experimental and 390 environmental conditions, are mainly the result of intrinsic, mostly genetic, differences between host 391 or symbiont taxa.

392 Network analyses can also be strongly affected by the choice of null models (Gotelli and Graves 393 1996). This is why we conducted a thorough evaluation of the performance of several null models 394 with simulations (Supplementary Methods 1). The null models should keep, as much as possible, 395 everything identical to the actual matrix apart from the pattern of interest, nestedness or 396 modularity. Many null models have unacceptably loose constraints. For example, null models that do 397 not force row or column marginal sums to be constant create distributions of taxa that do not match 398 those usually observed, leading to falsely positive nestedness (Brualdi and Sanderson 1999; Joppa et 399 al. 2010). Accordingly, high rates of false positives were observed with null models N and S in our 400 simulations (Tables S1 and S2). Since parasites typically differ greatly in the number of hosts they 401 exploit and the efficiency with which they exploit them, we did not want null models to detect 402 significant nestedness when the heterogeneity of infection was shuffled randomly among hosts, as 403 was frequently observed for null models N and S with test matrices M1R to M5R (Tables S1 and S2). 404 Null models R1 and R2 that force row marginal sums to be constant avoided this problem (Tables S1 405 and S2). The same was true for the scope and efficiency of resistance that differ greatly between 406 plant accessions. In that case, the C1 and C2 null models efficiently avoided an excess of falsely 407 positive nestedness due to the hererogeneity of resistance (because C1 and C2 are equivalent to R1 408 and R2 when the rows and columns of the matrix are exchanged, which leaves the nestedness scores 409 unchanged; data not shown). Overall, to account for both plant resistance and parasite infection 410 heterogeneities, we found that the CR1 (or CR2) null model, that combines null models C1 and R1 (or 411 C2 and R2, respectively), is the most efficient as it showed acceptable type I error rates (Supplementary Methods 1). Null model B, based on Patefield's (1981) algorithm, maintains both the 412 413 row and column marginal sums of the actual matrix. However, it does not maintain the connectance 414 (i.e. number of non-zero-valued cells of the matrix), which has a strong impact on the estimation of 415 nestedness. Consequently, the type I error rates associated with null model B were frequently higher 416 than those obtained with models CR1 or CR2. Moreover, using quantitative instead of binary data

417 contributed to lowering the nestedness false positive rate (Staniczenko et al. 2013; Dormann et al.418 2017).

Overall, we obtained strong and consistent evidence of nestedness for almost all matrices (except
matrices 21 and 32), whatever the parasite type, the plant species or the pathogenicity trait
measured. Nestedness was linked to two important features of quantitative plant-parasite matrices:
(i) scarcity and/or low level of statistical interactions between plant and parasite genotypes in terms
of infection intensity and (ii) lack of trade-offs between host range and pathogenicity among parasite
strains and between efficiency and scope of the resistance among plant accessions.

425 The former feature is supported by the fact that an additive linear model - containing only a plant 426 accession effect and a parasite strain effect with no interaction term - showed high multiple 427 coefficients of determination (from 0.49 to 0.98) across matrices (Table 1). This result is compatible 428 with a genetic model where pathogenicity in the parasite and resistance in the host plant are 429 determined by a varying number of QTLs, but the statistical interaction between effects of QTLs from 430 the parasite and QTLs from the host is rare and/or of small magnitude (Table 1; Fig. 1G). In other 431 words, plants and parasites differ by their QTL assemblage (i.e. QTL numbers and/or effects) but 432 plant resistance QTLs have similar effects towards all parasite strains and, reciprocally, parasite 433 pathogenicity QTLs have similar effects towards all plant genotypes. Quantitative models usually 434 used to analyse empirical data on plant-parasite interactions are quite simplistic, e.g. assuming or not 435 a statistical interaction between plant and parasite genotypes (Parlevliet 1977). Models that are 436 more complex have been proposed in the frame of theoretical modelling (*e.g.* Fenton et al. 2009) but 437 their relevance to represent biological data was not evaluated. Importantly, we do not argue that 438 evidence of nestedness supports a single genetic model of plant-parasite interaction. Instead, we 439 suggest that an additive linear model with a plant accession and a parasite strain effects is the 440 simplest model that accounts for the empirical data but we cannot exclude that other models could 441 be suitable, like the modified GFG model of Fenton et al. (2009). A future challenge, requiring more 442 in-depth genetic studies, would be to evaluate the adequacy of these different models to represent 443 empirical plant-parasite interactions. New analytical methods can provide a better understanding 444 and quantification of host-parasite genetic interactions, such as the host-parasite joint genome-wide 445 association analysis recently developed by Wang et al. (2018). Applied to the Arabidopsis thaliana-446 *Xanthomonas arboricola* pathosystem, this model showed that 44%, 2% and 5% of the phenotypic variance could be explained respectively by the parasite strain, the host accession and the parasite-447 448 host interaction. As in our results, only a small parasite-host interaction effect was detected.

449 The latter feature of quantitative plant-parasite matrices is supported by the fact that we observed a 450 majority of positive, rather than negative correlations (i.e. trade-offs), between the infectivity and 451 the breadth of host range of parasites on the one hand and, especially, between the efficiency and 452 scope of the resistance of plants on the other hand (Fig. 3). Few studies have examined the 453 relationships between the scope and efficiency of plant resistance. In contrast with our results, 454 Barrett et al. (2015) hypothesized evolutionary trade-offs between resistance efficiency and scope 455 because quantitative resistance had a broader scope compared to qualitative resistance in the Linum 456 marginale – Melampsora lini interactions. The difference between our studies could be that we 457 focussed on quantitative resistance and included few qualitative resistance genes in our dataset (or 458 these were overcome by most parasite strains). The positive correlation between parasite infectivity 459 and host range breadth contrasts with qualitative host-parasite interactions and especially the GFG 460 model, where the expansion of the host range of parasites is associated with a cost in fitness during 461 infection of the previous hosts. Such so-called "virulence costs" have been experimentally measured 462 in many plant-parasite systems, including viruses (Jenner et al. 2002; Desbiez et al. 2003; Janzac et al. 463 2010; Poulicard et al. 2010; Fraile et al. 2011; Ishibashi et al. 2012; Khatabi et al. 2013), fungi (Bahri 464 et al. 2009; Huang et al. 2010; Caffier et al. 2010; Bruns et al. 2014), oomycetes (Montarry et al. 2010), bacteria (Vera Cruz et al. 2000; Leach et al. 2001; Wichmann and Bergelson 2004) or 465 466 nematodes (Castagnone-Sereno et al. 2007), and could explain why universal pathogenicity is not 467 fixed in pathogen populations (Tellier and Brown 2011). For quantitative plant resistance, few studies 468 have estimated the occurrence of pathogenicity costs. Montarry et al. (2012) showed a cost for PVY 469 to adapt to a quantitative pepper resistance when inoculated to a susceptible pepper genotype, 470 whereas Delmas et al. (2016) showed, on the opposite, that there was no fitness cost associated with 471 the adaptation of *Plasmopara viticola* to partially resistant grapevine varieties. Fournet et al. (2016) 472 even highlighted that nematode populations that had adapted to potato quantitative resistance were 473 more pathogenic on a susceptible potato genotype than were naïve nematode populations. The 474 present study focused mostly on interactions between plants and parasites at the intraspecific level, 475 but other studies have revealed a similar trend when strains of a given parasite species are 476 confronted with numerous plant species. For example, a positive correlation was observed between 477 species host range and pathogenicity for *Pseudomonas syringae* (Morris et al. 2000, 2019). For this 478 bacterium, the most pathogenic strains were also the most ubiquitous in the environment, 479 suggesting also an absence of trade-off between host range and dispersal capability or survival in the 480 environment (Morris et al. 2010).

In contrast to nestedness, we obtained little evidence of modularity among the matrices that we
analysed. Modularity scores were low for all matrices. In only seven matrices, representing either

483 infection or resistance scores (i.e. reverse matrices), did we detect significant modularity with a 484 majority of null models (Tables 3 and 4; Fig. 4 and 5). For four of these matrices (matrices 5, 6, 14 and 485 15), modularity was linked to the presence of particular resistance genes or QTLs in the plant 486 accessions and, for the parasite strains, to the presence of particular avirulence genes or to a 487 common origin in terms of host genotype. For the remaining matrices (10, 11 and 17b), no common property could be found for plant accessions and parasite strains belonging to the same module. The 488 489 lack of modularity of infection matrices and of reverse matrices suggests that the MA and IMA 490 genetic models are either inadequate to represent the structure of quantitative plant-parasite 491 interactions or explain only marginally their structure (Fig. 1E,F).

492

493 Conclusion

494 The ubiquitous nested patterns observed in quantitative plant-parasite interaction matrices have

important implications for our understanding and management of plant diseases. They can help infer

496 the underlying genetic bases of quantitative aspects of disease manifestation and their evolution.

497 Our results are compatible with an additive model comprising a plant resistance effect, a parasite

498 pathogenicity effect and no (or little) plant-parasite interaction effect.

499 A major enigma that we highlight is the apparent lack of trade-off between pathogenicity and host 500 range breadth among strains of a parasite, which has important implications on the efficiency of 501 plant resistance management through cultivar rotation, mixtures or mosaics. Indeed, these strategies 502 rely at least in part on a counter-selection of the most pathogenic parasite strains by a diversification 503 of plant cultivars (Brown 2015). The efficiency of these strategies would certainly be reduced in 504 absence of costs of adaptation to plant resistance. Therefore, in absence of such costs, the efficiency 505 of the rotation, mixtures or mosaic strategies would rather depend on barrier effects designed to 506 limit parasite dispersal in agricultural landscapes.

507

508 Materials and Methods

509 Datasets

To be able to analyse plant-parasite interaction networks, we selected datasets containing at least 6
plant accessions and 6 parasite strains. A brief description of these datasets is provided in Table 1

512 and in the following text.

513

514 Matrices 1 to 4: *Pseudomonas syringae-Prunus armeniaca* (apricot)

515 Nine strains of *Pseudomonas syringae*, the causal agent of bacterial canker of apricot, were 516 inoculated on dormant tissues of twenty apricot cultivars chosen according to their differential 517 susceptibility in orchard conditions. The strains were chosen mainly within phylogroups 1 and 2, the 518 most abundant groups of *P. syringae* in contaminated apricot orchards in France (Parisi *et al.* 2019). 519 Seven strains were isolated from symptomatic trees and two in crop debris and soil. Bacterial 520 inoculum was prepared by cultivation on King's B medium for 48h at 24°C. The concentration of the 521 bacterial suspension was adjusted at 10^8 CFU.ml⁻¹. A volume of 25 µl of inoculum was deposited at 522 the level of a wound made superficially with a scalpel on the bark of one-year-old twigs grown in 523 orchard. Five months after inoculation, twigs were removed and the length of flat zone around the 524 inoculation point at the surface of the shoot (matrices 1 and 2) and the length of browning zone 525 around the inoculation point below the bark of the shoot (matrices 3 and 4) were measured. Two 526 independent tests were performed in 2017 (matrices 1 and 3) and 2018 (matrices 2 and 4).

527

528 Matrix 5: *Puccinia hordei-Hordeum vulgare* (barley)

529 Fourteen *Puccinia hordei* isolates (from Europe, Morocco, Israel and the USA) were inoculated on a

530 differential series of 12 *H. vulgare* lines carrying different *Rphq* QTLs (González et al. 2012). The first

seedling leaves of each barley line were inoculated with \approx 240 spores/cm². The relative latency period

532 (RLP) (Table 3 in González et al. 2012) was estimated by the number of hours from inoculation to the

533 moment at which 50% of the ultimate number of uredinia was visible.

534

535 Matrices 6 to 8: *Venturia inaequalis-Malus domestica* (apple tree)

Grafted plants of different apple accessions (*Malus domestica*) carrying resistance QTLs (*T1, F11, F17, F11 + F17* or *T1 + F11 + F17*) or no resistance QTL were inoculated in controlled conditions with isolates of *Venturia inaequalis*, a fungal pathogen responsable of apple scab. The percentage of sporulating leaf area was assessed from 8 to 21 days post inoculation (dpi) on a scale with eight levels: 0 = no visible symptom, 0.5 = 0-1%, 3 = 1-5%, 7.5 = 5-10%, 17.5 = 10-25%, 37.5 = 25-50%, 62.5 = 50-75%, and 87.5 = 75-100%. Matrix 6 (Laloi et al. 2017) consisted of interactions between 10 *V. inaequalis* isolates sampled in one

543 orchard (Angers, France) on apple trees carrying *T1*, *F11+F17*, *T1+F11+F17* or no QTL and 14 apple

544 accessions carrying the matching resistance QTL or no QTL.

545 Matrix 7 (Caffier et al. 2016) consisted of interactions between 14 *V. inaequalis* isolates sampled in one 546 orchard (Angers, France) on apple trees carrying or not *T1* and 12 apple accessions carrying or not *T1*

547 (with six accessions for each of the two classes). Matrices 6 and 7 represent the Area Under the Disease

548 Progress Curve (AUDPC) of the percentage of sporulating leaf area from eight to 21 dpi.

549 Matrix 8 (Caffier et al. 2014) consisted of interactions between 24 V. inaequalis isolates sampled in

550 two orchards (Lanxade and Villeneuve d'Ascq, France) on apple trees carrying F11, F17, F11+F17 or

- no QTL and eight apple accessions carrying the matching QTL or no QTL (with two accessions for each
- of the four classes). Matrix 8 represents the percentage of sporulating leaf area 14 dpi.

553

554 Matrix 9: Botrytis cinerea-Solanum lycopersicum / Solanum pimpinellifolium (tomato)

555 Leaves of 12 tomato accessions (six domesticated accessions of Solanum lycopersicum and six

accessions of the close wild relative *S. pimpinellifolium*) were infected with single droplets of spore

557 suspensions of 94 *B. cinerea* isolates. The size of lesions was measured from digital images 72 hours

after inoculation (Soltis et al. 2019). One isolate was poorly infectious on all tomato accessions (grade

559 0 after data transformation) and was withdrawn.

560

561 Matrices 10 and 11: Podosphaera xanthii-Cucumis melo (melon)

562 Nineteen melon differential lines were inoculated with 26 Podosphaera xanthii isolates collected in 563 2013 and 2014 in melon, squash, watermelon and cucumber crops in Southern Europe or Northern 564 Africa (France, Spain, Italy, Morocco, Turkey, Greece). Each P. xanthii isolate was propagated on 565 cotyledons of Lagenaria ciceraria for seven days and spores were blown on eight leaf disks per melon line-P. xanthii isolate combination using an inoculation tower (Perchepied et al. 2005). Sporulation 566 567 intensity was scored 14 days after inoculation and data were transformed in percentage of leaf disk 568 surface using the class mean as suggested by Nicot et al. (2002): 0 = 0%, 1 = 2.5%, 2 = 7.5%, 3 = 10%569 17.5%, 4 = 37.5%, 5 = 67.5%, 6 = 82.5%, 7 = 92.5%, 8 = 97.5%, and 9 = 100%. The mean score for 570 melon accession - P. xanthii isolate combinations was reported in matrix 10. For matrix 11, 31 571 isolates were inoculated to 19 differential lines on leaves of entire plants. The sporulation intensity was scored similarly as for leaf disks using a 0 to 9 scale. The mean score for melon accession - P. 572 xanthii isolate combinations was reported in matrix 11. 573

575 Matrices 12 to 15: *Zymoseptoria tritici-Triticum aestivum* (bread wheat) or *T. turgidum* subsp. *durum*

576 (durum wheat)

577 Matrices 12 and 13 were built by inoculating 12 lineages from a durum wheat landrace called 578 Mahmoudi with 15 Zymoseptoria tritici isolates. The 12 plant lineages were fixed from individivuals 579 coming from a single field at Journie in Tunisia and corresponded to 12 different multilocus genotypes 580 (MLGs) as defined previously by Ben Krima et al. (2020). The 15 isolates were collected in situ either 581 from the landrace Mahmoudi or from the cultivar Karim, at Journine in 2018. Matrices 14 and 15 were 582 built by inoculating 15 bread wheat cultivars (Triticum aestivum), 12 of which carrying different Stb 583 resistance genes, with 98 Z. tritici isolates collected mostly on cultivars Apache and Premio, all over 584 France between 2009 and 2010. These bread wheat cultivars belong to a series of differential 585 genotypes used to characterize the pathogenicity of Z. tritici isolates. All wheat-Z. tritici pairwise 586 confrontations were evaluated under controlled conditions, in growth chambers at 18°C/22°C 587 night/day and 16 hours light at 300 µmol.m⁻².s⁻¹. The first true leaf of 16-day-old seedlings were marked 588 with a black felt to delimit a 7.5 cm length that was inoculated with a solution of water containing 10⁶ 589 spores.mL⁻¹ and one drop of Tween[®] 20 per 15 mL. The inoculum was applied with a square-tipped flat 590 paintbrush six times on each leaf, repeated twice. After inoculation the plants were placed in 591 transparent polyethylene bags for 72 hours to initiate infection. At 10 dpi, *i.e.* before the appearance 592 of symptoms, leaves above the inoculated leaf were cut to homogenize light exposure. Visual 593 estimations of necrotic leaf area and sporulating leaf area were done at 14 dpi, 20 dpi and 26 dpi for 594 matrices 12 and 13, and only once at 21 dpi for matrices 14 and 15. For matrices 12 and 13, these 595 observations were used to calculate, for each plant lineage-isolate combination, an area under disease 596 progress curve (AUDPC) for the percentages of necrotic and sporulating leaf areas. The interactions for 597 matrices 12 and 13 were evaluated on three leaves repeated twice in time (total of six leaves) and for 598 matrices 14 and 15 on three leaves repeated thrice in time (total of nine leaves).

599

600 Matrices 16, 17 and 17b: *Phytophthora capsici-Capsicum annuum* (pepper)

To build matrix 16, the pathogenicity of six isolates of *Phytophthora capsici*, the causal agent of root and crown rot of chilli and bell peppers, collected in pepper fields in Algeria was measured in ten *Capsicum annuum* cultivars (F_1 hybrids or inbred lines) (Messaouda et al. 2015). Six plants per accession were inoculated by depositing a plug of 4 mm in diameter of mycelium of *P. capsici* cultivated on V8 medium on the fresh section of the primary stem extemporaneously decapitated (Lefebvre and Palloix 1996). Inoculated plants were kept in a growth chamber under controlled conditions with 12h photoperiod, a temperature of 22 ± 2°C and 100% relative humidity. *P. capsici* progresses to the

bottom of the stem causing a necrosis of the stem. The length of stem necrosis at 15 dpi is reported inmatrix 16.

610 For matrix 17, 53 accessions of C. annuum were inoculated by six isolates of P. capsici. The C. annuum 611 accessions originated from 20 countries from America, Europe, Asia and Africa, and included 612 accessions that had different levels of partial resistance to isolate P. capsici 'Pc101' and a few 613 susceptible accessions. The six P. capsici isolates were isolated from pepper plants in France and 614 Turkey, were of A1 mating type and differed in pathogenicity. A minimum of six plants per accession, 615 seven-eight week old, were inoculated as described for matrix 16. Inoculated plants were kept in a 616 growth chamber under controlled conditions with a photoperiod of 12h at 24°C under artificial light 617 and 22°C at obscurity. The length of stem necrosis was measured six times from three to 21 dpi and 618 the Area Under the Disease Progress Curve (AUDPC) of necrosis length was considered in matrix 17. 619 Because matrix 17 contained a large number of zero-values cells, matrix 17b was derived by

620 withdrawing redundant columns and columns entirely made of zero-valued cells.

621

622 Matrix 18: Phytophthora infestans-Solanum lycopersicum

Matrix 18 was built by inoculating eight Solanum sp. accessions with seven isolates of Phytophthora 623 624 infestans, the causal agent of tomato late blight. The accessions consisted of three inbred lines of 625 cultivated tomato (Solanum lycopersicum) and five accessions of the wild relative species S. pimpinellifolium, S. habrochaites and S. pennellii. Some of them are known to carry the Ph-1, Ph-2 or 626 627 Ph-3 genes, controlling resistance to races 0, 1 and 2 of P. infestans, respectively. The P. infestans 628 isolates were collected on tomato or potato plants in France and Poland and were chosen because 629 they varied in mating type (A1 or A2) and differed in pathogenicity. Mycelium was grown on pea juice-630 based agar medium for 10 days and six plants per accession, 3-4 week old, were inoculated using the 631 protocol described for matrix 16 (Danan et al. 2009). Inoculated plants were kept in a growth chamber 632 under controlled conditions with a photoperiod of 14h at 21°C under artificial light and 17°C at 633 obscurity. High humidity was maintained by artificial mist. Stem necrosis length was scored four times 634 from three to 14 dpi and the AUDPC was calculated.

635

636 Matrix 19: Aphanomyces euteiches-Fabaceae (pea, vetch, faba bean, alfalfa)

637 Eight accessions from four leguminous species (pea, alfalfa, vetch, faba bean), which previously

638 showed various levels of resistance, were inoculated with 34 *Aphanomyces euteiches* isolates

- 639 sampled from the main French pea growing regions in a growth chamber (thermo period: 25/23°C
- and 16h photoperiod). Seven-day-old plants (5 plants * 4 replicates * 2 experiments for each
- 641 accession-isolate combination) were inoculated by applying 5 mL of a zoospore suspension adjusted

to 5.10^3 spores / mL. After inoculation, the vermiculite substrate was saturated with water to provide 642 643 favorable conditions for infection. After 10 days, the plants were carefully removed from the 644 vermiculite, the roots were washed in tap water and disease severity (DS) was scored on each plant 645 using a 0-5 scale: 0 = no symptoms; 1 = traces of discoloration on the roots (<25%); 2 = discoloration 646 of 25 to 50% of the roots; 3 = discoloration of 50 to 75% of the roots; 4 = discoloration of >75% of the 647 roots; 5 = dead plant. ANOVA was performed with the DS score as the dependent variable, the A. 648 euteiches isolate and the plant accession as fixed factors and the replicate and experiment as random 649 factors. From the ANOVA, least square means (LSmeans) were calculated for each A. euteiches 650 isolate-plant accession combination. In the present study, LSmeans values of root DS scores were 651 analysed. More details are provided in Quillévéré-Hamard et al. (2018).

652

653 Matrix 20: Aphanomyces euteiches-Pisum sativum

Ten pea accessions were inoculated with 43 *A. euteiches* isolates sampled from the main French pea

655 growing regions in a growth chamber. The ten pea accessions consisted of (i) eight Near-Isogenic-

Lines (NILs) carrying one, two, three or five resistance alleles at main QTLs, in a common genetic

background and (ii) two control lines, including one susceptible variety and one highly resistant line.

The experimental design, inoculation procedure, disease scoring scale and statistical analysis were

659 similar to that described for matrix 19, except for inoculum concentration (2.10² spores / mL) and the

scoring date (seven days after inoculation). LSMean values of root DS scores were used. More details

661 are provided in Quillévéré-Hamard et al. (2020).

662

663 Matrices 21 and 22: *Plasmopara viticola-Vitis vinifera* (grapevine)

664 A set of 33 Plasmopara viticola strains, the causal oomycete of grapevine downy mildew, was 665 inoculated on eight grapevine varieties. The host panel was constituted of seven grapevine varieties 666 carrying the main resistance factors currently used in European breeding programs (Rpv1, Rpv3.1, 667 *Rpv3.2, Rpv5, Rpv6, Rpv10* and *Rpv12*) and one susceptible variety (Chardonnay). Cuttings from these 668 varieties were grown in a glasshouse under natural photoperiod. Each strain-variety combination was replicated on five leaf discs from five different plants that were excised in the fourth leaf below the 669 670 apex. Leaf discs were sprayed with 4 mL of a suspension of 10^5 / mL sporangia of *P. viticola*. They 671 were incubated in a climatic chamber for six days at 18°C with 12h/12h light/dark photoperiod. At six dpi, necrosis was rated on a scale of 0 to 4, based on the number of necroses counted per leaf disk (0 672 673 = no necrosis; 1 = <10 necroses; 2 = from 10 to 30 necroses; 3 = from 30 to 60 necroses; 4 = > 60

674 necroses) (matrix 21) and sporulation was assessed on leaf discs by automatic image analysis

675 (number of black pixels on the total leaf disc area) (matrix 22).

676

677 Matrices 23 and 24: Aphis gossypii-Cucumis melo

678 Matrices 23 and 24 were obtained through assessment of the resistance of 13 melon accessions to nine aphid (Aphis gossypii) clones (Boissot et al. 2016). The host panel consisted in twelve partially-679 680 resistant lines originating from Africa, India, China, Asia and Far East Asia, Mediterranean basin and 681 North America and a susceptible cultivar originating from Mediterranean basin. Two lines were wild 682 accessions and the others from breeding programs. They contained at least one to three homologs of 683 Vat, a gene conferring resistance to A. gossypii. The 13 melon lines belonged to three genetic groups 684 representative of melon diversity (Boissot et al., submitted). The aphid panel consisted in nine clones 685 collected in France and French West Indies. Except clone NM1 that was observed on plant species 686 belonging to six families, the clones have been observed exclusively (or almost exclusively) on 687 cucurbit plants and belong to the same genetic cluster.

For phenotyping, ten adult aphids were deposited on melon plantlets. Three days later, the number of aphids remaining on the plantlets was recorded as the 'Acceptance' parameter (matrix 23). Seven days after aphid deposition, the adults were counted, and the density of nymphs was estimated on a scale of 0 to 6. The 'Colonization' parameter was calculated as [density of nymphs + In(number of adults + 0.001)] (matrix 24). The 'Acceptance' and 'Colonization' parameters were collected for at least eight plantlets of each melon accession. Each test was conducted with one aphid clone on a subset of melon accessions.

695

696 Matrices 25 and 26: *Globodera pallida-Solanum tuberosum* (potato)

697 Matrix 25 was obtained through the inoculation of 20 populations of the potato cyst nematode 698 Globodera pallida on ten potato accessions. Those potato accessions were characterized by different levels of quantitative resistance. A susceptible potato cultivar, Désirée, was also used as a control. 699 700 Among the 20 G. pallida populations, 14 came from South-America (Peru and Chile) and six from 701 Europe. To perform *G. pallida* inoculation, ten cysts were locked in a tulle bag and placed in a pot 702 three-guarter filled with a soil mixture free of cysts (2/3 sand and 1/3 natural field soil). Four 703 replicates were performed for each potato accession - G. pallida population combination, i.e. for 704 each G. pallida population, four bags were inoculated to four tubers of the same potato accession. 705 One potato tuber was planted per pot and covered with the same soil mixture. Potato plants grew in

the greenhouse, under controlled conditions (15°C night during 8h and 20°C day during 16h), for 120
days. After 120 days, newly formed cysts were extracted from the soil, using a Kort elutriator. The
number of newly formed cysts was counted using a magnifying stereomicroscope, and divided by the
number of newly formed cysts produced on the susceptible cultivar Désirée (relative value).
For matrix 26, the measured fitness trait was the hatching of cysts which is induced by host root
exudates. It was produced using a cross-hatching assay between 13 populations of *G. pallida* and

- root exudates from 12 wild potato accessions, belonging to species *Solanum huancabambense*, *S*.
- 713 mochiquense, S. sogarandinum, S. ambosinum, S. medians, S. pampasense, S. santalallae, S.
- 714 marinasense, S. sparsipilum, S. raphanifolium, S. limbaniense and S. leptophyes, to test the
- 715 hypothesis of local adaptation between Peruvian *G. pallida* populations and Peruvian wild potato
- 716 accessions (Gautier et al. 2020). All details about *G. pallida* populations, root-exudates and the *in*
- vitro hatching assay are available in Gautier et al. (2020). Briefly, three cysts of each population were
- put on a sieve in 1.5 mL of root exudates (with four to five replicates) and after 30 days, the number
- of hatched juveniles was counted. At the end of the experiment, cysts were crushed and the number
 of unhatched viable eggs was counted, in order to calculate a hatching percentage.
- 721

722 Matrices 27 to 32: Potato virus Y-Capsicum annuum

723 The Capsicum annuum accessions were doubled-haploid lines issued from the F₁ hybrid between 724 accessions Perennial, carrying several Potato virus Y (PVY) resistance QTLs, and the susceptible 725 accession Yolo Wonder. They were chosen based on the lack of a major-effect resistance gene but 726 contrasted levels of quantitative resistance (Caranta et al. 1997). The PVY populations were issued 727 from cDNA clones of isolates SON41p and LYE84.2 and recombinants between these two cDNA 728 clones (Montarry et al. 2012). Capsicum annuum accessions were mechanically inoculated with the 729 different PVY populations and the virus load at the systemic level was estimated one month post 730 inoculation by quantitative DAS-ELISA as described in Quenouille et al. (2014) (matrices 27 and 28). In 731 addition, the area under the disease progress curve (AUDPC) was calculated using a semi-732 quantitative scoring scale as in Caranta et al. (1997) (matrices 29 and 30) and the dry weight of 733 infected relative to mock-inoculated plants was estimated as in Montarry et al. (2012) (matrices 31 734 and 32). Matrices 27, 29 and 31 on one side and matrices 28, 30 and 32 on the other side correspond 735 to two independent experiments with slightly different sets of PVY populations.

736

737 Network analyses

738 The nestedness and modularity of the different matrices were estimated, and their statistical 739 significance tested respectively with the 'bipartite' and 'igraph' packages of the R software version 740 3.5.1 (http://cran.r-project.org/). These analyses were initially developed for the study of social, then 741 of ecological, networks (or equivalently matrices) containing counts of links between individuals or between interacting species. Hence, to perform these analyses, the matrices should only contain 742 integer values. Moreover, some nestedness or modularity algorithms cannot run in the absence of 743 744 zero-valued matrix cells or in the presence of an excess of zero-valued cells leading to an 745 unconnected network.

Consequently, the first step consisted in transforming the actual matrices accordingly. In all matrices,

pathogenicity trait values were transformed into integers from 0 to 9. For this, ten intervals with

equal sizes and spanning the range of the pathogenicity trait values of the actual matrix were

defined. The bounds of these intervals are $[P_{min} + (P_{max} - P_{min})*i/10, P_{min} + (P_{max} - P_{min})*(i+1)/10]$,

with *i* being an integer in the [0,9] interval and P_{max} and P_{min} being the maximal and minimal

751 pathogenicity trait values in the whole matrix, respectively. Then, depending on its inclusion in a

given pathogenicity trait value interval defined as above, each matrix value was transformed into the

corresponding *i* integer value. When necessary, the matrix was modified in order that grades 0 and 9

correspond to the minimal and maximal pathogenicity classes, respectively, and not the opposite. A

continuous distribution of the pathogenicity grades was observed in 30 of 32 matrices (Fig. 2).

However, for matrices 17b and 22 that contained a large number of zero-values cells, phenotypic

values were log-transformed to spread out the data more evenly among the ten phenotypic classes.

758 As these log-transformed matrices produced similar results to the actual matrices in terms of

r59 significance of nestedness and modularity, only the latter are shown. To test if the matrices could fit

with the inverse-matching-allele model (Fig. 1), we also analyzed the "reverse matrices", where 0 and

9 correspond to the minimal and maximal plant resistance classes, respectively. Methods to estimate

nestedness and modularity are detailed in Weitz et al. (2013). Whereas many algorithms can

measure the nestedness of matrices containing binary data (0 and 1), only two algorithms were

available for matrices containing quantitative numeric data: the weighted nestedness metric based

on overlap and decreasing filling (wNODF algorithm) (Almeida-Neto et al. 2008) and the weighted-

766 interaction nestedness estimator (*WINE* algorithm) (Galeano et al. 2009). In the R software, the

765

⁷⁶⁷ 'nested' and 'wine' functions were used to estimate the *wNODF* and *WINE* scores, respectively.

768 Because none of the module detection algorithms developed to date provide consistently optimal

results in all matrices (Aldecoa and Marín 2013), we used seven different algorithms implemented

into the R software (see Supplementary Methods 1 for details). To determine the statistical

significance of the patterns (nestedness or modularity) of the plant-parasite interaction matrices, the

actual interaction matrices were compared to matrices simulated under several null models

773 (Supplementary Methods 1).

As the modularity algorithms (and nestedness algorithms to a lower extent) and null models

provided contrasted results (Tables 2 to 4), we used simulations to compare their performances

(type I and type II error rates) and help the interpretation of the results (Supplementary Methods 1;

777 Tables S1 to S18).

Two modularity algorithms (*walktrap* and *label prop*) provided modularity estimates of 0 (or near 0)

for almost all actual matrices and associated null models. Moreover, almost all simulations also

provided modularity estimates of 0 with these algorithms, hampering the evaluation of type I and

type II error rates (Supplementary Methods 1). Consequently, these two algorithms were not

782 considered for further analyses.

783

784 Acknowledgements

Marie-Claire Kerlan and Lionel Renault are acknowledged for there help to produce matrix number 785 786 25 and Anne Massire, Ghislaine Nemouchi, Thérèse Phaly, Bruno Savio and Patrick Signoret for their 787 assistance to produce matrix number 17. We thank Amine Slim from the National Gene Bank of Tunisia (NGBT) for providing seeds of the durum wheat landrace "Mahmoudi Joumine" used to build 788 789 the matrices 12 and 13, and we thank Aurélie Ducasse and Johann Confais for their help in acquiring 790 phenotypic data on the wheat-Zymoseptoria tritici pathosystem found in matrices 14 and 15. We 791 thank Isabelle Demeaux (INRAE, SAVE) for providing technical assistance with the downy 792 mildew/grapevine pathosystem. Anne Quillévéré-Hamard, Gwenola Le Roy and Christophe Le May 793 are acknowledged for having co-supervised, managed and/or significantly contributed to the production of matrices number 19 and 20. We thank Loup Rimbaud and Emmanuel Szadkowski 794 795 (INRAE, PACA) for their comments on an earlier version of the manuscript and Michel Pitrat (INRAE, 796 PACA) for his help for analyses of matrices 10 and 11. We thank the staff of the INRAE CRB-Leg 797 (https://www6.paca.inrae.fr/gafl/CRB-Legumes) who maintained the pepper and melon germplasm 798 collections of the GAFL research unit, and of the INRAE experimental facilities of the Plant Pathology 799 research unit (https://doi.org/10.15454/8DGF-QF70), the GAFL experimental unit and the PHENOTIC 800 core facility in Angers (https://doi.org/10.15454/U2BWFJ) who ensured the production of the plants 801 and maintenance of plant-growth facilities that allowed us to do this work. We thank the staff of the 802 INRAE experimental facilities of IGEPP for having provided and managed equipment for the 803 experiments.

804

805 Funding

The research was supported by the French National Research Agency (ANR) programs BIOADAPT 806 807 (grant no. ANR-12-ADAP-0009-04), ArchiV (grant no. ANR-18-CE32-0004-01), CEDRE (grant no. ANR-808 05-PADD-05) and PeaMUST (grant no. ANR-11-BTBR-0002), the PROGRAILIVE project (grant 809 RBRE160116CR0530019) funded by the Bretagne region, France and European FEADER grants, the 810 fundings of the Institut Carnot PLANT2PRO and the Comité Interprofessionnel des Vins de Bordeaux (CIVB), the INRAE departments "Santé des Plantes et Environnement" (project APÔGÉ and PhD thesis 811 of Safa Ben Krima) and "Génétique et Amélioration des Plantes", the INRAE métaprogramme SMaCH 812 813 (Sustainable Management of Crop Health), the French Ministry of Agriculture and Food for projects 814 "Recherche et mise au point de méthodes pour évaluer des résistances variétales durables à des 815 agents pathogènes" (CTPS project C2008-29), "Nouvelles sources de résistance à Aphis gossypii chez 816 le melon" (CTPS project C06/02) and "Caractérisation de la virulence de Podosphaera xanthii, agent 817 causal de l'oïdium du melon, et développement d'un système de codification des races" (CTPS 818 project C-2012-10). UMR1290 BIOGER benefits from the support of Saclay Plant Sciences-SPS (ANR-819 17-EUR-0007).

820

821 Conflict of interest disclosure

822 The authors of this manuscript declare that they have no financial conflict of interest with the

823 content of this article. Benoît Moury in one of the *Peer Community In Evolutionary Biology*

824 recommenders.

Matrix number	Parasite	Host plant	Matrix size (host ×	Phenotype	Multiple R ^{2a}	Reference or source
			parasite)			
Bacterium						
1	Pseudomonas syringae	Prunus armeniaca (apricot)	20 × 9	Length of flat zone around the inoculation point at the surface of the shoot	0.69	Omrani <i>et al.,</i> unpublished
2	P. syringae	P. armeniaca	20 × 9	Length of flat zone around the inoculation point at the surface of the shoot	0.84	Omrani <i>et al.,</i> unpublished
3	P. syringae	P. armeniaca	20 × 9	Length of browning zone around the inoculation point below the bark of the shoot	0.68	Omrani <i>et al.,</i> unpublished
4	P. syringae	P. armeniaca	20 × 9	Length of browning zone around the inoculation point below the bark of the shoot	0.75	Omrani <i>et al.,</i> unpublished
Fungi						
5	Puccinia hordei	Hordeum vulgare (barley)	12×14	Relative latent period	0.84	González <i>et al.,</i> 2012
6	Venturia inaequalis	Malus domestica (apple)	14×10	% sporulating leaf area (AUDPC)	0.64	Laloi <i>et al.,</i> 2017
7	V. inaequalis	M. domestica	12 × 14	% sporulating leaf area (AUDPC)	0.49	Caffier <i>et al.,</i> 2016
8	V. inaequalis	M. domestica	8 × 24	% sporulating leaf area	0.71	Caffier <i>et al.</i> , 2014
9	Botrytis cinerea	Tomato ^b	12 × 94	Lesion size on leaves	0.59	Soltis <i>et al.,</i> 2019
10	Podosphaera xanthii	Cucumis melo (melon)	19 × 26	Sporulation surface on leaf disks	0.93	Dogimont <i>et al.,</i> unpublished
11	P. xanthii	C. melo	19 × 31	Sporulation surface on plants	0.94	Dogimont <i>et al.,</i> unpublished
12	Zymoseptoria tritici	<i>Triticum turgidum</i> subsp. <i>durum</i> (durum wheat)	12 × 15	% necrotic leaf area (AUDPC)	0.77	Marcel et al., unpublished
13	Z. tritici	T. turgidum subsp. durum	12 × 15	% sporulating leaf area (AUDPC)	0.76	Marcel et al., unpublished
14	Z. tritici	<i>Triticum aestivum</i> (bread wheat)	15 × 98	% necrotic leaf area	0.63	Marcel et al., unpublished
15	Z. tritici	T. aestivum	15 × 98	% sporulating leaf area	0.63	Marcel et al., unpublished

Table 1: Datasets used to analyze the structure of quantitative plant-parasite interaction matrices. AUDPC : Area under the disease progress curve.

Oomycetes						
16	Phytophthora capsici	Capsicum annuum (pepper)	10 × 6	Necrosis length on stem (15 days post inoculation)	0.98	Messaouda et al., 2015
17	P. capsici	C. annuum	53 × 6	Necrosis length on stem (AUDPC)	0.78	Cantet et al., unpublished
17b ^c	P. capsici	C. annuum	42 × 6	Necrosis length on stem (AUDPC)	-	Cantet et al., unpublished
18	Phytophthora infestans	Solanum lycopersicum	8 × 7	Necrosis length on stem (AUDPC)	0.90	Ruellan <i>et al.,</i> unpublished
		(tomato), S. pimpinellifolium, S. habrochaites and S. pennellii				
19	Aphanomyces euteiches	Fabaceae ^d	8 × 35	Root disease severity	0.85	Quillévéré-Hamard <i>et al.,</i> 2018
20	A. euteiches	Pisum sativum	10 × 43	Root disease severity	0.86	Quillévéré-Hamard et al., 2020
21	Plasmopara viticola	Vitis vinifera (grapevine)	8 × 33	Necrosis on leaves	0.76	Paineau and Delmotte, unpublished
22	P. viticola	V. vinifera	8 × 33	Sporulation on leaves	0.80	Paineau and Delmotte, unpublished
Insect						
23	Aphis gossypii	C. melo	13 × 9	Acceptance of plants	0.61	Boissot <i>et al.,</i> 2016
24	A. gossypii	C. melo	13 × 9	Ability to colonize plants	0.59	Boissot et al., 2016
Nematode						
25	Globodera pallida	Solanum tuberosum (potato)	10 × 20	Cyst number (relative values)	0.58	Fournet et al., unpublished
26	G. pallida	Wild potato species	12 × 13	Cyst eclosion rate	0.81	Gautier <i>et al.,</i> 2020
Virus						
27	Potato virus Y (PVY)	C. annuum	7 × 8	Virus load	0.79	Doumayrou <i>et al.,</i> unpublished
28	PVY	C. annuum	9 × 7	Virus load	0.73	Doumayrou <i>et al.,</i> unpublished
29	PVY	C. annuum	8 × 7	Symptom intensity (AUDPC)	0.78	Doumayrou <i>et al.,</i> unpublished
30	PVY	C. annuum	7 × 7	Symptom intensity (AUDPC)	0.81	Doumayrou <i>et al.,</i> unpublished
31	PVY	C. annuum	8 × 7	Relative dry matter weight	0.66	Doumayrou <i>et al.,</i> unpublished
32	PVY	C. annuum	7 × 7	Relative dry matter weight	0.45	Doumayrou et al., unpublished

^{*a*} Fit of the linear model: pathogenicity \sim 'parasite strain' + 'plant accession' (multiple coefficient of determination).

^b Two species: cultivated tomato (*Solanum lycopersicum*) and wild tomato (*S. pimpinellifolium*).

^c Matrix 17b is identical to matrix 17 except that columns entirely made of zero-valued cells and redundant columns were removed.

^{*d*} Four species: three pea (*Pisum sativum*) accessions, two vetch (*Vicia sativa*) accessions, two faba bean (*Vicia faba*) accessions and one alfalfa (*Medicago sativa*) accession.

	WINE method								wNODF method							
Matrix	Nestedness				Null mode	b			Nestedness				Null model	b		
number	score ^a	В	Ν	C1	R1	S	C2	R2	score	В	Ν	C1	R1	S	C2	R2
1	0.78	0 ^c	0	0	0	0	0	0	30.9	0.05	0	0	0	0	0	0
2	0.81	0.01	0	0	0	0	0	0	43.7	0.06	0	0	0	0	0	0
3	0.82	0	0	0	0	0	0	0	47.6	0	0	0	0	0	0	0
4	0.82	0	0	0	0	0	0	0	46.9	0	0	0	0	0	0	0
5	0.83	0	0	0	0	0	0	0	23.2	0.24	0	0.42	0	0	0.36	0
6	0.70	0.12	0	0	0	0	0	0	55.4	0.15	0	0	0	0	0	0
7	0.60	0.49	0	0	0	0	0	0	43.9	0.41	0	0	0	0	0	0
8	0.58	0.01	0	0	0	0	0	0	49.4	0.66	0	0	0	0	0	0
9	0.46	0	0	0	0	0	0	0	42.4	0.01	0	0	0	0	0	0
10	1.01	0	0	0	0	0	0	0	72.7	0	0	0	0	0	0	0
11	1.04	0	0	0	0	0	0	0	75.4	0	0	0	0	0	0	0
12	0.69	0	0	0	0	0	0	0	10.1	0.68	0.85	0.67	1	0.73	0.54	0.90
13	0.73	0	0	0	0	0	0	0	30.0	0.16	0.38	0.48	0.07	0.35	0.39	0.52
14	0.76	0	0	0	0	0	0	0	22.3	0.76	1	1	1	0.06	1	0.22
15	0.68	0.12	0	0	0	0	0	0	41.9	0.31	0	0	0	0	1	0
16	0.84	0	0	0	0	0	0	0	38.6	0.09	0	0	0	0	0	0
17	0.84	0	0	0	0	0	0	0	51.0	0	0	0	0	0	0	0
18	0.93	0	0	0	0	0	0	0	59.2	0	0	0	0	0	0	0
19	0.79	0	0	0	0	0	0	0	9.4	0.89	0.01	0.01	0.80	0.04	0	0.01
20	0.80	0	0	0	0	0	0	0	15.0	0.98	0	0	0	0	0.12	0
21	0.75	0.90	0	0.07	0	0	0.46	0	27.6	0.33	0.42	0.68	0	0.51	1	0.59
22	0.91	0	0	0	0	0	0	0	49.2	0	0	0	0	0	0	0
23	0.75	0	0	0	0	0	0	0.04	6.1	0.65	0.82	0.28	1	0.82	0.48	0.85
24	0.68	0.12	0	0	0.01	0	0	0.02	22.4	0.29	0.98	0.96	0.72	0.95	0.93	0.72
25	0.82	0.01	0	0	0	0	0	0	44.1	0.20	0	0	0	0	0.02	0
26	0.86	0	0	0	0	0	0	0	34.3	0	0	0	0	0	0	0
27	0.69	0.37	0	0	0	0	0	0	51.2	0.41	0	0	0.01	0	0.01	0
28	0.63	0.46	0	0.01	0	0	0	0	58.0	0.27	0	0	0	0	0	0
29	0.78	0.01	0	0	0	0	0	0	22.3	0.97	0.81	0.62	0.02	0.88	0.96	0.18
30	0.84	0.03	0	0	0	0	0	0	66.8	0.01	0	0	0	0	0	0
31	0.77	0	0	0	0	0	0	0.01	21.3	0.05	0.30	0.49	0.04	0.21	0.35	0.06
32	0.52	0.31	0.06	0	0.36	0.06	0.01	0.71	11.1	0.13	0.65	0.55	0.90	0.62	0.51	0.74

Table 2: Analysis of nestnedness of plant-parasite interaction matrices with two methods.

^aMean of 100 estimates.

^bSee Supplementary Methods 1 for details of the null models.

^cNestedness significance: the probability value (p-value) indicates the frequency of null-model matrices showing a strictly higher nestedness score than that of the actual matrix. P-values ≤ 0.05 (significant nestedness) are in bold on grey cells and p-values > 0.95 (significant anti-nestedness) are in white on black cells.

				Spingla	SS				
Matrix		Number of				Null model ^c			
number	Modularity score ^a	modules ^b	В	Ν	C1	R1	S	C2	R2
1	0.058	-	0.69 ^d	0.76	0.79	0.71	0.93	0.89	0.93
2	0.070	-	0.86	1	1	0.84	1	1	0.92
3	0.084	-	0.32	0.68	0.38	0.42	0.36	0.20	0.22
4	0.095	-	0.95	1	1	0.97	0.99	0.98	0.89
5	0.070	2	0	0	0	0	0	0	0
6	0.102	3	0	0	0	0	0	0	0
7	0.079	-	0.97	1	1	1	0.99	0.96	0.95
8	0.069	-	0.07	0.53	0.35	0.05	0.70	0.66	0.34
9 ^e	0.069	-	0.96	1	1	0.97	0.89	0.97	0.86
10	0.077	3	0	0.07	0	0.03	0.01	0.05	0.04
11	0.086	3	0	0	0	0	0	0	0
12	0.057	-	0.98	0.98	0.99	0.96	1	0.99	0.91
13	0.072	-	0.08	0.27	0.23	0.06	0.73	0.43	0.38
14	0.062	2	0	0	0	0	0	0.01	0
15 ^e	0.079	-	0.06	0.61	0.14	0.68	0.13	0.08	0.39
16	0.078	-	0.20	0.39	0.32	0.37	0.66	0.41	0.86
17b ^f	0.097	3	0.05	0.25	0.15	0.06	0.05	0.01	0.02
18	0.097	-	0.77	0.98	0.97	0.93	0.95	0.71	0.97
19	0.051	-	1	1	1	1	1	1	1
20	0.040	-	1	1	1	1	1	1	1
21	0.092	-	0.44	0.97	0.59	1	0.99	0.56	0.98
22	0.083	-	0.15	NA^g	0.06	0.44	NA^g	0.02	0.30
23 ^e	0.072	-	0.41	0.39	0.27	0.36	0.65	0.57	0.54
24	0.063	-	0.30	0.52	0.58	0.27	0.81	0.77	0.53
25	0.091	-	0.75	0.99	0.78	0.99	0.75	0.58	0.45
26 ^e	0.045	-	0.79	0.91	0.86	0.90	1	0.99	1
27	0.130	-	0.73	0.83	0.74	0.85	0.76	0.74	0.89
28	0.090	-	0.96	0.98	0.98	1	0.91	1	0.98
29 ^e	0.078	-	0.89	0.79	0.91	0.79	0.93	1	0.89
30	0.095	-	0.49	0.80	0.82	0.56	0.59	0.58	0.49
31	0.061	-	0.98	1	0.98	1	1	1	0.99
32	0.065	-	1	0.99	1	0.99	0.97	0.97	0.99

Table 3. Analysis of modularity of plant-parasite interaction matrices with the *spinglass* method.

^{*a*}Maximum of 100 estimates.

^bThe optimal number of modules determined by *spinglass* is indicated only for matrices significantly modular with a majority of null models (Fig. 4).

^cSee Supplementary Methods 1 for details of the null models.

^{*d*}Modularity significance: the probability value (p-value) indicates the frequency of null-model matrices showing a strictly higher modularity score than that of the actual matrix. P-values ≤ 0.05 (significant modularity) are in bold on grey cells. Significant anti-modularity, when $\leq 5\%$ of null-model matrices show a strictly lower modularity degree than that of the actual matrix, are indicated in white on black cells. Note that some of the indicated p-values are ≥ 0.95 but do not correspond to significant anti-modularity because the modularity degrees of the actual matrix and of some null-model matrices are identical.

^eRows and/or columns entirely made of zero-valued cells were removed since the *spinglass* method cannot estimate the modularity under such circumstances (unconnected graphs).

^{*f*}Matrix 17b is identical to matrix 17 except that columns entirely made of zero-valued cells and redundant columns were removed.

^{*g*}NA: not available; many null-model matrices had rows and/or columns entirely made of zero-valued cells and the *spinglass* method could not estimate their modularity.

	Edge betweenness				Fast greedy					Louvai	n		Leading eigenvector			
Matrix	Modularity	N	lull model ^t	0	Modularity	Null model ^b		Modularity	dularity Null model ^b			Modularity	Null model ^b		b	
number	score ^a	S	C2	R2	score ^a	S	C2	R2	score ^a	S	C2	R2	score ^a	S	C2	R2
1	0.012	1 <i>c</i>	1	0.99	0.074	1	0.99	0.51	0.073	1	1	1	0.061	0.87	0.77	0.62
2	0.022	1	1	0.97	0.091	1	1	0.98	0.091	1	1	1	0.088	1	1	0.37
3	0.099	0.88	0.53	0.06	0.126	1	0.96	0.38	0.127	1	1	0.64	0.116	0.85	0.62	0.12
4	0	1	1	1	0.113	1	1	1	0.115	1	1	1	0.113	1	1	0.40
5	0.018	1	0.01	1	0.065	0.99	0	0.99	0.069	1	0	1	0.069	0.58	0	0.57
6	0.085	1	0.99	1	0.209	0.88	0.03	0.17	0.209	0.96	0.10	0.42	0.206	0.50	0.01	0.07
7	0.138	0.96	0.45	0.79	0.240	1	0.84	1	0.240	1	0.98	1	0.160	1	0.97	0.99
8	0.003	1	1	1	0.121	1	1	0.98	0.125	1	1	1	0.116	0.99	0.97	0.43
9	0	1	1	1	0.074	1	1	1	0.069	1	1	1	0.061	0.99	0.84	0.59
10	0	1	1	1	0.073	1	1	1	0.073	1	0.98	1	0.072	1	0.40	0.47
11	0	1	1	1	0.085	1	0.98	1	0.091	1	0.93	1	0.058	1	0.96	0.99
12	0.004	1	1	0.50	0.041	1	1	0.16	0.044	1	1	0.98	NA ^c	NA ^d	NA ^d	NA ^d
13	0.004	1	1	0.95	0.061	1	1	0.56	0.063	1	1	0.88	0.039	0.96	0.94	0.64
14	0	1	1	1	0.044	0.87	0.04	0.35	0.046	0.48	0.04	0.15	0.010	1	0.41	1
15	0	1	1	1	0.089	1	0.98	1	0.087	1	1	1	0.063	0.99	0.64	1
16	0.007	1	1	1	0.032	1	1	1	0.036	1	1	1	0.022	0.99	0.92	1
17	0.071	1	0.99	1	0.172	1	1	1	0.177	1	1	1	0.155	1	0.99	0.99
17b ^e	0.040	1	1	0.99	0.155	1	1	1	0.158	1	1	1	0.131	0.38	0.21	0.96
18	0.079	1	1	1	0.186	1	1	0.35	0.186	0.99	1	0.16	0.169	0.98	1	0.32
19	0	1	1	1	0.028	1	1	1	0.031	1	1	1	0	1	1	1
20	0	1	1	1	0.029	1	1	1	0.029	1	1	1	0.029	0.97	0.88	0.83
21	0.036	1	0.23	1	0.110	1	0	1	0.109	1	0.01	1	0.096	0.99	0	1
22	0.020	1	0.98	1	0.165	1	0.89	1	0.165	1	0.93	1	0.157	1	0.27	1
23	0.011	1	1	0.88	0.068	0.91	0.81	0.22	0.070	0.99	0.99	0.70	0.058	0.67	0.44	0.26
24	0.035	0.99	0.86	0.91	0.092	0.79	0.75	0.20	0.095	0.94	0.93	0.60	0.066	0.90	0.82	0.74
25	0.066	1	0.35	1	0.167	1	0.49	1	0.168	1	0.84	1	0.118	1	0.78	1
26	0	1	1	1	0.041	1	1	1	0.046	1	1	1	0.044	0.82	0.39	0.84
27	0.034	0.96	0.86	0.69	0.102	1	1	1	0.103	1	1	1	0.086	1	1	1
28	0	1	1	1	0.151	1	1	1	0.153	1	1	1	0.108	1	1	1
29	0.008	1	1	1	0.069	1	1	1	0.069	1	1	1	0.048	1	0.95	1
30	0.043	0.98	0.91	0.91	0.087	1	1	1	0.092	1	1	1	0	1	1	1
31	0.013	0.98	0.97	0.65	0.062	1	1	0.89	0.062	1	1	1	0.055	0.69	0.71	0.59
32	0.058	0.70	0.84	0.72	0.062	0.95	0.99	0.59	0.062	1	1	1	0.022	0.97	0.96	0.73

Table 4. Analysis of modularity of plant-parasite interaction matrices with four methods. Only the three null models S, C2 and R2 that provided the lowest rates of false positive modularity in our performance study (Supplementary Methods 1) are presented.

^{*a*}Maximum of 100 estimates.

^bSee Supplementary Methods 1 for details of the null models.

^cModularity significance: the probability value (p-value) indicates the frequency of null-model matrices showing a strictly higher modularity score than that of the actual matrix. P-values ≤ 0.05 (significant modularity) are in bold on grey cells. Significant anti-modularity, when $\leq 5\%$ of null-model matrices show a strictly lower modularity degree than that of the actual matrix, are indicated in white on black cells. Note that some of the indicated p-values are ≥ 0.95 but do not correspond to significant anti-modularity because the modularity degrees of the actual matrix and of some null-model matrices are identical.

^{*d*}NA: not available; the *leading eigenvector* algorithm failed to converge.

^eMatrix 17b is identical to matrix 17 except that columns entirely made of zero-valued cells and redundant columns were removed.



Figure 1. Matrices corresponding to different mechanistic, genetic and evolutionary models of qualitative or quantitative host-parasite interactions. In each case, host genotypes correspond to different columns and parasite genotypes to different rows) and black and white cells (or 1 and 0 grades) correspond to infection or lack of infection, respectively. A: Illustration of an imperfectly nested pattern. B: Illustration of a perfectly modular pattern (modules are delimitated with red lines). C and D: Gene-for-gene (GFG) models with partial or perfectly nested patterns. C: Case of two genes with two alleles in both hosts and parasites. Infection occurs only when no elicitor in the

parasite is recognized by a product of the resistance alleles in the host. In the other situations, resistance is induced and there is no infection. D: Case of a single gene with five alleles in both hosts and parasites. Resistance alleles have various levels of specificity: in some plant accessions resistance can be induced by several parasite strains. E: Matching-allele model. Infection occurs only if the product of the pathogenicity allele is recognized by the product of the susceptibility allele in the host. F: Variation of D with higher specificity: resistance is induced by a specific product present in a single parasite genotype. This model was named "inverse matching-allele" model (Thrall et al. 2016) and has an anti-modular structural pattern. G: Additive QTL model with no plant-parasite QTL × QTL interaction. For each parasite strain i with pathogenicity level P_i and each plant accession j with resistance level R_j, infection score corresponds to P_i x (1-R_j).

Superscript figures correspond to alleles of a given gene whereas normal font figures correspond to different genes. Matching genes or alleles at resistance and pathogenicity loci in host and parasite genotypes share the same figure. For simplicity, hosts and parasites are considered haploid. R: resistance allele; r or R⁺: susceptibility allele; P: allele controlling lack of pathogenicity; p: pathogenicity allele.



Figure 2. Overview of the 32 analyzed plant-parasite matrices (Table 1). Different plant accessions and parasite strains correspond to different columns and rows, respectively. White to black shades in each cell correspond to an increasing gradient of pathogenicity or infectivity (corresponding to 0 to 9 values in the analysed matrices) for a given plant and parasite pair. Rows and columns were ordered by increasing marginal totals, revealing the nested patterns. Red numbers correspond to significant nestedness (*WINE* algorithm) (Table 2).



Figure 3. Distributions of Pearson's coefficients of correlation (r) between parasites host range breadth and pathogenicity (left) or between plant resistance efficiency and scope (right) across the 32 analysed matrices for different thresholds separating hosts and non-hosts (or parasites included or not included in the resistance scope). Each threshold corresponds to a percentage of the maximal pathogenicity value in each matrix (only results obtained with thresholds corresponding to 30%, 50% and 70% of the maximal pathogenicity value are shown; results were similar for other thresholds). In blue and red: significantly negative or positive r values (p-value < 0.05). For some thresholds and some matrices, the coefficient of correlation could not be calculated because too few pathogenicity data remained.



Figure 4. Overview of the six plant-parasite matrices showing significant modularity with the *spinglass* algorithm (Table 3). Rows and columns were ordered by modules, delimited by red lines. See legend of Figure 2 for the representation of matrices.



Figure 5. Overview of the four plant-parasite matrices showing significant modularity with the *spinglass* algorithm when matrices were transformed such that 0 values correspond to the maximal plant susceptibility and 9 values to the maximal plant resistance (but note that the matrices are represented such that 0 to 9 values correspond to a plant resistance to susceptibility gradient, as in the original matrices). Rows and columns were ordered by modules, delimited by red lines. See legend of Figure 2 for the representation of matrices.

References

- Aldecoa, R., Marín, I. 2013. Exploring the limits of community detection strategies in complex networks. Sci. Rep. 3:2216.
- Almeida-Neto, M., Ulrich, W. 2011. A straightforward computational approach for measuring nestedness using quantitative matrices. Environ. Model. Softw. 26:173-176.
- Almeida-Neto, M., Guimaraes, P., Guimaraes, P.R., Loyola, R.D., Ulrich, W. 2008. A consistent metric for nestedness analysis in ecological systems: reconciling concept and measurement. Oikos 117:1227–1239.
- Bahri, B., Kaltz, O., Leconte, M., de Vallavieille-Pope, C., Enjalbert, J. 2009. Tracking costs of virulence in natural populations of the wheat pathogen, *Puccinia striiformis* f.sp.*tritici*. BMC Evol. Biol. 9:26.
- Bartoli, C., Roux, F. 2017. Genome-wide association studies in plant pathosystems: Toward an ecological genomics approach. Front. Plant Sci. 8:763.
- Ben Krima, S., Slim, A., Gelisse, S., Kouki, H., Nadaud, I., Sourdille, P., Yahyaoui, A., Ben M'barek, S., Suffert, F., Marcel, T.C. 2020. Life story of Tunisian durum wheat landraces revealed by their genetic and phenotypic diversity. bioRxiv 2020.08.14.251157.
- Barrett, L.G., Encinas-Viso, F., Burdon, J.J., Thrall, P.H. 2015. Specialization for resistance in wild hostpathogen interaction networks. Front. Plant Sci. 6:761.
- Bascompte, J., Jordano, P., Melián, C.J., Olesen, J.M. 2003. The nested assembly of plant–animal mutualistic networks. Proc. Natl. Acad. Sci. USA 100:9383–9387.
- Bent, A. F., Mackey D. 2007. Elicitors, effectors, and R genes: the new paradigm and a lifetime supply of questions. Annu. Rev. Phytopathol. 45:399-436.
- Blondel, V.D., Guillaume, J.-L., Lambiotte, R., Lefebvre, E. 2008. Fast unfolding of communities in large networks. J. Stat. Mech.: Theory Exp. 10:P10008.
- Boissot, N., Thomas, S., Chovelon, V., Lecoq, H. 2016. NBS-LRR-mediated resistance triggered by aphids: viruses do not adapt; aphids adapt via different mechanisms. BMC Plant Biol. 16:25.
- Brown J.K.M. 2015. Durable resistance of crops to disease: a Darwinian perspective. Annu. Rev. Phytopathol. 53:513-539.
- Brualdi, R.A., Sanderson, J.G. 1999. Nested species subsets, gaps, and discrepancy. Oecologia 119:256-264.
- Bruns, E., Carson, M., May, G. 2014. The Jack of all trades is master of none: a pathogen's ability to infect a greater number of host genotypes comes at a cost of delayed reproduction. Evolution 68:2453-2466.
- Caffier, V., Didelot, F., Pumo, B., Causeur, D., Durel, C.E., Parisi, L. 2010. Aggressiveness of eight *Venturia inaequalis* isolates virulent or avirulent to the major resistance gene *Rvi6* on a non-*Rvi6* apple cultivar. Plant Pathol. 59:1072-1080.
- Caffier, V., Lasserre-Zuber, P., Giraud, M., Lascostes, M., Stievenard, R., Lemarquand, A., Van De Weg, E., Expert, P., Denancé, C., Didelot, F., Le Cam, B., Durel, C.E. 2014. Erosion of quantitative host resistance in the apple - Venturia inaequalis pathosystem. Infect. Genet. Evol. 27:481-489.
- Caffier, V., Le Cam, B., Al Rifaï, M., Bellanger, M.N., Comby, M., Denancé, C., Didelot, F., Expert, P., Kerdraon, T., Lemarquand, A., Ravon, E., Durel, C.E. 2016. Slow erosion of a quantitative apple

resistance to *Venturia inaequalis* based on an isolate-specific Quantitative Trait Locus. Infect. Genet. Evol. 44:541-548.

- Caranta, C., Lefebvre, V., Palloix, A. 1997. Polygenic resistance of pepper to potyviruses consists of a combination of isolate-specific and broad-spectrum quantitative trait loci. Mol. Plant-Microbe Interact. 10:872–878.
- Castagnone-Sereno, P., Bongiovanni, M., Wajnberg E. 2007. Selection and parasite evolution: A reproductive fitness cost associated with virulence in the parthenogenetic nematode *Meloidogyne incognita*. Evol. Ecol. 21:259-270.
- Clauset, A., Newman, M.E.J., Moore, C. 2004. Finding community structure in very large networks. Phys. Rev. E 70:066111.
- Danan, S., Chauvin, J.-E., Caromel, B., Moal, J.-D., Pellé, R., Lefebvre, V. 2009. Major-effect QTLs for stem and foliage resistance to late blight in the wild potato relatives *Solanum sparsipilum* and *S. spegazzinii* are mapped to chromosome X. Theor. Appl. Genet. 119:705–719.
- Delmas, C.E.L., Fabre, F., Jolivet, J., Mazet, I.D., Cervera, S.R., Delière, L., Delmotte F. 2016. Adaptation of a plant pathogen to partial host resistance: selection for greater aggressiveness in grapevine downy mildew. Evol. Appl. 9:709–725.
- Desbiez, C., Gal-On, A., Girard, M., Wipf-Scheibel, C., Lecoq, H. 2003. Increase in *Zucchini yellow mosaic virus* symptom severity in tolerant zucchini cultivars is related to a point mutation in P3 protein and is associated with a loss of relative fitness on susceptible plants. Phytopathology 93:1478-1484.
- Dormann, C.F., Fründ, J., Schaefer, H.M. 2017. Identifying causes of patterns in ecological networks: Opportunities and limitations. Annu. Rev. Ecol. Evol. Syst. 48:559-584.
- Feng, W, Takemoto, K. 2014. Heterogeneity in ecological mutualistic networks dominantly determines community stability. Sci. Rep. 4:5912.
- Fenton, A., Antonovics, J., Brockhurst, M.A. 2009. Inverse-gene-for-gene infection genetics and coevolutionary dynamics. Am. Nat. 174:E230-E242.
- Flor, H.H. 1956. The complementary genic systems in flax and flax rust. Adv. Genet. 8:29–54.
- Flores, C.O., Meyer, J.R., Valverde, S., Farr, L., Weitz, J.S. 2011. Statistical structure of host-phage interactions. Proc. Natl. Acad. Sci. USA 108: E288–97.
- Flores, C.O., Valverde, S., Weitz, J.S. 2013. Multi-scale structure and geographic drivers of cross-infection within marine bacteria and phages. ISME J. 7:520-532.
- Fortuna, M.A., Barbour, M.A., Zaman, L., Hall, A.R., Buckling, A., Bascompte, J. 2019. Coevolutionary dynamics shape the structure of bacteria–phage infection networks. Evolution 73:1001–1011.
- Fournet, S., Eoche-Bosy, D., Renault, L., Hamelin, F.M., Montarry, J. 2016. Adaptation to resistant hosts increases fitness on susceptible hosts in the plant parasitic nematode *Globodera pallida*. Ecol. Evol. 6:2559-2568.
- Fraile, A., Pagán, I., Anastasio, G., Saez, E., García-Arenal, F. 2011. Rapid genetic diversification and high fitness penalties associated with pathogenicity evolution in a plant virus. Mol. Biol. Evol. 28:1425-1437.
- Galeano, J., Pastor, J.M., Iriondo, J.M. 2009. Weighted-Interaction Nestedness Estimator (WINE): A new estimator to calculate over frequency matrices. Env. Model. Soft. 24:1342-1346.

- Gallois, J.-L., Moury, B., German-Retana, S. 2018. Role of the genetic background in resistance to plant viruses. Int. J. Mol. Sci. 19:2856.
- Gautier, C., Fournet, S., Piriou, C., Renault, L., Yvin, J.C., Nguema-Ona, E., Grenier, E., Montarry, J. 2020. Plant-parasite coevolution: a weak signature of local adaptation between Peruvian *Globodera pallida* populations and wild potatoes. Ecol. Evol. 10:4156-4163.
- González, A.M., Marcel, T.C., Niks, R.E. 2012. Evidence for a minor gene-for-minor gene interaction explaining nonhypersensitive polygenic partial disease resistance. Phytopathology 102:1086-1093.
- Gotelli, N.J., Graves, G.R. 1996. Null models in ecology. Smithsonian Institution Press, Washington D.C.
- Grosberg, R.K., Hart, M.W. 2000. Mate selection and the evolution of highly polymorphic self/nonself recognition genes. Science 289:2111-2114.
- Huang, Y.J., Balesdent, M.-H., Li, Z.Q., Evans, N., Rouxel, T., Fitt, B.D.L. 2010. Fitness cost of virulence differs between the *AvrLm1* and *AvrLm4* loci in *Leptosphaeria maculans* (phoma stem canker of oilseed rape). Eur. J. Plant Pathol. 126:279-291.
- Ishibashi, K., Mawatari, N., Miyashita, S., Kishino, H., Meshi, T., Ishikawa, M. 2012. Coevolution and hierarchical interactions of *Tomato mosaic virus* and the resistance gene *Tm-1*. PLoS Pathog. 8:e1002975.
- Janzac, B., Montarry, J., Palloix, A., Navaud, O., Moury, B. 2010. A point mutation in the polymerase of *Potato virus Y* confers virulence towards the *Pvr4* resistance of pepper and a high competitiveness cost in susceptible cultivar. Mol. Plant-Microbe Interact. 23:823-830.
- Jenner, C.E., Wang, X.W., Ponz, F., Walsh, J.A. 2002. A fitness cost for *Turnip mosaic virus* to overcome host resistance. Virus Res. 86:1-6.
- Jonhson, S., Domínguez-García, V., Muñoz, M.A. 2013. Factors determining nestedness in complex networks. PLOS ONE 8:e74025.
- Joppa, L.N., Montoya, J.M., Solé, R., Sanderson, J., Pimm, S.L. 2010. On nestedness in ecological networks. Ecol. Evol. Res. 12:35–46.
- Khatabi, B., Wen, R.H., Hajimorad, M.R. 2013. Fitness penalty in susceptible host is associated with virulence of *Soybean mosaic virus* on *Rsv1*-genotype soybean: a consequence of perturbation of HC-Pro and not P3. Mol. Plant Pathol. 14:885-897.
- Kidner, J., Moritz, R.A.F. 2013. The Red Queen process does not select for high recombination rates in haplodiploid hosts. Evol. Biol. 40:377–84.
- Laloi, G., Vergne, E., Durel, C.-E., Le Cam, B., Caffier, V. 2017. Efficiency of pyramiding of three quantitative resistance loci to apple scab. Plant Pathol. 66:412-422.
- Lambrechts, L. 2010. Dissecting the genetic architecture of host–pathogen specificity. PLoS Pathog. 6:e1001019.
- Leach, J.E., Vera Cruz, C.M., Bai, J.F., Leung, H. 2001. Pathogen fitness penalty as a predictor of durability of disease resistance genes. Annu. Rev. Phytopathol. 39:187-224.
- Lefebvre, V., Palloix, A. 1996. Both epistatic and additive effects of QTLs are involved in polygenic induced resistance to disease: a case study the interaction pepper-*Phytophthora capsici* Leonian. Theor. Appl. Genet. 93:503-511.

- Marcel, T.C., Gorguet, B., Truong Ta, M., Kohutova, Z., Vels, A., Niks, R.E. 2008. Isolate specificity of quantitative trait loci for partial resistance of barley to *Puccinia hordei* confirmed in mapping populations and near-isogenic lines. New Phytol. 177:743-755.
- Messaouda, B., Guechi, A., Mézaache-Aichour, S. 2015. Susceptibility of Algerian pepper cultivars (*Capsicum annuum* L.) to *Phytophthora capsici* strains from different geographic areas. Afr. J. Biotechnol. 14:3011-3018.
- Montarry, J., Hamelin, F.M., Glais, I., Corbière, R., Andrivon, D. 2010. Fitness costs associated with unnecessary virulence factors and life history traits: evolutionary insights from the potato late blight pathogen *Phytophthora infestans*. BMC Evol. Biol. 10:283.
- Montarry, J., Cartier, E., Jacquemond, M., Palloix, A., Moury, B. 2012. Virus adaptation to quantitative plant resistance: erosion or breakdown? J. Evol. Biol. 25:2242–2252.
- Morris, C.E., Moury, B. 2019. Revisiting the concept of host range of plant pathogens. Annu. Rev. Phytopathol. 57:63–90.
- Morris, C.E., Lamichhane, J.R., Nikolić, I., Stanković S., Moury, B. 2019. The overlapping continuum of host range among strains in the *Pseudomonas syringae* complex. Phytopathology Research 1:4.
- Morris, C.E., Glaux, C., Latour, X., Gardan, L., Samson, R., Pitrat, M. 2000. The relationship of host range, physiology and genotype to virulence on cantaloupe in *Pseudomonas syringae* from cantaloupe blight epidemics in France. Phytopathology 90:636-646.
- Morris CE, Sands DC, Vanneste JL, Montarry J, Oakley B, Guilbaud C, Glaux C (2010). Inferring the evolutionary history of the plant pathogen *Pseudomonas syringae* from its biogeography in headwaters of rivers in North America, Europe and New Zealand. mBio 1: e00107-10.
- Newman, M.E.J. 2006. Finding community structure using the eigenvectors of matrices. Phys. Rev. E 74:036104.
- Newman M.E.J., Girvan, M. 2004. Finding and evaluating community structure in networks. Phys. Rev. E 69:026113.
- Nicot, P.C., Bardin, M., Dik, A.J. 2002. Basic methods for epidemiological studies of powdery mildew:
 Culture and preservation of isolates, production and delivery of inoculum, and disease assessment.
 Pages 83-99 in: The Powdery Mildews: A Comprehensive Treatise. R. R. Bélanger, W. R. Bushnell, A. J.
 Dik, and T. L. W. Carver, eds. The American Phytopathological Society, St. Paul, MN.
- Parisi, L., Morgaint, B., Blanco Garcia, J., Guilbaud, C., Chandeysson, C., Bourgeay, J.-F., Moronvalle, A., Brun, L., Brachet M.-L., Morris, C.E. 2019. Bacteria from four phylogroups of the *Pseudomonas syringae* complex can cause bacterial canker of apricot. Plant Pathol. 68:1249-1258.
- Parlevliet, J. E. 1977. Evidence of differential interaction in the polygenic *Hordeum vulgare Puccinia hordei* relation during epidemic development. Phytopathology 67:776-778.
- Patefield, W.M. 1981. Algorithm AS159. An efficient method of generating r x c tables with given row and column totals. J. Royal Stat. Soc. 30:91–97.
- Perchepied, L., Bardin, M., Dogimont, C., Pitrat, M. 2005. Relationship between loci conferring downy mildew and powdery mildew resistance in melon assessed by quantitative trait loci mapping. Phytopathology 95:556-565.
- Peters, A.R., Zhang, Z., Richards, J.K., Friesen, T.L., Faris, J.D. 2019. Genetics of variable disease expression conferred by inverse gene-for-gene interactions in the wheat-*Parastagonospora nodorum* pathosystem. Plant Physiol. 180:420-434.

- Pons, P., Latapy, M. 2006. Computing communities in large networks using random walks. J. Graph Algorithms Appl. 10:191–218.
- Poulicard, N., Pinel-Galzi, A., Hébrard, E., Fargette, D. 2010. Why *Rice yellow mottle virus*, a rapidly evolving RNA plant virus, is not efficient at breaking *rymv1-2* resistance? Mol. Plant Pathol. 11:145-154.
- Quenouille, J., Paulhiac, E., Moury, B., Palloix, A. 2014. Quantitative trait loci from the host genetic background modulate the durability of a resistance gene: a rational basis for sustainable resistance breeding in plants. Heredity 112:579-587.
- Quillévéré-Hamard, A., Le Roy, G., Moussart, A., Baranger, A., Andrivon, D., Pilet-Nayel, M.-L., Le May, C.
 2018. Genetic and pathogenicity diversity of *Aphanomyces euteiches* populations from pea-growing regions in France. Front. Plant Sci. 9:1673.
- Quillévéré-Hamard, A., Le Roy, G., Lesné, A., Le May, C., Pilet-Nayel, M.-L. 2020. Aggressiveness of diverse French *Aphanomyces euteiches* isolates on pea Near-Isogenic-Lines differing in resistance QTL. Phytopathology, doi: 10.1094/PHYTO-04-20-0147-R.
- Raghavan, U.N., Albert, R., Kumara, S. 2007. Near linear time algorithm to detect community structures in large-scale networks. Phys. Rev. E 76:036106.
- Reichardt, J., Bornholdt, S. 2006. Statistical mechanics of community detection. Phys. Rev. E 74:016110.
- Sacristán, S., García-Arenal, F. 2008. The evolution of virulence and pathogenicity in plant pathogen populations. Mol. Plant Pathol. 9:369-384.
- Saintenac, C., Lee, W.-S., Cambon, F., Rudd, J.J., King, R.C., Marande, W., Powers, S.J., Bergès, H., Phillips, A.L., Uauy, C., Hammond-Kosack, K.E., Langin, T., Kanyuka, K. 2018. Wheat receptor-kinase-like protein *Stb6* controls gene-for-gene resistance to fungal pathogen *Zymoseptoria tritici*. Nat. Genet. 50:368-374.
- Soltis, N.E., Atwell, S., Shi, G., Fordyce, R., Gwinner, R., Gao, D., Shafi, A., Kliebenstein D.J. 2019. Interactions of tomato and *Botrytis cinerea* genetic diversity: Parsing the contributions of host differentiation, domestication, and pathogen variation. Plant Cell 31:502–519.
- Staniczenko, P.P.A., Kopp, J.C., Allesina, S. 2013. The ghost of nestedness in ecological networks. Nat. Commun. 4:1391.
- Suweis, S., Simini, F., Banavar, J.R., Maritan, A. 2013. Emergence of structural and dynamical properties of ecological mutualistic networks. Nature 500:449–452.
- Tellier, A., Brown, J.K.M. 2011. Spatial heterogeneity, frequency-dependent selection and polymorphism in host-parasite interactions. BMC Evol. Biol. 11:319.
- Thrall, P.H., Barrett, L.G., Dodds, P.N., Burdon, J.J. 2016. Epidemiological and evolutionary outcomes in gene-for-gene and matching allele models. Front. Plant Sci. 6:1084.
- Traag, V.A., Bruggeman, J. 2009. Community detection in networks with positive and negative links. Phys. Rev. E 80:036115.
- Valverde, S., Elena, S.F., Solé, R. 2017. Spatially induced nestedness in a neutral model of phage-bacteria networks. Virus Evol. 3:vex021.
- Valverde, S., Jordi Piñero, J., Corominas-Murtra, B., Montoya, J., Joppa, L., Solé, R. 2018. The architecture of mutualistic networks as an evolutionary spandrel. Nat. Ecol. Evol. 2:94–99.

- Vera Cruz, C.M., Bai, J.F., Ona, I., Leung, H., Nelson, R.J., Mew, T.W., Leach J.E. 2000. Predicting durability of a disease resistance gene based on an assessment of the fitness loss and epidemiological consequences of avirulence gene mutation. Proc. Natl. Acad. Sci. USA 97:13500-13505.
- Wang, M., Roux, F., Bartoli, C., Huard-Chauveau, C., Meyer, C., Lee, H., Roby, D., McPeek, M.S.,
 Bergelson, J. 2018. Two-way mixed-effects methods for joint association analysis using both host and pathogen genomes. Proc. Natl. Acad. Sci. USA 115:E5440-E5449.
- Weitz, J.S., Poisot, T., Meyer, J.R., Flores, C.O., Valverde, S., Sullivan, M.B., Hochberg, M.E. 2013. Phagebacteria infection networks. Trends Microbiol. 21:82–91.
- Wichmann, G., Bergelson, J. 2004. Effector genes of *Xanthamonas axonopodis* pv. *vesicatoria* promote transmission and enhance other fitness traits in the field. Genetics 166:693-706.
- Zhong, Z., Marcel, T.C., Hartmann, F.E., Ma, X., Plissonneau, C., Zala, M., Ducasse, A., Confais, J., Compain, J., Lapalu, N., Amselem, J., McDonald, B.A., Croll, D., Palma-Guerrero, J.C. 2017. A small secreted protein in *Zymoseptoria tritici* is responsible for avirulence on wheat cultivars carrying the *Stb6* resistance gene. New Phytol. 214:619-631.