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OPINION

Improving sustainable crop protection using population genetics concepts

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Abstract

Growing genetically resistant plants allows pathogen populations to be controlled and reduces the use of pesticides. However, pathogens can quickly overcome such resistance. In this context, how can we achieve sustainable crop protection? This crucial question has remained largely unanswered despite decades of intense debate and research effort. In this study, we used a bibliographic analysis to show that the research field of resistance durability has evolved into three subfields: (1) "plant breeding" (generating new genetic material), (2) "molecular interactions" (exploring the molecular dialogue governing plant–pathogen interactions) and (3) "epidemiology and evolution" (explaining and forecasting of pathogen population dynamics resulting from selection pressure[s] exerted by resistant plants). We argue that this triple split of the field impedes integrated research progress and ultimately compromises the sustainable management of genetic resistance. After identifying a gap among the three subfields, we argue that the theoretical framework of population genetics could bridge this gap. Indeed, population genetics formally explains the evolution of all heritable traits, and allows genetic changes to be tracked along with variation in population dynamics. This provides an integrated view of pathogen adaptation, in particular via evolutionary–epidemiological feedbacks. In this Opinion Note, we detail examples illustrating how such a framework can better inform best practices for developing and managing genetically resistant cultivars.

KEYWORDS
citation network, genetic drift, host-pathogen coevolution, plant immunity, resistance durability, transient dynamics

1 | GENETIC RESISTANCE DURABILITY

Growing genetically resistant plants helps regulate pathogen populations while considerably reducing pesticide use. Genetic resistances are used extensively in crops to confer partial or complete host immunity. Whereas some resistance genes, especially those relying on pathogen recognition, can be defeated quickly by pathogens, leading to a loss of efficiency (Brown, 2015; REX Consortium, 2016), others can remain undefeated for decades (Cowger & Brown, 2019; Piffanelli et al., 2004). The two crucial questions are thus: (1) why is there such variation in the durability of resistances, and (2) how can resistance durability be enhanced? This Opinion Note embraces an

evolutionary view of plant–pathogen interactions for a better understanding of pathogen adaptation in the face of plant resistances, highlighting the role of theoretical population genetics in achieving sustainable management of plant diseases.

2 | THE PLANT RESISTANCE DURABILITY LITERATURE COMPRISES THREE DISTINCT SUBFIELDS

This Opinion Note was prompted by an analysis of the literature on plant resistance durability (Supporting information, Annex S1, Figures S1–S8) that revealed a large split among studies. A keyword co-occurrence analysis distinguished three subfields of research (Figure 1), hereafter referred to as "plant breeding", "molecular interactions" and "epidemiology and evolution", each of which addresses a different scale of pathogen adaptation to plant resistances. These subfields share the potential to ultimately improve plant health and increase the durability of crop protection, but they tackle these issues in very different ways (Box 1).

The observed split may have originated from at least two causes of divergence. First, these subfields focus on different stages, upstream or downstream of resistance durability, ranging from the identification of new resistances to resistances being defeated, in particular because of their wide deployment in agroecosystems. Typically, the selection of new plant resistances is the goal of the "plant breeding" subfield. Second, for studies that focus on already identified plant resistances, the split originates from a difference in viewpoint. "Molecular interactions" studies focus on the mechanisms of resistance, whereas "epidemiology and evolution" studies aim to define better management policies. This amounts to a classical partition between proximal and distal points of view that examine the causes and consequences of a phenomenon, respectively. More recently, we have observed some changes in paradigms, for example, the search for the Holy Grail of durable resistance mechanisms versus the sustainable management of not-necessarily durable resistances (Rimbaud et al., 2021). As such, the origins of this gap remain multifactorial, and further characterization warrants a dedicated epistemological study, which is beyond the scope of this Opinion Note.

An analogous split had already been documented in terms of resistance to pesticides (REX Consortium, 2010). Insights from multiple fields can leap forward scientific progress. Isolated contributions preclude the emergence of an integrated knowledge. Regarding the question of resistance durability, the split ultimately compromises the sustainable management of genetic resistances. Here, we

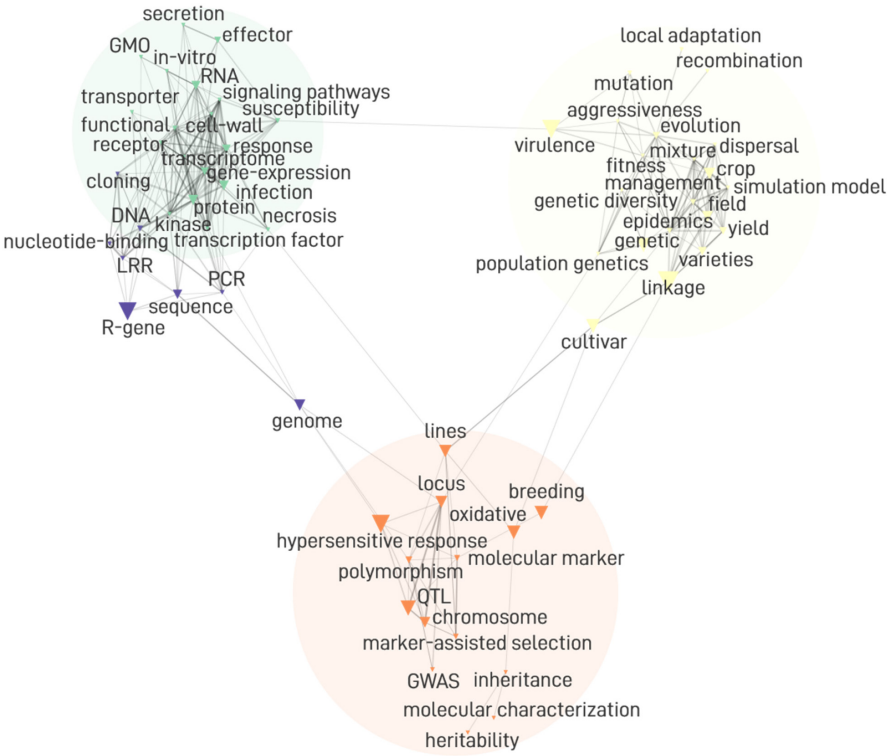

FIGURE 1 Network of the co-occurrence of article keywords. Drawings were prepared using the network mapping tool on CorTexT manager platform (https://www.cortext.net/), based on the refined list of 62 keywords and 1783 articles from the "plant breeding", "molecular interactions", and "epidemiology and evolution" clusters (see supporting information Annex S1 for details, Table S1). The proximity threshold was fixed at 0.44, and all other parameters were set to default values. Nodes represent keywords; lines between nodes represent links that measure the mutual occurrence of the keywords among articles. The closer the nodes, the tighter the association. An interactive version of this figure is available at: https://documents.cortext.net/lib/mapexplorer/explorerjs.html?file=https://assets.cortext.net/docs/438fce7b216d23e2d2316cab168d14e9)

BOX 1 Three-way split among plant resistance durability studies

"Plant breeding" studies focus on the creation of new plant varieties with, among other goals, intrinsically durable resistances. Historically, plant breeding relied on traditional phenotypic selection, and later integrated molecular markers by applying marker-assisted selection based on the identification of quantitative trait loci (Ribaut & Hoisington, 1998). The denser the markers, the more accurate the marker–trait association. More recently, the advent of next-generation sequencing techniques, and the resulting drop in whole-genome sequencing costs, led to the appearance of genomic selection, which uses the highest density of molecular markers to predict the performance of candidate genotypes for breeding. This method reduces the costs and time required for variety development (Crossa et al., 2017). This shift in methodology also enables screening of an ever-growing source of new genetic resistances (from natural genetic variability to mutant lines). Notably, mutagenesis experiments have already produced very efficient and durable resistances, for example the *mlo-9* allele in barley (Jørgensen, 1992).

Because it confers complete host immunity, the gene-for-gene model (Flor, 1971) has attracted a great deal of interest and breeding efforts to select for varieties carrying qualitative resistances. According to the gene-for-gene model, resistance often relies on the recognition of a specific pathogen molecule (e.g., an effector protein, called an avirulence protein when recognized by a cognate resistance protein) by a plant receptor (Jones & Dangl, 2006). In such cases, pathogens can evolve with the loss or modification of the recognized molecule and thus escape host recognition, thereby restoring infectivity (Hartmann et al., 2017). Nevertheless, overcoming genetic resistance is not systematic (García-Arenal et al., 2003; Nilusmas et al., 2020). The speed at which a given resistance is overcome is one of the main determinants of the duration of its use. Quantitative resistances have regained attention in recent years as a longer resistance durability can be expected (Cowger & Brown, 2019). Indeed, by conferring only a partial level of resistance to the plant, they also reduce the selection pressure on pathogen populations. Quantitative resistances can also increase the durability of qualitative resistances when combined within the same variety (Brun et al., 2010; Fournet et al., 2013; Laloi et al., 2017; Palloix et al., 2009). However, in a theoretical study, Gandon and Michalakis (2000) predicted that using quantitative resistance would select for increased levels of host damage. This agrees with empirical studies in which quantitative resistances have been shown to select for higher aggressiveness (Cowger & Mundt, 2002; Pariaud et al., 2009). Finally, resistances that are not based on pathogen recognition can be far more durable. For example, barley plants carrying the recessive loss-of-function alleles (*mlo*) preventing hyphal penetration (Kusch & Panstruga, 2017) have so far proven resistant against all known isolates of the powdery mildew fungus *Blumeria graminis* f. sp. *hordei* (Brown, 2015; Lyngkjær et al., 2000; Piffanelli et al., 2004).

"Molecular interactions" studies examine how plant pathogens promote infection by altering plant defence reactions and plant cellular processes, and how plants recognize pathogens and trigger immunity. Technological innovations (i.e., genomics, bioinformatics) and strong conceptual models (i.e., recognition-based immunity, or the zig-zag model; Jones & Dangl, 2006) guide this subfield. In particular, cloning of resistance genes and associated avirulence genes (see, e.g., Dangl et al., 2013) has led to three important discoveries that could help manage resistances and predict their durability:

1. The switch to virulence may have a fitness cost. Inactivation of avirulence genes or generation of near isogenic strains of fungi differing by the presence/absence of one avirulence gene allow measurement of potential fitness costs associated with a switch to virulence (Huang et al., 2006). These fitness costs differ depending on the avirulence gene (Nováková et al., 2016), and have major consequences on resistance durability and, therefore, on management strategies (Fabre et al., 2012; Leach et al., 2001).
2. The switch to virulence often results from alteration of the avirulence gene. Several molecular mechanisms are involved in the switch to virulence, with direct or indirect alteration of the avirulence gene. Depending on the avirulence effectors and their importance for pathogenesis, we observe either drastic mechanisms of gene inactivation (deletions, accumulation of mutations) or mechanisms that make it possible to escape recognition while maintaining the effector function (point mutations, intervention of another effector that masks recognition of the first) (Gómez et al., 2009; Louet et al., 2022; Rouxel & Balesdent, 2017; Sánchez-Vallet et al., 2018). The variability of these mechanisms of transition to virulence can have important evolutionary consequences. Knowledge of such mechanisms could give clues as to the importance of the targeted effectors for the pathogen, and therefore the potential durability of the corresponding resistances (Janzac et al., 2009).
3. The gene-for-gene model fails to describe "unconventional" molecular interactions. While an increasing number of avirulence genes have been identified in pathogens infecting agronomically important crops, "unconventional" gene-for-gene interactions have also been reported. The recognition of one avirulence gene by several resistance genes, or epistatic interactions between avirulence genes, are typical examples of such interactions. All these interactions have different consequences for the switch from avirulence to virulence and, hence, on resistance gene management (for a review, see Petit-Houdenot & Fudal, 2017).

"Epidemiology and evolution" studies decipher the evolutionary causes and consequences of pathogen adaptation at the population scale, employing both empirical and modelling approaches. To improve understanding of resistance durability, these studies first aim to identify the key drivers of durability. Several strategies differing in the type of resistance used and their deployment in time and space can be distinguished (Brown, 2015; REX Consortium, 2016). While knowledge in the "molecular interactions" field is spurred by technological advances brought about in the -omics era, "epidemiology and evolution" studies are driven mostly by field observations and include a large corpus of modelling works (Brown, 2015; Rimbaud et al., 2021). A major recent change in "epidemiology and evolution" studies is the increasing interest in quantitative resistances, as evidenced in our bibliographic analysis (Annex). Historically, epidemiological modelling studies started with the simple situation of plants bearing a single qualitative resistance. Recent studies encompass more complexity, in line with the observation of the overcoming of qualitative resistance alleles following their deployment. This prompted the field to increase investigation of the contribution of multiple and quantitative resistances on resistance durability (Lo Iacono et al., 2012; Rimbaud, Papaïx, Rey, et al., 2018; Zhan et al., 2015). Some studies compare two resistance types with different deployment strategies, such as resistance mixtures and pyramiding (Djidjou-Demasse et al., 2017; REX Consortium, 2016; Rimbaud, Papaïx, Barrett, et al., 2018). During the last two decades, there has been a trend to widen the quest for intrinsic durable resistance—resulting from the properties of resistance genes only—towards including the consideration of durable strategies of resistance management as an emerging property of clever agricultural practices (Rimbaud et al., 2021). A key notion for increasing resistance durability would be to break the continuity in the selection pressure imposed by modern agricultural practices (Brown, 2015; Zhan et al., 2015). Overall, this research subfield has led to three main findings so far:

1. It is crucial to take pathogen population biology into account. In particular, McDonald and Linde (2002) reviewed the typology of risk of overcoming resistance dependent on pathogen life cycle, finding that pathogens with large population sizes, mixed reproductive modes (i.e., both sexual and asexual reproduction) and massive, long-distance dispersal, have the highest evolutionary potential.
2. There is no absolute rule about the best deployment strategy to achieve resistance durability. All factors being equal, gene pyramiding will perform better in the case of de novo mutations, whereas other strategies (e.g., crop rotations and mixtures) are better suited to impeding pathogen evolution from standing genetic variation (Djidjou-Demasse et al., 2017; REX Consortium, 2016; Rimbaud, Papaïx, Barrett, et al., 2018).
3. Chosen management strategies may differ depending on the time scale considered: short-term disease control or long-term mitigation of pathogen evolution (Brown, 2015; Papaïx et al., 2018).

suggest it might be possible to combine these three subfields of research to improve plant health and increase the durability of crop protection.

3 | POPULATION GENETICS PROVIDES A CONCEPTUAL LINK ACROSS RESEARCH SUBFIELDS

In this Opinion Note, we advocate that population genetics provides us with the dedicated theory to merge the efforts of all three subfields (Box 2). Evolution results from changes in the frequencies of gene states (alleles), or any other heritable character. It results from the combined action of evolutionary forces, namely selection, migration, mutation, and drift. Population genetics is one of the rare established and efficient theoretical paradigms of biology, and relies strongly on mathematical modelling (Wakeley, 2005). Recent technological advances in investigations of molecular variations and genotyping have important ramifications for experimental sciences. Here, we build our proposal by considering that population genetics—more precisely, demogenetics—provides the concepts for knitting communities together by its inherent ability to integrate biological features and species interactions over time and space. This view differs from the current and traditional use of population genetics mostly as a tool to describe the genetic structure of populations within a species (see Supporting Information for details). In the following, our proposal tackles how population genetics can help better explore plant–pathogen interactions towards the rational breeding and clever management of plant genetic resistances.

4 | KNITTING COMMUNITIES TOGETHER WITH POPULATION GENETICS TO IMPROVE PLANT HEALTH DURABILITY

Our proposal is based on our analysis of the specificities of each of the three subfields, and identification of key research topics that would aid better subfield integration.

4.1 | Consider evolutionary trajectories to highlight transient dynamics

We propose that "epidemiology and evolution" studies focus on demogenetic trajectories by taking demographic fluctuations of pathogen populations into account more systematically when studying plant resistance durability. To best characterize evolutionary trajectories, we have to consider the interplay between epidemiology

BOX 2 A brief history of population genetics

Population genetics is a research field with a long and productive history. Our goal here is not to draw a detailed picture of this area. Rather, we summarize the main points of interest to the reader from the viewpoint of this Opinion Note. Population genetics is a key element in evolutionary synthesis, because it formally explains the evolution of all heritable biological features for any defined transmission rule. The term "population genetics" was coined nearly one century ago, most famously by Fisher (1930), Wright (1930) and Haldane (1924–1934). At its origin, the main contribution of this field was to show that a phenotype, even if distributed continuously, can be explained by the contribution of discrete entities called genes (Fisher, 1930). Nowadays, population genetics provides a valuable framework to fill the gap between genetic variation at an individual level (the genotypic state, i.e., a given combination of alleles, that determines a phenotype) and the change in this genetic variation at the population level. As such, it provides us with a sound approach for investigating molecular evolution. It also accounts for changes in genetic variation at different scales of time and space. Its applications range from point molecular variations to very complex genetic architectures as long as transmission rules from generation to generation are known (Ewens, 2004). More recently, population genetics have explicitly incorporated population dynamics in a so-called demogenetic approach, and hence is able to track feedback between epidemiology and evolution (see Section 4.1). Lastly, population genetics reasoning can be extended to multiple species to monitor their joint fate in time and space (Mueller, 2019). For example, in studying host–plant interactions, population genetics allows analyses of the reciprocal selection pressures exerted by host and pathogen species and hence reveals their joint evolutionary trajectories (Brown & Tellier, 2011).

and evolution, and treat them as having equal footing. Evolutionary forces shape epidemiological dynamics (for example when a new virulence leads to drastic epidemics on the resistant host). These population dynamics in turn impact population evolution (for example, because the size of the pathogen population influences the probability that a new mutation occurs). Population genetics constitutes a valuable approach as it considers the changes in both genotype states and numbers (Box 2), thus capturing this interplay between epidemiology and evolution. Such a modelling framework has been proposed by Day and Proulx (2004) and Day and Gandon (2007); notably, the latter study showed the existence of transient states that can be overlooked in studies focusing on final evolutionary equilibria only. These transient states are expected to emerge after a perturbation and can have strong epidemiological and evolutionary consequences. For example, the transient dynamics resulting from the onset of vaccination can lead to severe epidemics and the possible emergence of more virulent strains before epidemiological dynamics reach a new equilibrium (Gandon & Day, 2007).

The evolutionary epidemiology framework is worth applying to the management of plant resistances. Agricultural landscapes change rapidly, resulting in regular perturbations being applied to pathogen populations (Stukenbrock & McDonald, 2008; Zhan et al., 2015). In the literature, we observe a change in paradigm from the short-term control of pathogen populations by means of epidemiology-driven regulation to the long-term control of the evolutionary trajectories of pathogen populations (Brown, 2015; Papaïx et al., 2018). We thus need a proper definition of resistance durability that embraces both short- and long-term control of pathogen populations. Indeed, the initial definition according to Johnson (1984), "a resistance remaining effective in a cultivar for a long period of time during its widespread cultivation", is based on an arbitrary criterion. A more precise definition of resistance durability goes back to the study of Van den Bosch and Gilligan (2003). This latter study was distinctive as it proposes several measures of resistance durability as well as a modelling framework coupling a classical epidemiological model to a population genetics approach. Hence, whereas some of their criteria for resistance durability are related to epidemic intensities, such as healthy area duration, other criteria, such as the time elapsing before a virulent allele to become fixed in the pathogen population, are typically derived from population genetics. Later, theoretical studies by Rimbaud, Papaïx, Barrett, et al. (2018) and Papaïx et al. (2018) built on this distinction and proposed criteria related to epidemiological control and criteria related to evolutionary control. Importantly, they highlighted that strategies aiming to maximize epidemiological control are not necessarily those maximizing evolutionary control (Papaïx et al., 2018; Rimbaud, Papaïx, Barrett, et al., 2018). Typically, landscapes planted with a high proportion of the resistant cultivar in low aggregation confer the best short-term epidemiological control, but are far from optimal for resistance durability (Papaïx et al., 2018).

Another interesting feature of the evolutionary epidemiology framework is that, with the same mathematical formalism, it can handle the dynamics of adaptation of pathogen populations towards both qualitative and quantitative resistances (Fabre et al., 2022; Lo Iacono et al., 2012). Furthermore, this formalism allows the dynamics of pathogen life history traits targeted by quantitative resistances to be derived (Lo Iacono et al., 2012). Yet, this framework has seldom been applied in theoretical studies. One reason for this might be that it can lead to complex mathematical models, especially when dealing with quantitative resistances (Fabre et al., 2022). Still, new models have to be developed, even considering the simpler genetic determinisms that govern qualitative interactions.

4.2 | Build new contextual models that include detailed understanding of biological processes

We propose that "epidemiology and evolution" studies develop more realistic models of pathogen evolution. Pathogen genetics allows us

to integrate the molecular mechanisms underlying pathogen adaptation through an explicit description of the genotypic states and the probabilities of their changes. Losses of resistance efficacy can result from a variety of molecular mechanisms leading to alteration of the avirulence gene (Box 1). Knowledge of these key biological processes is of paramount importance to feed into epidemiological models and, ultimately, to forecast the risk of pathogen adaptation (Hessenauer et al., 2021; Milgroom & Peever, 2003). Some mechanisms have already been taken into account in theoretical studies. For example, models consider both qualitative and quantitative resistances as general features, although quantitative resistances remain underrepresented (see table 1 in Rimbaud et al., 2021). However, our current knowledge of molecular mechanisms and pathogen biology ranges far beyond current modelling assumptions. We propose that modellers build contextual models that integrate our current understanding of biological processes. These models would be less generic but would lead to more accurate predictions on given classes of organisms. The following four examples illustrate the importance of considering such a wider array of biological processes underlying pathogen adaptation.

1. Life history traits affected by quantitative resistances drive resistance durability. Contrary to qualitative resistances that prevent infection, quantitative resistances can affect different steps of the infection cycle without completely preventing infection. Rimbaud, Papaïx, Rey, et al. (2018) predicted that resistance durability would differ depending on the trait impacted by quantitative resistance genes. In particular, this theoretical study showed that quantitative resistance targeting the pathogen latent period has the best potential to increase resistance durability. Similarly, evolution can lead in theory to a monomorphic or dimorphic pathogen population, depending on the life history trait impacted by quantitative resistance (sporulation curve vs. infection efficiency) (Fabre et al., 2022). This result highlights the importance of the choice of the quantitative resistance genes operated by plant breeders as a driver of pathogen diversification (Fabre et al., 2022).
2. Molecular mechanisms rule pathogen adaptation. For example, the type and number of mutations is key to understanding pathogen adaptation. Population genetics allows us to set the probabilities of genotypic changes and to monitor pathogen evolution at the finest molecular scale. In the case of virus adaptation to qualitative resistances, the epidemiological control provided by qualitative resistance to a plant virus is impacted strongly by the number of mutations that the virus must accumulate to overcome resistance (Djidjou-Demasse et al., 2017; Fabre et al., 2012; Janzac et al., 2009). Here, typically, a population genetic concept, the mutation-selection equilibrium, allows molecular data (Janzac et al., 2009) and an evolutionary-epidemiological model (Djidjou-Demasse et al., 2017; Fabre et al., 2012) to be linked. Furthermore, few theoretical models consider epistatic interaction among avirulence gene loci, although molecular investigations have proved that it can occur (Plissonneau et al., 2016). Finally, consider the example of priming, that is, the induction of plant defence by specific infection conferring cross-protection to all pathogen genotypes. A theoretical study by Clin et al. (2021) found that considering priming changes predictions for the use of cultivar mixtures. With priming, a given proportion of resistant and susceptible host genotypes is optimal to reduce disease prevalence, whereas, without priming, maximal reduction is obtained with a monoculture of pure resistant plants.
3. The diverse, and sometimes complex, reproductive modes of pathogens are seldom considered. In particular, models often neglect the role of sexual reproduction (Rimbaud et al., 2021). Yet, pathogens undergoing sexual reproduction generate, in theory, less gene diversity but greater evenness in genotypic distributions than asexual pathogens (Birky, 1996; Frank, 1993; Halkett et al., 2005; Reichel et al., 2016; Stoeckel et al., 2021). In addition, mixed sexual and asexual reproductions could lead to higher risk of pathogen adaptation via an increased evolutionary potential: on the one hand sexual reproduction generates genotypic diversity and on the other hand asexual reproduction maintains and favours the most adapted combinations of alleles (Bazin et al., 2014; McDonald & Linde, 2002).
4. Few evolutionary epidemiology models take into account pathogen ploidy. Most studies assume haploid pathogens. Yet, diploid pathogens can follow different evolutionary trajectories. Following the gene-for-gene model, the recessivity of the virulence allele in diploids results in delayed and more stochastic invasion dynamics (see the modelling study by Saubin et al., 2021). Moreover, pathogen life cycle variability can impact the relative importance of each evolutionary force on the resulting resistance durability. In particular, host alternation in pathogen life cycle can reduce the probability of virulence emergence but once a virulence emerges it can speed up resistance overcoming because host alternation increases gene flow (Saubin et al., 2021).

More broadly, we argue that there are plenty of other molecular mechanisms and biological processes that need to be better considered in theoretical studies. This would lead to more contextualized and accurate studies of resistance durability.

4.3 | Do not neglect genetic drift as a source of stochasticity in evolutionary trajectories

The diversity of pathogen life cycles translates into diversity in pathogen demography and population sizes. Small population sizes at any time in a pathogen life cycle increase genetic drift and, hence, stochasticity in evolutionary trajectories. We expect drift to impede pathogen adaptation, a weakness we can exploit to enhance resistance durability. The most recent theoretical models consider the stochasticity of pathogen evolutionary trajectories thanks to demogenetic models. However, few modelling works consider the effects of genetic drift (Rimbaud et al., 2021). For some pathogen species, effective population sizes are shown to be large enough to

confidently neglect genetic drift. This is the case for many fungal species (e.g., *Botrytis cinerea*, Walker et al., 2017; *Zymoseptoria tritici*, Zhan et al., 2001). Other organisms have smaller population sizes and their evolution can be impacted more strongly by stochasticity: in particular, recent experimental studies highlighted the non-negligible effect of genetic drift on the dynamics of adaptation of diverse pathogens (e.g., in nematodes, Jan et al., 2016; Montarry et al., 2019).

Besides, some pathogen populations undergo large demographic fluctuations. Among the various pathogen life cycles, specific phases induce drastic drops in population size (i.e., bottlenecks). These include, for example, overwintering (Castel et al., 2014; Djidjou-Demasse et al., 2017; Fabre et al., 2012, 2015; Hamelin et al., 2011; Lo Iacono et al., 2013), host alternation (Saubin et al., 2021) and plant-to-plant transmission (Moury et al., 2007). Quantitative resistances can also promote drift by reducing within-host population size (Rousseau et al., 2017). Drift should therefore be considered more in modelling works (e.g., as in Rousseau et al., 2019; Saubin et al., 2021), as a direct consequence of demographic fluctuations, and in breeding processes as a leverage to slow pathogen adaptation (Montarry et al., 2019; Quenouille et al., 2014). In that respect, it could also be worth considering evolutionary processes in which genetic drift is particularly strong, such as reproductive modes that impact effective population sizes and bottleneck events. For example, during bottleneck events, evolutionary rescue can occur, when genetic adaptation prevents population extinction and leads to demographic recovery (Alexander et al., 2014). This would shed new light on the effect of landscape management strategies on changes in pathogen population sizes in relation to their dynamics of adaptation.

However, we identify some limits to this proposed leverage. First, selection can occur at the parcel scale rather than within-host (Bergstrom et al., 1999). This is the case when there are recurrent migration events among hosts (horizontal transmission), which increases the effective size of the pathogen population. This challenges the possibility to take advantage of genetic drift by deploying quantitative resistances. Second, the increase in genetic drift would lead to more stochastic pathogen evolutionary trajectories, making it more difficult to forecast pathogen adaptation and to adapt landscape management accordingly.

4.4 | Take into account the temporal dimension in empirical studies

In addition to detailed investigations on molecular interactions, empirical studies should consider temporal samples to better elucidate rapid changes in molecular weaponries. Pathogens offer the unique opportunity to study contemporaneous evolution (McDonald, 2010) and to disentangle the interplay of the evolutionary forces at work. The recent advances in molecular studies promoted by omic approaches have helped deciphering the diversity of effectors and the multiplicity of evolutionary mechanisms that can lead to the emergence of virulence (Fouché et al., 2018; Rouxel & Balesdent, 2017; Stergiopoulos et al., 2007; Stukenbrock & Bataillon, 2012). Detailed studies have examined the diversity of virulence determinants within pathogen populations (Daverdin et al., 2012; Huang et al., 2014) or evolutionary patterns in effector diversification (Stukenbrock & McDonald, 2009). Yet, a temporal dimension in pathogen population surveys is often lacking, or is too narrow to trace evolutionary dynamics in detail, as has been done using phylogenomic approaches in human diseases (Geoghegan & Holmes, 2018). Examining genetic variation on a snapshot sample can give access to only a restricted part of the evolutionary history and hides phenomena that remain unsuspected without the use of temporal samples (e.g., population replacement, as evidenced in Persoons et al., 2017 and Louet et al., 2022). We encourage long-term sampling efforts to build large collections of isolates over extended time periods (Gandon et al., 2016).

4.5 | Use the determinants of reciprocal interactions to forecast and stabilize evolutionary trajectories of pathogen populations

Finally, we propose better consideration of the reciprocity of interactions between hosts and pathogens within an evolutionary framework. In agroecosystems, host populations and their genetic diversity is strictly controlled by humans. As such, it is not correct to draw analogies between evolution in agroecosystems and the coevolution that occurs in nature. Yet, we argue that an understanding of the theoretical outcomes of host–pathogen coevolution can provide insights into the best ways to manage such host diversity for durable control of pathogen populations. Theoretical population genetics models show that coevolutionary dynamics can stabilize (or not) polymorphism, depending on how evolution of pathogen and host populations is coupled (Tellier & Brown, 2011). Strong and reciprocal interactions lead to unstable spirals, leading to evolutionary arms races through epidemic outbreaks. These occur when pathogen fitness depends on the abundance of a host plant that imposes directional selection. This is often typically observed in human-managed systems, with boom and bust cycles resulting from the strong and unidirectional selection pressures exerted by the intensive use of a single qualitative resistance (Persoons et al., 2017; Phan et al., 2020; Zhan et al., 2015). A rupture of continuous selection pressure can enhance resistance durability, as observed for deployment of the *mlo* gene in barley against powdery mildew. A striking feature of this deployment is the long-term and lasting choice to refrain from introducing it in winter barley (Dreiseitl, 2020). The obligate powdery mildew pathogen is deemed to infect winter varieties to overwinter. Therefore, despite the massive use of the *mlo* gene in spring varieties for more than four decades, each year the pathogen populations experience an interruption of selection pressure on winter varieties. More generally, ecological processes that maintain the genetic diversity of host and pathogen populations are expected to regulate epidemic cycles and prevent outbreaks (Laine & Barrès, 2013). This

can occur, for example, in natural systems with perennial hosts or seed banks (Tellier & Brown, 2009). Host and pathogen diversity is a key element in explaining the success of cultivar mixtures in disease control, in both the short and long term (Clin et al., 2021), as recently observed by Perronne et al. (2021) in wheat. We should therefore promote and use the diversity of plant material provided by plant breeders. More generally, diversifying crops in agricultural landscape would be beneficial (Vialatte et al., 2021). A remaining question is how to go beyond the epidemiological approach in integrating coevolutionary dynamics, to make best use of this diversity.

The theory of coevolution indicates that polymorphism stability depends on the costs associated with host resistance(s) and pathogen virulence(s). Even if the fitness costs of virulence have been documented in all pathogen kingdoms (Leach et al., 2001), it is not a strict and generalized rule (see e.g., Fournet et al., 2016; Maupetit et al., 2021). Quantitative resistances offer the opportunity to exploit putative trade-offs among pathogen fitness traits to better stabilize the system (Laine & Barrès, 2013). Early theoretical models of plant–pathogen coevolution focussed on gene-for-gene interactions. New models incorporating the genetic architecture of quantitative traits in both plants and pathogens should be developed.

Ultimately, a theoretical understanding of host–pathogen evolutionary trajectories should enable us to forecast pathogen evolution conditionally on the selection exerted by crops. Direct epidemiological surveys can allow us to know the current and past pathogen population dynamics and genetic characteristics, and to adequately adapt cultivated landscapes. Understanding the reciprocity between the human-mediated evolutionary trajectories of hosts and pathogens would make it possible to tailor plant breeding not only to current, but also to anticipated states of evolution of pathogen populations, provided plant resistance is evaluated early enough in the breeding process. This understanding and prediction of pathogen evolutionary trajectories would then lead to more durable management strategies of host resistance, including adaptive adjustments of the varietal landscape. In addition to using all available genetic diversity developed by plant breeders to break unidirectional selection pressures, we advise strengthening plant breeding efforts by including pathologists, molecular biologists, and modellers as early as possible when developing breeding schemes.

5 | CONCLUDING REMARKS

Population genetics is a central framework that can improve our understanding of the durability of plant resistance, by knitting together "plant breeding", "molecular interactions", and "epidemiology and evolution" analyses. However, this research field is still underrepresented, both empirically and theoretically, and often used only as a simplified tool. We believe that enhanced dialogue across the three identified subfields will pave the way to a better knowledge of the evolutionary trajectories of pathogen populations and help improve the sustainable management of genetic resistances. Developing interdisciplinary work is challenging. It may be costly and risky in the short term, compared with traditional studies deeply rooted in each subfield. Incentives must, however, be strong enough to bypass these initial difficulties and ensure that teams with complementary expertise work together in a long-term effort. Ultimately, we advocate forming interdisciplinary teams by bringing together researchers from the three subfields and truly sharing the same goal—namely the development and deployment of durable resistances. Our prediction is that this will lead to significant progress in the sustainable management of plant diseases.

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CONFLICT OF INTEREST

The authors declared no conflict of interest for this article.

OPEN RESEARCH BADGES

This article has earned an Open Data Badge for making publicly available the digitally-shareable data necessary to reproduce the reported results. The data is available at https://www.webofscience.com.

DATA AVAILABILITY STATEMENT

All the files extracted from the ISI Web of Science portal (https://www.webofscience.com) and the list of keywords used for the bibliographic analysis are available on Zenodo repository (DOI: 10.5281/zenodo.6651957)

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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