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Models of Plant Resistance Deployment

Loup Rimbaud,[1,2] Frédéric Fabre,[3] Julien Papaïx,[4] Benoît Moury,[1] Christian Lannou,[5] Luke G. Barrett,[2] and Peter H. Thrall[2]

[1]INRAE, Pathologie Végétale, 84140 Montfavet, France; email: loup.rimbaud@inrae.fr, benoit.moury@inrae.fr

[2]CSIRO Agriculture and Food, Canberra, ACT 2601, Australia; email: luke.barrett@csiro.au, peter.thrall@csiro.au

[3]INRAE, Bordeaux Sciences Agro, SAVE, 33882 Villenave d'Ornon, France; email: frederic.fabre@inrae.fr

[4]INRAE, BioSP, 84914 Avignon, France; email: julien.papaix@inrae.fr

[5]INRAE, BIOGER, 78850 Thiverval-Grignon, France; email: christian.lannou@inrae.fr

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adaptation, durability, evolution, host–microbe interaction, immunity, simulation

Abstract

Owing to their evolutionary potential, plant pathogens are able to rapidly adapt to genetically controlled plant resistance, often resulting in resistance breakdown and major epidemics in agricultural crops. Various deployment strategies have been proposed to improve resistance management. Globally, these rely on careful selection of resistance sources and their combination at various spatiotemporal scales (e.g., via gene pyramiding, crop rotations and mixtures, landscape mosaics). However, testing and optimizing these strategies using controlled experiments at large spatiotemporal scales are logistically challenging. Mathematical models provide an alternative investigative tool, and many have been developed to explore resistance deployment strategies under various contexts. This review analyzes 69 modeling studies in light of specific model structures (e.g., demographic or demogenetic, spatial or not), underlying assumptions (e.g., whether preadapted pathogens are present before resistance deployment), and evaluation criteria (e.g., resistance durability, disease control, cost-effectiveness). It highlights major research findings and discusses challenges for future modeling efforts.

1. INTRODUCTION: WHY WE NEED TO MANAGE RESISTANCE DEPLOYMENT AND HOW MODELS CAN HELP

Resistance durability: initially defined as the time during which a given resistance remains effective in spite of an environment favorable to disease; the term has since gained a wide range of accepted usages

Resistance-adapted pathogens: pathogen variants adapted to a plant resistance gene. Also referred to as infective, virulent, and resistance-breaking in other contexts

Deployment of plant resistance is a relatively low-input, cost-effective way to protect agricultural crops from plant pathogens (68, 126). Plant resistance has been used in plant breeding programs to control diseases of various crops (e.g., 4, 6, 59). However, pathogens have frequently evolved to quickly break down resistance following field deployment (38, 52, 107), sometimes resulting in catastrophic epidemics and massive use of pesticides. High pathogen evolutionary potential, coupled with the standardization and intensification of modern agriculture across large cultivated areas, has generally led to recurrent cycles of resistance deployment followed by rapid pathogen adaptation, often described as boom-and-bust cycles (79). When the resistance of a cultivar becomes ineffective, economic losses can be considerable because of the direct impact of epidemics and the cost of alternative control methods. Moreover, breeding for resistance is costly, time consuming, and often constrained by the limited availability of genetic resistance sources (41, 149). Resistance genes should therefore be considered an exhaustible resource deserving careful stewardship.

The design and implementation of strategies that improve resistance durability would therefore be of great benefit to agricultural productivity, sustainability, and profitability. However, a key point is that resistance durability and epidemiological control are not necessarily correlated (13, 53). Thus, any strategy designed to control the emergence of resistance-adapted pathogens in agro-ecosystems has the potential to conflict with epidemic control in both the short-term (from standing pathogenic variants) and long-term, should resistance break down.

Pathogen spread and adaptation are favored by the low host genetic diversity that is representative of intensive agricultural systems (125). Therefore, many proposed strategies rely on the selection of diverse resistance sources and their spatiotemporal deployment to engineer biodiverse cropping systems (9, 13, 78, 85, 126). The goal is to confront pathogens with eco-evolutionary challenges and thus avoid or delay their adaptation to plant resistance while maintaining effective epidemiological protection (15, 149). Particularly for airborne plant pathogens, deployment strategies are more likely to be effective if implemented across landscapes at large spatial scales (41). However, experimental tests of landscape-based strategies are rarely feasible for obvious practical reasons (but see 27, 58, 152).

To overcome the difficulties of experimentation with plant resistance deployment at large spatiotemporal scales, numerous mathematical models have been developed (see the sidebar titled Complementarity Between Models, Experiments, and Observations). However, models are typically faced with the challenges of combining several aspects of resistance deployment (e.g., type of plant–pathogen interaction, spatiotemporal scale of deployment; see Section 2), incorporating realistic parameters and assumptions with respect to epidemiological and evolutionary processes (see Section 3), and generating usable outputs (see Section 4). In this review, we identify 69 studies that use models to assess or optimize deployment strategies (**Table 1**; details in the **Supplemental Table**). Our aim is to provide a comprehensive overview of these modeling approaches, noting that the diversity of model structures, assumptions, and outputs makes direct comparisons difficult. Regardless, we examine their main features from both epidemiological and evolutionary perspectives and highlight major findings of relevance to resistance durability and epidemiological control.

Supplemental Material >

2. MODELING RESISTANCE DEPLOYMENT FROM GENE TO LANDSCAPE SCALES

The main strategies considered in plant resistance deployment act across scales from genes to landscapes. They rely on the appropriate choice of resistance sources, which can be combined

COMPLEMENTARITY BETWEEN MODELS, EXPERIMENTS, AND OBSERVATIONS

Numerical experiments performed using computer models represent an alternative way of generating results while circumventing logistical, financial, legal, and ethical constraints associated with traditional experiments in laboratory or field conditions (31). Models are powerful tools to predict epidemics and guide disease management. With respect to the use of plant resistance, a huge number of deployment strategies can now be tested via such models thanks to the growing capacity of modern computers, even if the number of possible calculations will always be limited by the computational cost (i.e., the time required to perform the calculations). However, we are now confronted with the difficulty of manipulating, analyzing, and synthesizing results obtained from high dimension systems. And more fundamentally, modeling is insufficient on its own. Modelers need empirical knowledge and data acquired from experimental and observational approaches in the laboratory or the field to develop their model, calibrate its parameters, and validate or test its predictions.

in the same cultivar (gene pyramiding), alternated within rotations, mixed within fields, or segregated across a mosaic of fields (**Figure 1**). Because these have been extensively described in previous reviews (e.g., 9, 13, 85, 126, 149), we focus on mathematical models developed to assess, compare, and improve these strategies (**Table 1**, **Supplemental Table**). We note that the evolutionary processes underlying pathogen and pest adaptation to plant resistance are analogous to those associated with the emergence of resistance to chemicals. Therefore, the deployment strategies we consider have counterparts in the management of resistance to pesticides in crops, drugs used for the treatment of animals and humans, and vaccines (for reviews, see 110, 111, 129, 137).

2.1. Choosing Appropriate Resistance Sources

The smallest scale that impacts deployment lies in the choice of resistance sources to be deployed. Plant resistance has often been classified as either qualitative complete or quantitative partial, although considerable empirical evidence suggests that this dichotomy should be revised (see the sidebar titled Should the Traditional Dichotomy of Plant Resistance Be Reconsidered?).

2.1.1. Modeling qualitative and quantitative resistance. Qualitative resistance usually refers to major resistance genes, which code for specific host proteins able to recognize a specific pathogen molecular pattern or effector. Such gene-for-gene interactions are traditionally modeled using a two-by-two matrix describing the occurrence of disease as an outcome of the interaction between host genotype (with or without the resistance gene) and pathogen genotype (nonadapted or adapted) (35) (**Figure 2*d***). Only resistance-adapted pathogens can infect resistant hosts. Depending on whether or not they are present in the initial pathogen population, they may need to be introduced (e.g., via immigration from distant areas, mutation or recombination; see Section 3.2). In this context, pathogen adaptation leads to resistance breakdown, i.e., complete restoration of pathogen infectivity on resistant hosts. However, adaptation is often penalized by a fitness cost on susceptible hosts (60, 68, 140), resulting in a decreased ability of resistance-adapted genotypes to infect susceptible hosts compared to nonadapted pathogens (131). The inclusion of a fitness cost parameter makes the plant–pathogen interaction matrix (**Figure 2*b***) relevant for both the gene-for-gene (**Figure 2*d***) and matching allele (**Figure 2*e***) concepts (1, 117, 130). Indeed, the classic matching allele concept states that pathogen adaptation to a new host makes infection of other hosts impossible (i.e., the fitness cost is maximal).

Quantitative resistance traditionally refers to the additive effects of multiple minor resistance genes, resulting in a continuous distribution of pathogen adaptation (21, 91, 124). From the

Supplemental Material >

Qualitative: distributed in discrete classes (by homology with statistics)

Complete: resistance is complete when it completely blocks the infectious cycle of nonadapted pathogens (e.g., by preventing infection or the production of propagules)

Quantitative: continuously distributed (by homology with statistics)

Partial: resistance is partial when infection by maladapted pathogens is not blocked but reduced, resulting in the attenuation of pathogenicity traits

Genotype: plant genotype refers here to the set of susceptibility/resistance genes, and pathogen genotype refers to the set of pathogenicity genes

Table 1 List of mathematical models used to test, optimize, or compare plant resistance deployment strategies against pathogens or predict their evolutionary consequences

Deployment strategy	Resistance efficiency[a]	Distribution of pathogen genotypes[b]	Model structure	Evolution mechanisms	Preexistence of adapted pathogens	Host spatial structure	Seasonality[c]	Outputs[d]			References
								Epidemiological	Evolutionary	Socioeconomic	
Purely demographic models											
MI	Nonhost	NA	DE	NA	No	SE	No	×			64
MI*	Nonhost	NA	DE	NA	No	SE	No	×			54, 87–89
MI	Nonhost	NA	IDE	NA	No	SE	No	×			122
MI	Nonhost	NA	ODE	NA	No	SE	No	×			128
MI	Nonhost	NA	Other	NA	No	NS	No	×			139
MO+RO	Nonhost	NA	Other	NA	No	SE	Yes	×			73
MI	Nonhost	NA	RDE+STOCH	NA	No	SE	No	×			120
MO	Nonhost	NA	STOCH	NA	No	SE	No	×			100
MI	Nonhost or partial	NA	DE+STOCH	NA	No	SE	No	×			40
RO	Nonhost or partial	NA	ODE	NA	No	NS	No	×			23
MO	Nonhost or partial	NA	STOCH	NA	No	SE	No	×			105
MO or MO+MI	Partial	NA	IDE+STOCH	NA	No	SE	No	×			123
MI	Partial	NA	ODE	NA	No	NS	No	×			51
TO or MI	Partial	NA	ODE	NA	No	NS	Yes	×			57
MO*	Partial	NA	ODE+STOCH	NA	No	NS	No			×	141
MO	Partial	NA	ODE+STOCH	NA	No	NS	No	×		×	121
MO	Partial	NA	Other	NA	No	SE	Yes	×			48
Demogenetic models of adaptive dynamics											
RO	Nonhost	Continuous	ODE	S-M	No	NS	Yes		×		132
Pure stand or MO	Nonhost or partial	Continuous	ODE	S-M	No	NS	No		×		37
MO	Partial	Continuous	DE	S-M	No	SE	No		×		103
MI*	Partial	Continuous	ODE	S-M	No	NS	No		×		133
Pure stand	Partial	Continuous	ODE	S-M	No	NS	No	×	×		135, 138

(*Continued*)

Table 1 (*Continued*)

Deployment strategy	Resistance efficiency[a]	Distribution of pathogen genotypes[b]	Model structure	Evolution mechanisms	Preexistence of adapted pathogens	Host spatial structure	Seasonality[c]	Outputs[d]			References
								Epidemiological	Evolutionary	Socioeconomic	
Demogenetic models											
MO	Complete	Classes	ODE	S-M	No	SE	Yes	×	×	×	96, 97
MO or MO+PY	Complete	Classes	ODE	S-M	No	SE	Yes	×		×	98
TO, MO, PY, or MO+PY	Complete	Classes	IDE+STOCH	S-M-D	Yes/no	SE	Yes		×		74
MI* or MI*+PY	Complete	Classes	ODE	S	Yes	NS	No	×			95
MO	Complete	Classes	ODE	S	Yes	SI	Yes	×			33
MO or dynMO	Complete	Classes	ODE	S	Yes	SI	Yes	×	×		34
MI*	Complete	Classes	ODE	S-I-M	Yes/no	NS	No	×	×		136
MO, dynMO, PY, or dynMO+PY	Complete	Classes	ODE	S-M	Yes	SI	Yes	×			29
RO	Complete	Classes	ODE	S-M	Yes	NS	Yes	×			93, 94
MO+PY	Complete	Classes	ODE (within plant), STOCH (between plant)	S-M-D	No	NS	No		×		32
MO or MI	Complete	Classes	ODE+STOCH	S-I-M-D	Yes	NS	No	×			70
MI	Complete	Classes	Other	S	Yes	NS	No		×		45
TO, MO, PY, or MO+PY	Complete	Classes	Other	S	Yes	SI	Yes		×		75
MI*	Complete	Classes	Other	S-M	Yes	NS	No		×		127
MI or MI+PY	Complete	Classes	RDE	S-R	Only single mutants	SE	Yes	×	×		118

(*Continued*)

Table 1 (*Continued*)

Deployment strategy	Resistance efficiency[a]	Distribution of pathogen genotypes[b]	Model structure	Evolution mechanisms	Preexistence of adapted pathogens	Host spatial structure	Seasonality[c]	Outputs[d]			References
								Epidemiological	Evolutionary	Socioeconomic	
MO	Complete	Classes	STOCH	S-M	No	SE	No		×		144
MO, MI, RO, or PY	Complete	Classes	STOCH	S-M-D	No	SE	Yes	×	×		112
MO	Complete	Continuous	STOCH	S-M-D	No	SE	Yes	×	×		104
MI	Complete + induced R	Classes	DE	NA	Yes	SE	No	×			65
MI*	Complete + induced R	Classes	ODE	S	Yes	NS	No	×			19
MI	Complete or partial	Classes	ODE	S	Yes	NS	No	×	×		81
MO*	Complete or partial	Classes	ODE	S	Yes	SE	Yes	×			143
MI	Complete or partial	Classes	STOCH	S-M	No	SI	No	×	×		17
MO or MI	Complete or partial	Classes or continuous	IDE	S-M	No	NS	No	×			71
MI or MI+PY	Complete or complete + partial	Classes or classes + continuous	DE	S	Yes	NS	No		×		62
MI* or MI*+PY	Complete or complete + partial	Classes	STOCH	S-M-D	Yes	NS	No	×			115
MO or MO+PY	Complete or partial or complete + partial	Classes or continuous or classes + continuous	STOCH	S-M-D	No	SE	Yes	×	×		114
MI	Nonhost or partial	Classes	STOCH	S	Yes/no	SE	No	×			148
RO	Partial	Continuous	ODE	S-M	No	NS	Yes	×	×	×	3

(*Continued*)

Table 1 (*Continued*)

Deployment strategy	Resistance efficiency[a]	Distribution of pathogen genotypes[b]	Model structure	Evolution mechanisms	Preexistence of adapted pathogens	Host spatial structure	Seasonality[c]	Outputs[d]			References
								Epidemiological	Evolutionary	Socioeconomic	
MI	Partial	Classes	DE	S	Yes	SE	Yes	×	×		66, 67
MI*	Partial	Classes	ODE	S	Yes	NS	Yes	×	×		108
PY+ Fungicides	Partial	Classes	ODE	S-M	No	NS	Yes		×		16
MI	Partial	Classes	Other	S	Yes/no	NS	No	×		×	134
MI	Partial	Classes	RDE	S	Yes	SE	No	×			119
Pure stand, RO, or RO+PY	Partial	Classes	STOCH	S-R	Yes	NS	Yes	×	×		22
MI or MI+RO	Partial	Classes	STOCH	S-D	Yes	SE	Yes	×			147
PY+MI	Partial	Classes	STOCH	S-R-D	Only single mutants	SE	Yes		×		146
Pure stand	Partial	Continuous	IDE	S-M	No	NS	No		×		28
Pure stand or PY	Partial	Continuous	STOCH	S-M	No	NS	No	×	×		8
MO	Partial	Continuous	STOCH	S-M-D	No	SE	Yes		×		102

[a]Resistance may be completely or partially efficient. Nonhost is used when a cultivar is completely resistant to a pathogen without evolution (i.e., the pathogen can never adapt and infect such a host).

[b]A distribution in classes refers to qualitative resistance (to which a pathogen adapts via a sudden breakdown), and a continuous distribution refers to quantitative resistance (to which a pathogen gradually adapts via erosion).

[c]Seasonality refers to a periodic host dynamic imposing a recurrent reduction in pathogen population size (but not necessarily with genetic drift).

[d]Epidemiological, evolutionary, and socioeconomic outputs used in modeling studies, relative to plant health and pathogen population size, pathogen population genetic composition, and crop yield or economic profit, respectively.

Abbreviations: D, genetic drift; DE, difference equations; dynMO, dynamic mosaic; I, immigration; IDE, integro-differential equations; M, mutation; MI, mixture; MO, mosaic; NA, not applicable; NS, nonspatial; ODE, ordinary differential equation; PY, pyramiding; R, recombination; RDE, reaction–diffusion equations; RO, rotation; S, selection; SE, spatially explicit; SI, spatially implicit; STOCH, stochastic equations (accounting for demographic stochasticity); TO, turnover.

Plus signs represent a combination.

Asterisks indicate models in which mosaics and mixtures cannot be distinguished.

A detailed version can be found in the **Supplemental Table**.

Supplemental Material >

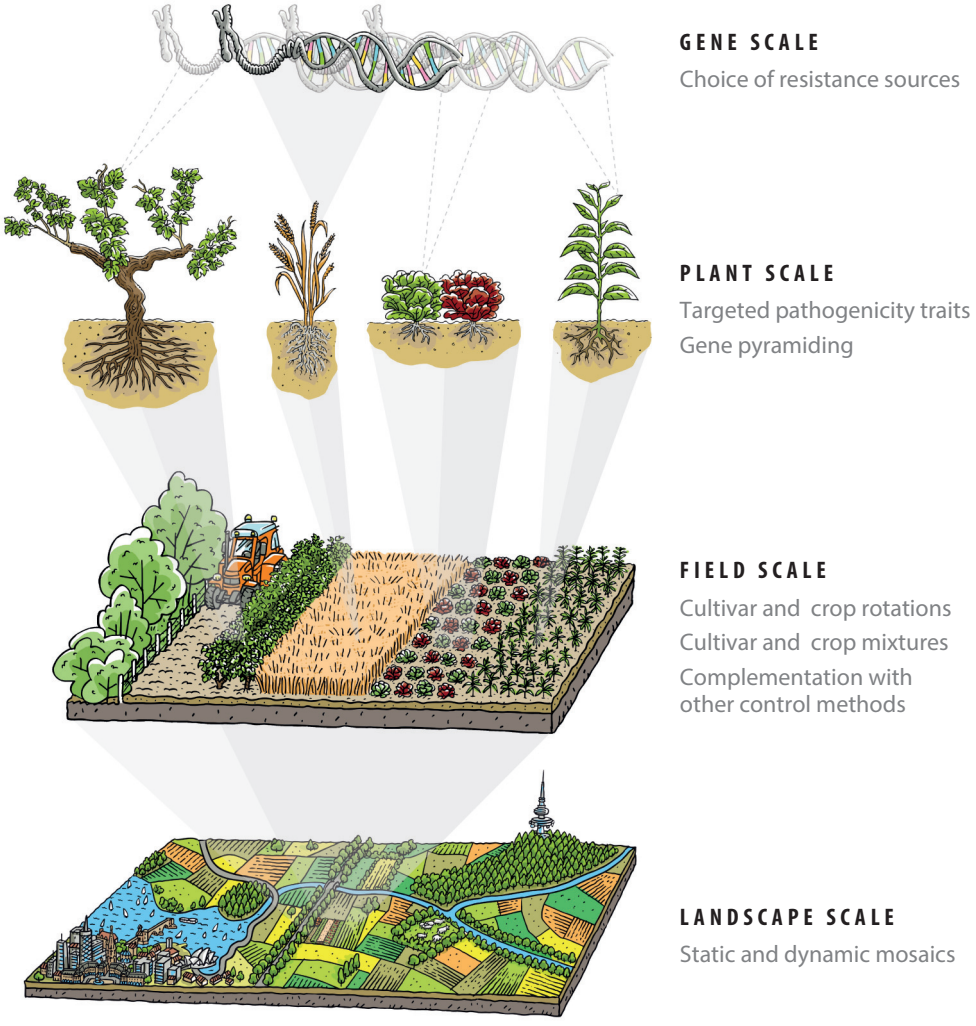

Figure 1

Nested scales of plant resistance deployment. A global deployment strategy is a combination of, first, the appropriate selection of effective genetic resistance sources (e.g., qualitative or quantitative, complete or partial) and, second, their spatiotemporal deployment at plant, field, and landscape scales with the aim of mitigating pathogen spread and evolution. Such deployment may be complemented by agronomic practices, biological control, and chemical treatments. Possible options available at each scale are indicated.

Resistance breakdown: loss of effectiveness (complete or partial, sudden or gradual) of plant resistance as a consequence of pathogen adaptation

plant perspective, pathogen adaptation corresponds to an erosion phenomenon (9, 79, 106) (**Figure 2*a*,*c***). Quantitative resistance is classically considered to be partially efficient, i.e., resistant hosts can be infected by maladapted pathogens, although disease development is reduced. Models with compartmental architecture (Section 3.1) can disentangle the effect of partial resistance on different pathogenicity traits (63): plant infection rate by pathogen propagules (e.g., fungal or bacterial spores, insect vectors carrying viral particles), latent and infectious periods, and propagule production rate (**Figure 3*a***). According to the few modeling studies that have compared the performance of quantitative resistance against different pathogenicity traits from

SHOULD THE TRADITIONAL DICHOTOMY OF PLANT RESISTANCE BE RECONSIDERED?

Plant resistance is traditionally classified into two distinct categories. Qualitative resistance is described as monogenic [conferred by a single major resistance gene typically coding for an NLR (nucleotide-binding domain leucine-rich repeat)-containing protein], which is complete, race-specific (i.e., effective only for some strains of a pathogen species), and often considered nondurable. Quantitative resistance is described as polygenic (conferred by the additive action of several minor resistance genes), partial, and race-nonspecific and often hypothesized as durable. However, oversimplification sometimes leads to erroneous assumptions, and several excellent reviews have pointed out exceptions to this long-standing dichotomy (91, 92, 124), such as the wheat gene *Lr34* against rusts and the barley gene *mlo* against powdery mildew (these genes do not belong to the NLR family and confer almost complete, race-nonspecific, and durable resistances). Consequently, we think it is important to disentangle the phenotype (complete versus partial), specificity, genetic inheritance (monogenic versus polygenic), molecular mechanism, and durability of resistance. Furthermore, we argue that pathogen genotypes can be structured qualitatively (i.e., in discrete classes, either adapted or not to the resistance) or quantitatively (i.e., continuously, more or less adapted).

a disease management perspective, the most promising target trait for quantitative resistance is latent period, followed by infection rate and propagule production rate (71, 114).

However, qualitative resistance is not always complete, and quantitative resistance is not necessarily partial (see the sidebar titled Should the Traditional Dichotomy of Plant Resistance Be Reconsidered?). For example, many qualitative resistance genes actually allow some infection, whether they may be partially broken down, environmentally sensitive, developmentally regulated, or simply weak (20, 92, 124). In models, inclusion of a resistance efficiency parameter in the plant–pathogen interaction matrix (**Figure 2*b***) allows the representation of partially efficient qualitative resistance.

2.1.2. Deployed resistance sources must be inherently hard to break down. One of the few models accounting for the molecular mechanisms of pathogen adaptation to resistance highlighted the effect of the number, nature (transition or transversion), and rate of the required mutations and associated fitness costs on the durability of major resistance genes (32). The impact of mutation rate and fitness cost has also been demonstrated in models focusing on phenotypic aspects of qualitative resistance (33, 34, 112; see also Section 3.2). Similarly, for quantitative resistance, models indicate that the strong fitness costs of pathogen adaptation slow resistance erosion (71, 102, 104). However, resistance erosion is sensitive to pathogen mutational processes (i.e., the number of mutations required to completely erode quantitative resistance) (8). Collectively, these results support the importance of identifying and deploying resistance sources that are inherently hard to break down. These findings have been confirmed experimentally for plant viruses (50, 79, 109).

High resistance efficiency (i.e., the targeted pathogenicity trait is drastically reduced for maladapted pathogens) reduces pathogen epidemiological impact (105, 114, 119). However, the effect of this parameter on resistance durability is less well documented, probably because it is generally associated with quantitative resistance, for which defining durability is still a challenge (Section 4.2). A study on pesticide resistance showed that high application doses slow the appearance of adapted pathogens but hasten their invasion once present (46). These conclusions agree with results obtained for partially efficient major genes when resistance-adapted pathogens are initially present (22, 108).

Fitness: ability to transmit genes to the next generation. Here, pathogen fitness is mostly the relative adaptation to different host genotypes

Nonadapted pathogens: pathogen variants not adapted to plant resistance. Also referred to as avirulent or wild type in other contexts

Maladapted pathogens: pathogen variants not fully adapted to plant resistance, i.e., infection is possible, although the resulting disease is reduced

Pathogenicity traits: measures of pathogen ability to develop and spread (e.g., infection, reproduction and survival rates, latent and infectious periods)

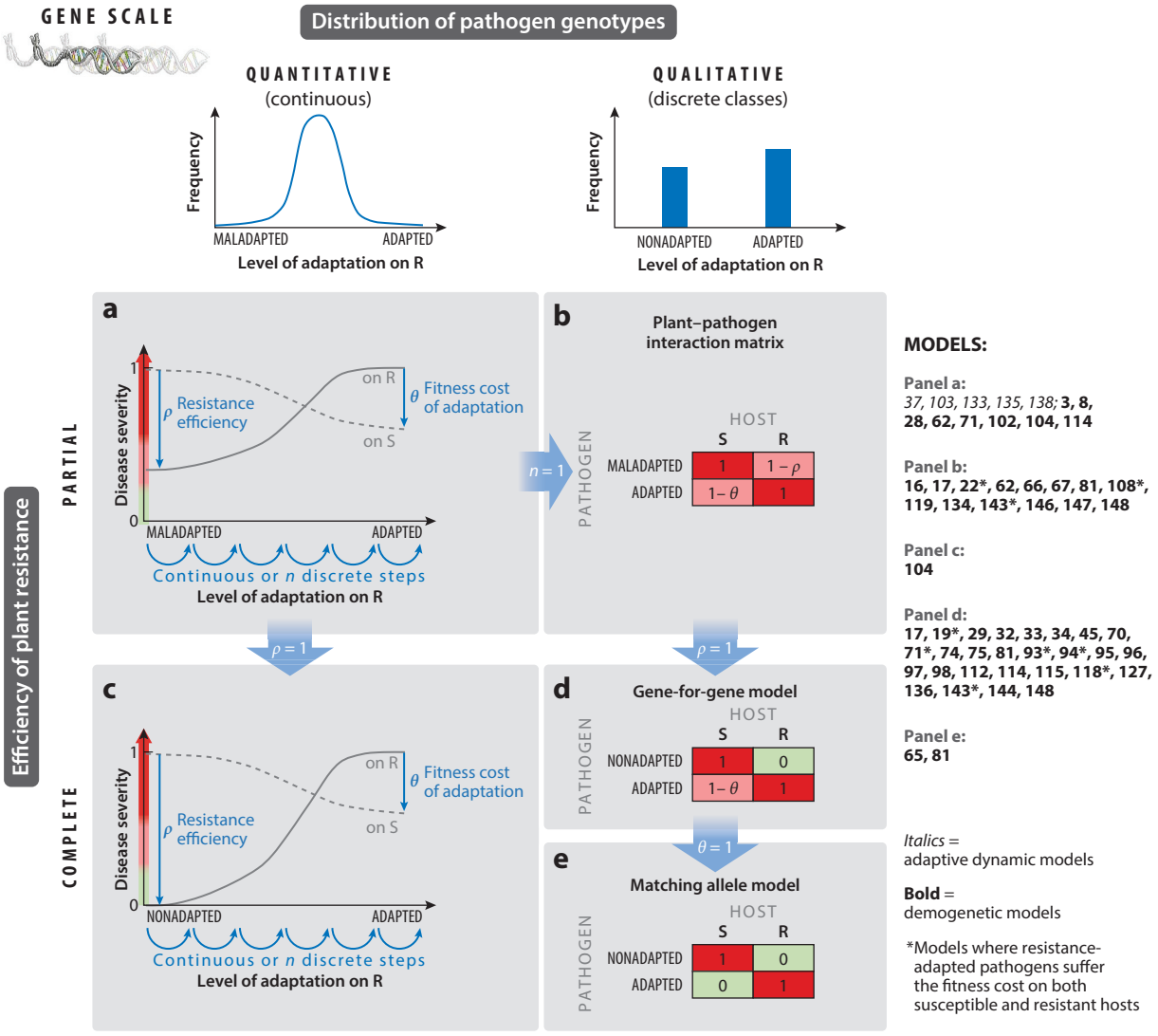

Figure 2

Modeling the phenotype of plant–pathogen interactions for resistance deployment. (*a*) The quantitative description of plant–pathogen interactions provides a general framework. Parameters of interest in plant resistance deployment are indicated in blue text. In this depiction, the degree of pathogen adaptation to the resistance source is distributed continuously in the population. Gradual pathogen adaptation via multiple adaptive steps ($n > 1$, each step involving one or more genetic mutations) results in resistance erosion [R (resistant hosts)], with a potential fitness cost (θ) paid on susceptible hosts (S). (*b*) When the pathogen population is split into two genotypic classes (adapted or nonadapted to the resistance), resistance is broken down in a single step (i.e., $n = 1$), resulting in a simple matrix that describes a gene-for-gene interaction. Independent of the distribution of pathogen genotypes, resistance can be partial (i.e., infection is possible with reduced efficiency $\rho < 1$; panels *a* and *b*) or complete (i.e., it provides total immunity, $\rho = 1$; panels *c*–*e*). Numbers refer to adaptive dynamic and demogenetic models that have used these formalizations.

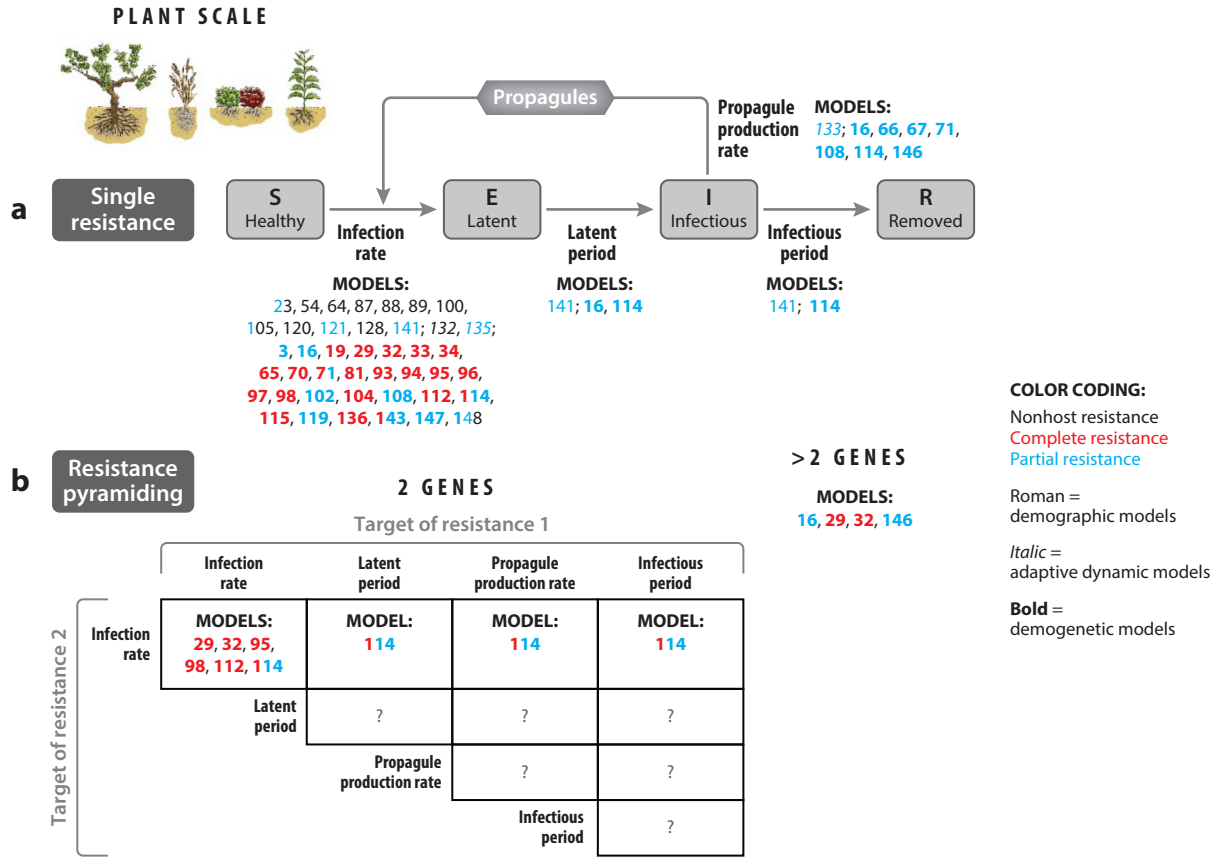

Figure 3

Modeling resistance deployment options at plant scale. (*a*) Different resistance types have varying phenotypic effects on plants when challenged by a pathogen: lower infection rate and propagule production rate, shorter infectious period, or longer latent period. Potentially, all these pathogenicity traits could be completely or partially impeded by plant resistance, but in published models, complete resistance has mostly been associated with infection rate. (*b*) Different sources of resistance can be stacked into the genome of a single plant as a pyramid. Numbers refer to demographic, adaptive dynamic, and demogenetic SEIR (susceptible-exposed-infectious-removed) models representing a wide range of pathosystems (numbers with multiple fonts or colors belong to multiple categories). Abbreviations: R, resistant; S, susceptible.

2.2. Spatiotemporal Strategies for Deploying Different Resistance Sources

Once resistance sources are chosen, they must be deployed at plant, field, and landscape scales in such a way that pathogen spread and evolution are mitigated.

2.2.1. Resistance genes can be combined at plant scale. Multiple resistance sources can be stacked into a single plant genotype as a pyramid (30, 36, 83). Although different resistance types can be combined, published models have mostly focused on pyramids of major resistance genes (**Figure 3*b***). In line with theoretical predictions (9, 68, 85) and results obtained with single genes (Section 2.1), models have shown that the durability of this strategy increases with the number of mutations required to break down all the genes composing the pyramid and the strength of associated fitness costs (29, 32, 112, 114). However, the durability of pyramids can be compromised if pyramid gene components are simultaneously deployed individually (74, 118) or

pathogens adapted to one or more of these components are already present in the population (74) (see also Section 3.2). Pyramid cultivars must therefore be deployed carefully, especially because their breakdown results in the emergence of multiadapted pathogens.

Multiadapted pathogens: pathogen variants adapted to several resistance genes. Also referred to as multivirulent pathogens and superpathogens in other contexts

Extensive empirical evidence has demonstrated the efficacy of combining qualitative and quantitative resistance in a pyramid (11, 86, 99, 109), but few models have investigated these scenarios. These models have shown that the breakdown of a major resistance gene can be delayed when pyramided with the appropriate quantitative resistance. Promising target traits include the latent period (114) and pathogen effective population size (i.e., the size of an idealized population showing the same degree of randomness in allele frequencies as the real population, noting that small effective sizes amplify genetic drift; see Section 3.2) (115). Several sources of quantitative resistance may also be pyramided (61, 124). The only model investigating this scenario highlighted the potential of targeting pathogenicity traits whose evolution is constrained by trade-offs (i.e., evolution to improve one trait penalizes another trait) (8).

2.2.2. Resistance genes can be segregated at field and landscape scales. At field scale, varieties carrying different resistance sources (or resistant and susceptible varieties) can be cultivated in the same patch, simultaneously in mixtures or alternating within rotations. Crop varieties can also be segregated into a mosaic of fields within a broader regional strategy (79, 85). Furthermore, varying the different components of mixtures, rotations, and mosaics, their relative proportions and spatial (for mixtures and mosaics) or temporal (for rotations and mosaics) organization offer a multitude of deployment options (**Figure 4**).

The value of combining cultivars in mixtures or mosaics is likely to increase with the number and heterogeneity of components. Given the fitness costs of pathogen adaptation to different hosts, heterogeneous host populations are expected to favor diversifying selection, i.e., to select for higher pathogen specialization (5). This should result in reduced disease spread owing to a (*a*) dilution effect (i.e., reduced colonization rate of a specialized pathogen in host cultivars to which the pathogen is adapted because of increased distance among the hosts, with the remainder of the host population acting as a propagule sink), (*b*) barrier effect (i.e., hosts of a given genotype acting as physical barriers to pathogen spread owing to their architecture), and (*c*) competition effect (i.e., different pathogen genotypes competing for the same host individual) (14, 55, 145). In accordance with empirical results (39, 49), models confirm the potential for dilution effects by showing that the amount of disease in mixtures is often smaller than the arithmetic mean of the amount of disease obtained from these components in pure stands (51, 54, 66, 67, 119). Assuming fitness costs of adaptation to different components, models have also demonstrated that higher numbers of mixture components amplify dilution effects (29, 81) and delay the emergence of multiadapted pathogens through competition with more specialized pathogens (45, 62, 66). In addition to dilution, barrier, and competition effects, mixtures and to a lesser extent mosaics may facilitate plant immune system activation via various mechanisms, including induced resistance (151). Induced resistance (for any kind of pathogen) or cross protection (for viruses) can occur when a cultivar becomes resistant to a resistance-adapted pathogen when previously challenged by a nonadapted pathogen coming from another cultivar (150). The only two models we are aware of that have investigated induced resistance in mixtures highlighted the impact on disease reduction of the duration and level of protection of induced resistance (19, 65) and the size of the area protected (65).

In practice, the spatial organization of a mixture is often linked to the degree of heterogeneity of its components. Multiline cultivars differing in only a few genes (10), nonfixed populations showing high genetic diversity (e.g., landraces), and mixtures of different cultivars from the same species (145) may be sown after mixing seeds, resulting in completely random mixtures.

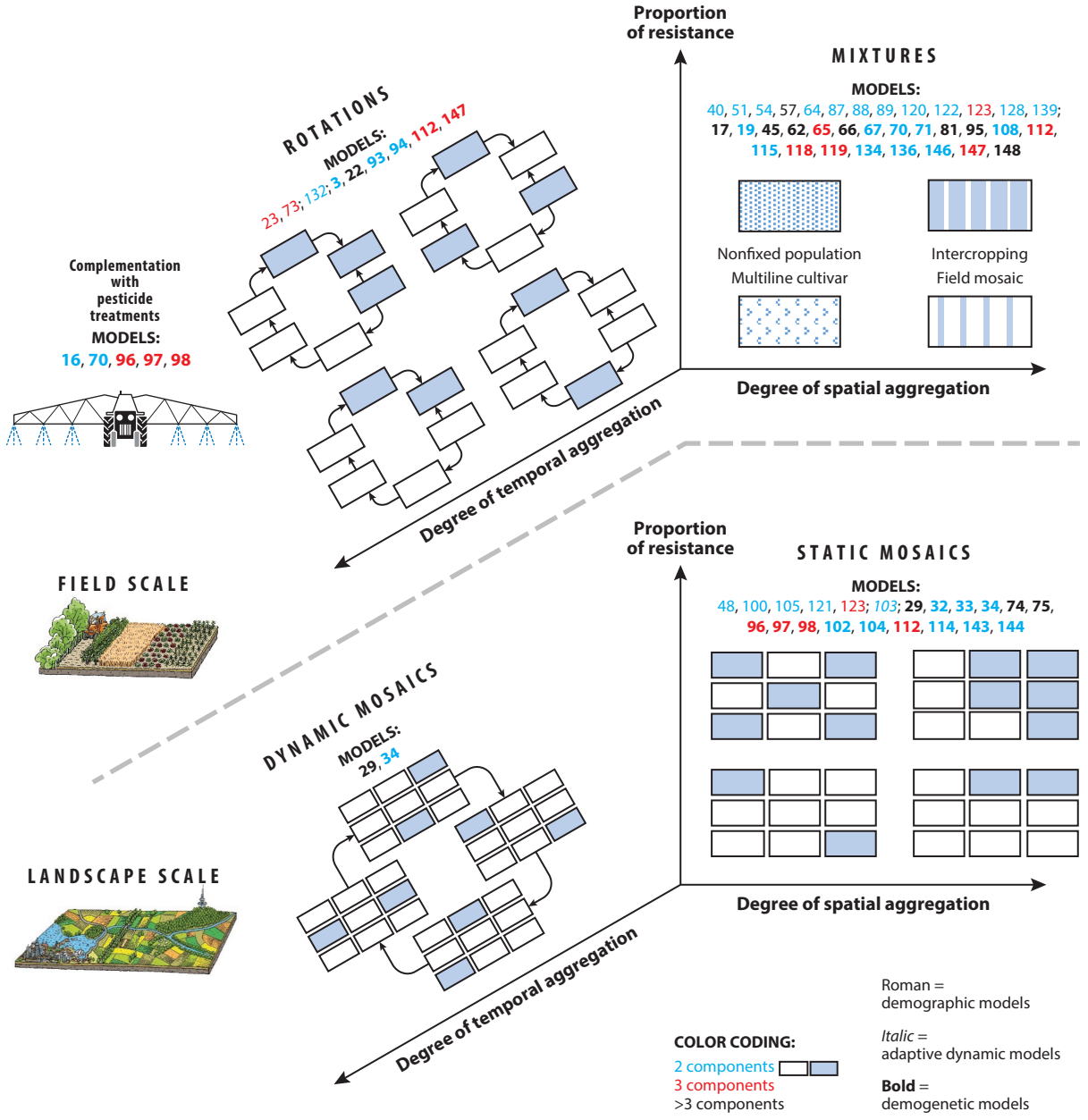

Figure 4

Modeling resistance deployment options at field and landscape scales. Field-scale strategies mostly include mixtures and rotations, which can vary with regard to the relative proportion of each component and their degree of aggregation in space (mixtures) or time (rotations). These may be complemented with other control methods (e.g., pesticide treatments). Landscape-scale strategies refer to mosaics of fields where resistance is deployed in controlled proportions and controlled degrees of spatiotemporal aggregation. Numbers refer to demographic, adaptive dynamic, and demogenetic models that have explored these different options.

Conversely, intercropping different species (7), as well as some cultivar mixtures, often requires planting in blocks or rows to facilitate crop segregation at harvest (84, 152). Accordingly, mixtures are qualitatively similar to mosaics (hence, the term field mosaic is sometimes used), the main difference being the average distance between components (the size of a genetic unit), noting that this distance must match the scale of pathogen dispersal for effective disease management (42, 120). In fact, results obtained from studies of mixtures and mosaics are likely to be highly correlated (87). This is especially true for nonspatial models in which the scale of the host population structure could be interchangeably represented as a field or a landscape (**Table 1**).

Models have found that when resistance-adapted pathogens are initially absent, high proportions of resistant hosts in a field or broader region with low aggregation of cultivars (or weak connectivity between hosts of a given cultivar) favor good disease control (40, 48, 71, 97, 100, 104, 105, 112, 119, 123, 128, 139, 148). However, intermediate proportions of resistant cultivars are often preferable when adapted pathogens are initially present, with the precise proportion that maximizes disease control being sensitive to their initial frequency (33, 95). This results in a competition between adapted and nonadapted pathogens, which can be amplified in the presence of induced resistance (19). This U-shape effect is in line with the effect of the proportion of resistance on its durability (17, 104, 112, 136). The U shape is attributable to the fact that high proportions of resistance considerably reduce pathogen population size (resulting in a low probability of the appearance of adapted mutants), whereas small proportions minimize selection pressure and reduce the probability that an adapted pathogen successfully disperses to a resistant field. With respect to spatial aggregation, in contrast to its effect on disease control, well-mixed landscapes (i.e., low aggregation) tend to have a higher probability of resistance breakdown, as this increases the interface between resistant and susceptible components and thus the exposure of resistant hosts to potential adapted pathogens emerging from susceptible cultivars (17, 104, 112).

The effect of cultivar rotations on resistance durability is less well documented than the effect of mixtures and mosaics, especially in models. Nevertheless, one expectation is that for each rotation cycle, the number of components, their degree of heterogeneity, and their temporal sequence all affect pathogen survival (equivalent to dispersal in time) (12) in a conceptually analogous way to pathogen spatial dispersal in mixtures and mosaics. Accordingly, models predict that resistance will be more durable when used in small proportions (93) and with rapid turnover (112) within the temporal sequence. Furthermore, although most landscape-scale studies use a static landscape (i.e., crop allocation to fields is fixed), some models have demonstrated that resistance deployment can be improved by temporal variation in the proportion of resistance in the landscape (29, 34, 73). This finding emphasizes the potential of dynamic mosaics in which the number and spatial location of resistant fields vary in time (**Figure 4**).

In addition to the strategies discussed above, resistance deployment can benefit from complementary control methods (84). Any control method that reduces the effective or census size of the pathogen population (e.g., chemical application, biological control, removal of infected crop residues, and other agronomic practices) should increase resistance durability, provided that the pathogen does not adapt to this additional control method (16).

The diversity of resistance types, spatiotemporal scales of deployment, and complementary control methods results in an extensive range of possibilities whose combinations merit further investigation. Based on the few results from modeling studies, some combinations, such as rotations and mosaics (29, 34, 112) or rotations and mixtures (147), are expected to maximize both epidemiological control and resistance durability. Other combinations are yet to be explored, e.g., those involving different types of resistance (e.g., complete and partial, qualitative and quantitative) at different spatiotemporal scales via pyramids (**Figure 3**), mosaics, mixtures, and rotations (**Figure 4**). Models are powerful tools to assess and compare deployment options. Nevertheless, a

clear understanding of their structure and assumptions is essential to make appropriate interpretations and comparisons.

3. MODEL STRUCTURE AND ASSUMPTIONS

Following the long-standing tradition of compartmental models in theoretical epidemiology (56), diverse models have been developed to investigate resistance deployment. They are mainly distinguished by how the genetic and spatiotemporal structures of host and pathogen populations are modeled and how epidemiology and evolution are accounted for.

3.1. Modeling Epidemics

The basic SIR (susceptible, infected, removed) model consists of a set of coupled nonlinear ordinary differential equations (ODEs) representing the temporal dynamics of S(t), I(t), and R(t), i.e., the numbers of susceptible (i.e., healthy in this context), infected, and removed (i.e., epidemiologically inactive) individuals in the host population, respectively (76). For pathogens such as viruses that trigger systemic infection, host individuals are often entire plants. For other pathogens such as fungi that trigger localized clonal lesions, individuals may be considered as plant tissue units such as a leaf or part thereof (**Supplemental Table**). If the basic SIR model considers a population of genetically identical hosts, compartmental models can handle several host genotypes by including dedicated compartments for each plant cultivar. Such models remain purely demographic from the pathogen perspective, as a single pathogen strain characterized by a unique set of pathogenicity traits (e.g., transmission rate, infection rate; see Section 2.1) is considered (**Table 1**). ODEs naturally apply to tropical crops with continuous planting and harvest throughout the year. Nevertheless, the seasonality of temperate climates (as well as cultivar rotations; see Section 2.2) can be represented in semidiscrete models. They undergo continuous ODE dynamics and experience discrete dynamics at given time points, typically at pathogen overwintering (77; see also **Supplemental Table**). Regardless of their structures, ODEs rely on a deterministic framework in which a set of given inputs invariably yields the same outputs. However, epidemic dynamics as well as pathogen demography are impacted by uncertainty affecting individual life events (demographic stochasticity) or imposed by the environment (environmental stochasticity) (68). Demographic stochasticity is typically important during the initial phase of an epidemic. Using stochastic SIR models is then a way to account for the probability of epidemic extinction when the number of infected hosts is small.

Deterministic: a framework in which a set of given inputs invariably yields the same outputs. Deterministic models inform on mean output tendencies

Demographic stochasticity: the intrinsic uncertainty associated with the life events of each individual in a population (reproduction, dispersal, mutation, death)

Environmental stochasticity: random perturbations imposed on a population by its environment

Stochastic: a framework in which random events are accounted for. Stochastic models inform on mean tendencies and variability of the outputs

Supplemental Material >

3.2. Accounting for Pathogen Evolution

Addressing questions about resistance durability requires modeling of pathogen evolution. Historically, theoretical studies of pathogen evolution mainly relied on the framework of adaptive dynamics (26). Assuming that a single pathogen strain is present at its endemic steady state, the method determines under what conditions a second mutant strain, introduced at low frequency, will invade the population. Adaptive dynamics supposes that epidemiological and evolutionary processes do not interfere with each other or act at different timescales. It essentially focuses on long-term predictions for endemic diseases and has been used to study pathogen evolution in response to resistance deployment (**Table 1**). For example, the effect of resistance genes targeting different pathogenicity traits on the evolution of virus multiplication rates has been investigated (135, 138). Through computation of stable evolutionary equilibria, it is possible to resolve evolutionary trade-offs like those between virulence (in this context, virulence refers to host damage caused by pathogen infection) and transmission (37, 132), survival and transmission (132), and

Phenotype: refers here to the occurrence (and amount) of disease and is mostly determined by the plant–pathogen–environment interaction

generalism and specialization (103). However, in agro-ecosystems, interest is generally focused on short-term epidemics, which impact both pathogen population size and composition. Day & Proulx (25) and Day & Gandon (24) introduced a framework to simultaneously model the dynamics of epidemics and evolution for any pathogenicity trait. This approach, termed evolutionary epidemiology, is inspired by quantitative genetics and is well suited to model the evolution of quantitative traits. To date, it has been applied to study the erosion of quantitative resistance targeting different pathogenicity traits (28, 71).

As for plant cultivars, multiple pathogen strains are considered in multistrain compartmental models. By doing so, models explicitly switch from demographic to demogenetic representations of the pathogen population (**Table 1**). Many models solely consider the effect of selection and assume that all pathogen genotypes are initially present, with adapted genotypes initially present at low frequencies. These assumptions ignore the time required for the appearance and establishment of adaptive mutations in pathogen populations (136). Although this may be an acceptable assumption for pathogens with large population sizes, it can considerably overestimate the speed of adaptation of pathogens with smaller effective population sizes, especially for strategies involving gene pyramids (Section 2.2).

A further step is to explicitly model the effects of mutation or migration on the establishment of resistance-adapted pathogens that are initially absent. Taking into account the classical genetic mutation rate (number of genetic mutations/generation/nucleotide) is difficult, as it requires correct identification of the genetic architecture (number, type, location, and phenotypic effects of genetic mutations) underlying phenotypic trait variation. Presently, this knowledge is considered only for virus adaptation to major resistance genes using the concept of mutation-selection balance (29, 33, 34). For most pathogens, the links between genotype and phenotype are ignored. Most models instead consider a phenotypic mutation rate representing a displacement into the pathogen phenotypic space (e.g., 8, 71, 74, 97, 112). Empirically largely unknown, this rate theoretically integrates the phenotypic effects of genetic mutations into the multidimensional space of pathogenicity traits as well as potential correlations within and between host genotypes. Immigration of pathogen strains from external sources has also been considered as an alternative source of new genetic variants (70, 136). Although the rate of appearance of new genetic variants via mutation depends on the size of the pathogen population, with immigration this rate is generally constant and independent of the epidemiological status of the system.

Besides mutation, genetic recombination (occurring during virus replication, bacterial conjugation, transformation, and transduction, or the fungal sexual cycle) also generates new variants. For example, recombination can accelerate pathogen adaptation via the reassortment of adaptive mutations controlled by independent loci. This enables the emergence of multiadapted pathogens and thus favors the breakdown of resistance pyramids. Thus, ignoring its role can result in severe bias (2). Only a few models (73, 118, 146) included recombination to study the emergence of multiadapted genotypes of a pathogen having one sexual phase at the beginning of each cropping season (**Table 1**).

Demographic stochasticity shapes the effect of these evolutionary processes and can be dealt with in stochastic models. This is of particular importance when (*a*) events are inherently rare (e.g., due to low mutation rates) and (*b*) pathogen population size is low (e.g., just after a mutant strain appears). Therefore, depending on subtle interactions between effective population size (Ne), selection coefficient (s), and mutation rate (μ), the evolutionary dynamics of a population can be mainly deterministic or stochastic (116). For example, if $Ne \times \mu \ll 1$, the waiting time of mutations conferring adaptation could be substantial and is thus subject to large random fluctuations that can hardly be ignored if adapted pathogens are initially absent. If $Ne \times s \ll 1$, genetic drift generates random fluctuations in pathogen genetic diversity, with the potential to purge

variants regardless of their selective value. Most models reviewed here ignore the effect of genetic drift (**Table 1**). Dealing with such evolutionary force requires specific consideration of *Ne* and its variation, especially bottlenecks from which only some individuals will be randomly sampled and survive to reproduce (18). Lo Iacono et al. (70) used the size of the infected host population as an indirect proxy of such variation, whereas other authors have explicitly modeled bottlenecks occurring at crop harvest and during the off-season (74, 104, 114, 146, 147), intraplant movement in viral infection (115), and viral transmission by insect vectors (32).

3.3. Representing the Spatial Structure of Host Populations

In nonspatial models (**Table 1**), each infected individual is equally likely to establish an infectious contact with any other healthy individual, regardless of its geographic location. Accounting for space is critical for accurate assessment of deployment strategies relying on the spatial segregation of different cultivars (e.g., mixtures and rotations; see Section 2.2), especially when the pathogen disperses primarily at short distances compared to the field size.

New compartments leading to more realistic contact structures between individuals can be introduced in spatially implicit models. A metapopulation of well-mixed host patches in which pathogen spread rates differ within and between patches provides a typical example (43). Addressing this question more deeply requires spatially explicit approaches in which pathogen dispersal is represented using reaction–diffusion equations (47) or via dedicated kernels (90) within integro-differential equations. Notably, dispersal kernels allow the explicit representation of long-distance infection events (80). In any case, variables of interest depend on a vector of spatial coordinates x in addition to time t [e.g., $S(t,x)$, $I(t,x)$], providing a straightforward way to investigate the effect of habitat geometry (e.g., spatial aggregation; see Section 2.2). Stochastic models are often used to randomly segregate pathogen propagules across different landscape elements. They are also used to explicitly consider environmental stochasticity associated with random fluctuations of landscape structure (40, 100, 102, 104, 105, 112, 114, 143) as well as cultivar allocations (74, 147) or pesticide treatments (70, 97) year after year in different parts of the landscape.

4. MODEL OUTPUTS: CRITERIA TO ASSESS DEPLOYMENT STRATEGIES

As described for fungicide application (137), the assessment of resistance deployment strategies depends strongly on evaluation criteria. Importantly, the objectives of different stakeholders (e.g., growers, breeders) are not always compatible. Indeed, minimizing epidemiological impacts, maximizing resistance durability, and minimizing costs of disease management are all sensible targets that may lead to different optimal strategies (104, 112, 136). This section considers potential key variables used in models (**Table 1**, **Supplemental Table**) for assessing resistance deployment strategies from epidemiological, evolutionary, and socioeconomic perspectives.

Supplemental Material >

4.1. Epidemiological Outputs

Epidemiological outputs characterize the ability of deployment strategies to reduce disease impact in a given region over a given time period (15). In the field, disease impact is classically evaluated using the proportion of infected hosts (disease prevalence) (76) or a quantitative assessment of symptoms on infected hosts (disease severity) (76). In models, disease impact is usually measured by the proportion of infected individuals (i.e., infection units; see Section 3.1), equating to prevalence when an individual is a single plant and severity when an individual is an infection site. Thus, prevalence and severity can be distinguished only when plant architecture is explicitly modeled in

terms of number of infection sites per plant (e.g., 40, 146–148). Because prevalence and severity change over time, the challenge is to summarize them using representative point estimates to compare different deployment options. One approach focuses on epidemiological status at the end of a given period (119, 123, 128) or at stable evolutionary equilibrium (81, 95, 135, 138). Another approach relies on the integration of prevalence or severity over time into an area under disease progress curve (AUDPC) (19, 29, 33, 34, 112, 114).

Alternatively, the number of infected hosts can be deduced from the number of healthy hosts (95, 101, 135, 138). Similar to the computation of AUDPC, the dynamic of healthy hosts may be integrated over time into a variable representing the cumulative amount of photosynthetic tissue, assumed to be proportional to crop growth and yield (142). Modeling studies variously refer to this as healthy area duration (HAD) (104), healthy surface (71, 100, 105), green leaf area (114), or green area canopy duration (108). Depending on the study objectives, AUDPCs and HAD-like variables may be computed for the whole host population or individually for each cultivar (e.g., 108) and for the whole simulation run or specific periods (e.g., before and after resistance breakdown) (104, 112). It may be expressed in absolute value or relative to a reference context, e.g., to assess, compared to a fully susceptible landscape, the additional number of healthy hosts resulting from resistance deployment (70, 71, 136, 143) or the intensity of epidemics (29, 33, 34).

Finally, the dynamic of infected hosts in a region can be summarized by other metrics such as the speed of the epidemic expansion front (122, 134, 139), the total distance traveled (105), or the final area covered by the epidemic (123, 128).

4.2. Evolutionary Outputs

Evolutionary outputs mainly assess the ability of deployment strategies to prevent or slow down pathogen adaptation and are often summarized by resistance durability. In models in which pathogen genotypes are classified as nonadapted or adapted (see Section 2.1), resistance durability has been calculated using criteria such as the point in time when resistant hosts become as severely affected as susceptible hosts (108), when adapted pathogens first appear (32), or when the prevalence (57, 112, 114) or frequency in the pathogen population (16, 74, 75, 97, 108, 136) of these adapted variants exceeds an arbitrary threshold. The value of this threshold determines which of the three characteristic phases of resistance breakdown is targeted. These phases, analogous to an ecological invasion process of the cropping landscape by adapted pathogens, consist of (*a*) introduction via immigration or appearance (via mutation, recombination, horizontal gene transfer, or sexual reproduction); (*b*) establishment, i.e., when extinction becomes unlikely despite potential competition with nonadapted pathogens; and (*c*) spread (or propagation) within the formerly resistant host population, potentially causing severe yield losses. Thus, model results can be significantly impacted by the chosen threshold above which resistance is considered to have broken down (75) but also by model assumptions (e.g., whether or not adapted pathogens are initially present) (74; see also Section 3.2). When several resistance genes are deployed, and in particular for pyramid cultivars, resistance durability can also be assessed based on the dynamics of the multiadapted pathogen (22, 45, 66, 67, 112).

Measuring pathogen adaptation to resistance when it is continuously distributed is still a challenge. The few approaches that have been proposed rely on the speed of pathogen evolution (103) or resistance erosion (114) as well as on the time point when the proportion of healthy hosts drops below an arbitrary threshold (16, 102, 104).

4.3. Socioeconomic Outputs

Despite the importance of identifying deployment strategies that are not only efficient and durable but also cost-effective and feasible for growers, socioeconomic factors are rarely accounted for in

resistance deployment models. Although planting density, growth rate, and contribution to crop yield are often assumed to be uniform, this is rarely the case in practice. For potato late blight in the Netherlands (97) and blackleg of winter oilseed rape (72, 73), crop yield was computed as a function of crop cultivar, disease severity, and climatic variables. Accounting for yield enables the resolution of trade-offs between the reduction of damage resulting from the use of resistant cultivars and associated costs, e.g., reduced growth (97) or smaller yield (141) of resistant varieties. However, yield data are generally not available and can be challenging to estimate (or predict), particularly the yield of a cultivar carrying a broken-down resistance.

Organizational and social aspects (e.g., feasibility criteria accounting for farming practices) of resistance deployment have rarely been considered. Yet these factors drive farmers' decisions and have a considerable impact on the adoption of a deployment strategy, as illustrated for potato late blight (96). Milne et al. (82) predict that adoption by farmers of a resistant maize cultivar (which offers better protection against European corn borers but is potentially more expensive to grow) producing a *Bacillus thuringiensis* toxin depends on their communication network and sensitivity to risk. In this context, the use of visual interfaces and model-based scenarios can help communicate results to the farmer community and stimulate stakeholder discussions in workshops on plant resistance management (e.g., 98).

5. GENERAL CONCLUSIONS

Models of resistance deployment can be used to deliver insights into the epidemiological, evolutionary, and economic performance of deployment strategies (e.g., gene pyramiding, crop rotations, cultivar mixtures, landscape mosaics) at spatiotemporal scales beyond the scope of empirical experimentation. However, it is important to note that most of the models reviewed here are not designed to precisely predict resistance durability or the level of epidemiological control in real-world systems. Rather, their purpose is to identify key parameters, provide mechanistic insight into the consequences of different deployment strategies, and allow decision-makers to understand their relative merits (44).

Given this focus, is it possible to use the models to collectively identify a single best strategy for resistance deployment? The diversity of assumptions underlying the different modeling approaches, of scenarios considered, and of evaluation criteria used makes it almost impossible to rank strategies. Based on the very few studies that allow such a comparison, all other things being equal, pyramiding seems the most epidemiologically efficient and evolutionarily durable strategy to deploy complete resistance in the absence of preadapted pathogen genotypes (74, 112) (**Figure 5**). However, pyramiding can suffer important limitations, as (*a*) it is challenging to effectively identify the existence of preadapted genotypes that could be maintained at very low frequencies, (*b*) other cultivars or wild relatives can represent evolutionary steps facilitating the adaptation of the pathogen population, and (*c*) several precious genetic resources are lost at the same time when a pyramid is overcome. Mosaics and rotations are alternative solutions to cope with these limitations and are predicted to be more efficient (29, 112) and durable (74) when resistance-adapted genotypes are present prior to resistance deployment. In addition, by increasing the overall diversity of the crop, these strategies confer a portfolio effect, i.e., increased resilience to other biotic and abiotic constraints. These conclusions should not be overgeneralized to any crop production situation or pathosystem, as they have mostly been obtained in specific contexts. This brings us face-to-face with the modeler's dilemma: It is not possible to maximize generality, realism, and precision in the same model (69).

To conclude, we argue that there is no universal strategy. The optimal deployment approach depends on the desired objective, the epidemiological and evolutionary context, and the

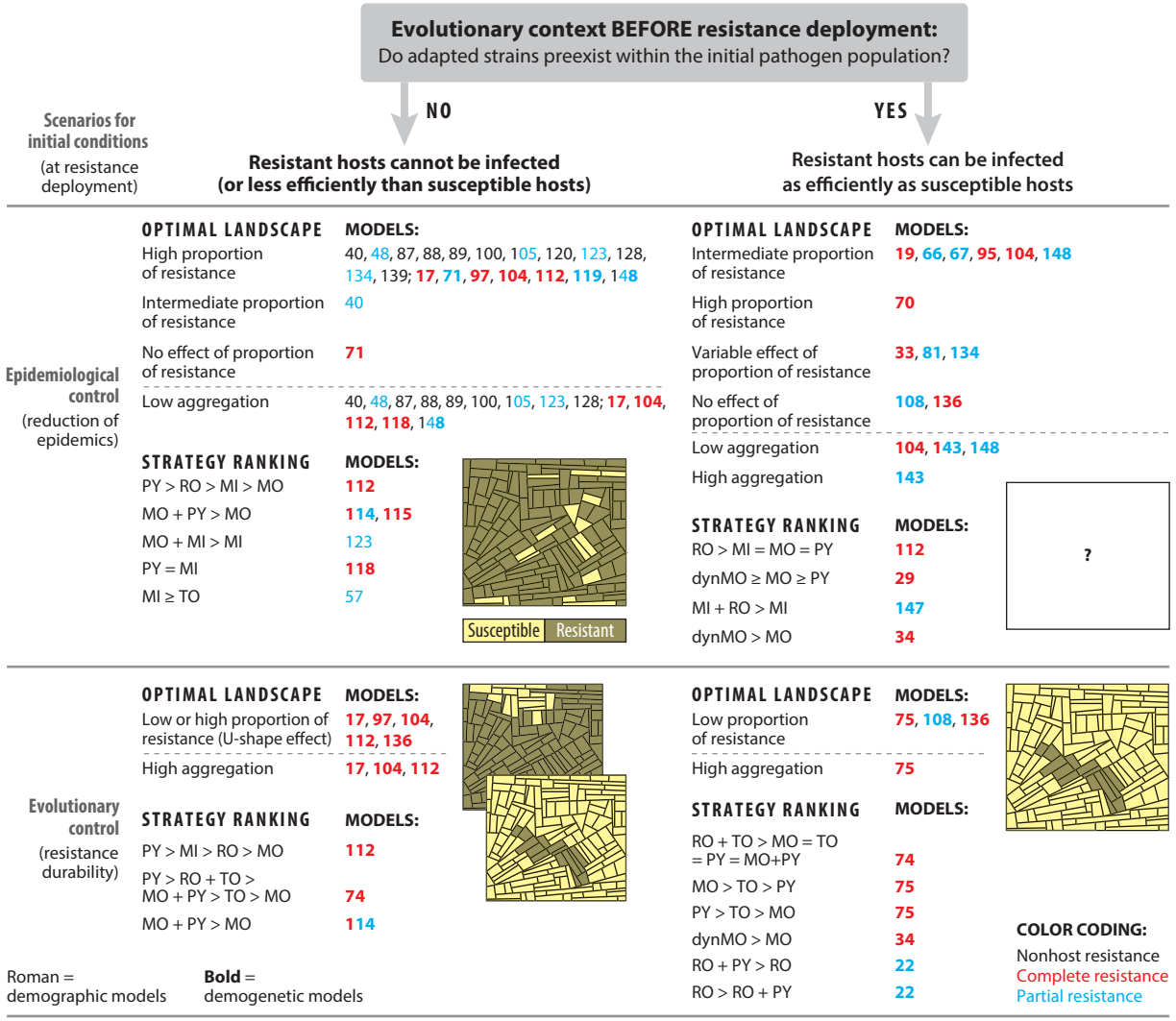

Figure 5

What models tell us about optimal landscape organizations and deployment strategies to manage plant resistance with respect to epidemiological and evolutionary disease control. Conclusions considerably differ depending on the existence or absence of resistance-adapted genotypes in the pathogen population prior to resistance deployment. Illustrations are examples of optimal landscape organizations. The plus sign stands for combination. Numbers refer to demographic and demogenetic models representing different pathosystems (numbers with multiple fonts or colors belong to multiple categories). Abbreviations: dynMO, dynamic mosaic; MI, cultivar mixture; MO, landscape mosaic; PY, gene pyramiding; RO, cultivar rotation; TO, turnover of cultivars.

pathosystem considered, among other elements. This is in line with what Mundt (86, p. 792) wrote in a recent review: "There are multiple approaches to increasing durability of resistance. . .none of which should be considered inherently superior to the other, and all of which likely benefit from being combined." We hope this review paves the way for future modeling investigations toward a more efficient, sustainable, cost-effective, and feasible deployment of plant resistance.

SUMMARY POINTS

1. During the past twenty years, there has been a paradigm shift from the idea of durable resistance to one of durable management of resistance. This implies that durability is no longer considered an intrinsic property of a resistance gene but rather the result of a clever combination of effects operating at different scales. Accordingly, plant resistance against pathogens must be carefully designed (by breeders) and organized in space and time (by farmers) to be both efficient and durable in spite of pathogen evolutionary potential.
2. The multiplicity of deployment strategies, resulting from the huge diversity of choices made from gene to landscape scales (**Figure 1**), impedes their comparison with empirical experimentation. In this context, models provide powerful tools to explore possible deployment options (**Figures 2–4**) and can help identify promising strategies (**Figure 5**) that, in turn, may be amenable to experimental verification.
3. The profusion of modeling approaches offers a wide range of possibilities to model epidemics while accounting for pathogen evolution and spatiotemporal organization of host plants (**Table 1**, **Supplemental Table**). Their epidemiological, evolutionary, and socioeconomic outputs allow the evaluation of deployment options with respect to multiple criteria.
4. There is no silver bullet deployment strategy: Optimal deployment approaches vary depending on the desired objective, the epidemiological and evolutionary context, and the pathosystem considered. Any deployment option has its own advantages and drawbacks; thus, there are likely benefits from hybrid strategies.

Supplemental Material >

FUTURE CHALLENGES

1. Future models should encompass the diversity of plant immunity mechanisms (including tolerance, which reduces pathogen-induced host damage without affecting pathogen development) and consider the full range of pathogen adaptation mechanisms.
2. Recognizing that predictions about real-world systems often require relatively complex models, we must take advantage of computers' current capacity to model complex resistance deployment scenarios that combine different deployment options and complementary control measures at multiple spatiotemporal scales. Such scenarios should also include adaptive strategies that are continuously updated based on real-time data.
3. A unified modeling framework will help compare deployment strategies, all other things being equal, and understand the impact of ecological, epidemiological, evolutionary, and genetic factors for a diversity of pathosystems. This is one of the objectives of the model *landsepi*, freely accessible through an R package (113).
4. More efforts should be made to collect and share epidemiological data sets to help calibrate and validate models with empirical data.
5. Models must account for socioeconomic and organizational constraints of real farming systems to identify solutions that are both feasible and likely to be adopted by breeders and growers.

6. Results and recommendations need to be communicated to relevant stakeholders in a way that is accessible and likely to be acted upon. The use of dedicated pedagogical interfaces facilitates such interactions (98; see also the prototype for a pedagogical interface for *landsepi*: **https://shiny.biosp.inrae.fr/app_direct/landsepi/**).

DISCLOSURE STATEMENT

The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

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