Evolution of pathogen traits in response to quantitative host resistance in heterogeneous environments

R. Djidjou-Demasse[a], S. Lion[b], A. Ducrot[c], J.-B. Burie[d,e], Q. Richard[a], F. Fabre[f]

[a] *Univ. Montpellier, MIVEGEC, IRD, CNRS, Montpellier F-34394, France*

[b] *CEFE, CNRS, Univ. Montpellier, Univ. Montpellier 3 Paul-Valéry, EPHE, IRD, Montpellier F-34293, France*

[c] *Normandie Univ, UNIHAVRE, LMAH, FR-CNRS-3335, ISCN, 76600 Le Havre, France*

[d] *Univ. Bordeaux, IMB, UMR 5251, F-33400 Talence, France*

[e] *CNRS, IMB, UMR 5251, F-33400 Talence, France.*

[f] *UMR 1065 SAVE, INRA, Bordeaux Sciences Agro, Villenave d'Ornon F-33882, France*

March 26, 2020

Abstract

Despite considerable studies on the adaptation of plant pathogens to qualitative resistance, few theoretical studies have investigated whether and how quantitative resistance can select for increased pathogen aggressiveness. In this paper, we formulate an integro-differential model with nonlocal effects of mutations to describe the evolutionary epidemiology of fungal plant pathogens in heterogeneous agricultural environments. Parasites reproduce clonally and each strain is characterized by several pathogenicity traits corresponding to the basic infection steps (infection efficiency, latent period, sporulation capacity depending on the age of infection). We first derive a general expression of the basic reproduction number $\mathcal{R}_0$ for fungal pathogens in heterogeneous host environments, typically several cultivars cultivated in the same field (cultivar mixtures) or in different fields landscape (mosaics). Next, by characterizing the evolutionary attractors of the coupled epidemiological evolutionary dynamics, we investigate how the choice of quantitative resistances altering different pathogenicity traits impact the evolutionary dynamics of the pathogen population both at equilibrium and during transient epidemiological dynamics. We show that the model admits an optimization principle relying on an $\mathcal{R}_0$ maximization approach for traits involved in the infection cycle after spore germination. We also highlight that within-host correlation between such traits (typically between the latent period and total number of spores produced during the infectious period) impact resistance durability and, more generally, how one may take advantage of evolutionary

dynamics to increase the durability of quantitative resistance. Our analyses can guide experimentations by providing testable hypotheses and help plant breeders to design breeding programs.

Key words. Basic reproduction number; Evolutionary epidemiology; Fungal pathogen; Invasion fitness; Quantitative resistance; Lifetime Reproduction success; Spore producing pathogens; Resistance durability.

1 Introduction

Resistance to parasites, i.e. the capacity of a host to decrease its parasite development (Raberg et *al.*, 2009; Restif & Koella , 2004), is a widespread defense mechanism in plants. Qualitative resistance usually confers disease immunity in such a way that parasites exhibit a discrete distribution of their disease phenotype ("cause disease" versus "do not cause disease") (McDonald & Linde, 2002). Quantitative resistance leads to a reduction in disease severity (Poland et *al.*, 2009; St. Clair, 2010) in such a way that parasites exhibit a continuous distribution of their quantitative pathogenicity (McDonald & Linde, 2002; St. Clair, 2010; Lannou, 2012). Quantitative pathogenicity, also termed aggressiveness, can be estimated in laboratory experiments through the measure of a small number of pathogenicity traits (Pariaud et *al.*, 2009; Lannou, 2012) expressed during the basic steps of the host-pathogen interaction. Quantitative resistance genes alter their expression, sometimes through pleiotropic effects (*i.e.* effects on more than one trait (Parlevliet, 1986; Richardson et *al.*, 2006)). Quantitative resistance has gained interest in plant breeding for pathogen control in low-input cropping systems, in particular due to their supposed higher durability compared to qualitative resistance (Mundt, 2014; Niks et *al.*, 2015). However plant pathogens also adapt to quantitative resistance (see Pilet-Nayel et *al.* (2017) for a review). The resulting gradual "erosion" of resistance efficiency (McDonald & Linde, 2002) corresponds, from the pathogen side, to a gradual increase in quantitative pathogenicity.

Few theoretical studies have investigated how the deployement of quantitative resistance in agrosystems impact pathogen aggressiveness (Iacono et *al.*, 2012; Bourget *al.*, 2015; Rimbaud et *al.*, 2018). These studies must address the fundamental short- and long-term objectives of sustainable management of plant diseases (Zhan et *al.*, 2015; Rimbaud et *al.*, 2018): the short-term goal focuses on the reduction of disease incidence, whereas the longer-term objective is to reduce the rate of evolution of new pathotypes. The evolutionary epidemiology analysis are well-suited for this purpose (see *e.g.*, Day & Proulx (2004); Day & Gandon (2006)). Essentially inspired by quantitative genetics, it accounts for the interplay between epidemiological and evolutionary dynamics on the same time scale. As such it can be used to monitor the simultaneous dynamics of epidemics and evolution of any set of pathogen life-history trait of interest. It can also handle heterogeneous host populations resulting, for example, from differences in their genetic composition (Gandon & Day, 2007). This

is typically the case of field mixtures, where several cultivars are cultivated in the same field, and of landscapes mosaics, with cultivars cultivated in different fields.

In this article, we follow this approach and study the evolutionary epidemiology of spore-producing pathogens in heterogeneous agricultural environments. Plant fungal pathogens (*sensu lato, i.e.* including Oomycetes) are typical spore-producing pathogens responsible for nearly one third of emerging plant diseases (Anderson et *al.*, 2004). Here we use an integro-differential model where the pathogen traits are represented as a function of a N-dimensional phenotype. This model extends previous results of Djidjou-Demasse et *al.* (2017) to heterogeneous plant populations mixing cultivars with different quantitative resistances. First, we investigate how the choice of quantitative resistances altering different pathogenicity traits impact the pathogen population structure at equilibrium. This question is addressed by characterizing the evolutionary attractors of the coupled epidemiological evolutionary dynamics. A particular emphasis will be put here on the differences between the cornerstone concepts of $\mathcal{R}_0$ in epidemiology (Diekmann et *al.*, 1990; van den Driessche & Watmough, 2008) and invasion fitness in evolution. Secondly we investigate how this choice also impacts the transient behavior of the coupled epidemiological evolutionary dynamics.

2 A structured model of epidemiological and evolutionary dynamics

2.1 Host and pathogen populations

We consider an heterogeneous host population with $N_c \geq 2$ host classes infected by a polymorphic spore-producing pathogen population. Here, host heterogeneity may refer to different host classes, typically plant cultivars, but more generally it can handle different host developmental stages, sexes, or habitats. The host population is further subdivided into two compartments: susceptible or healthy host tissue (S) and infectious tissue (I). In keeping with the biology of fungal pathogens, we do not track individual plants, but rather leaf area densities (leaf surface area per m^2). The leaf surface is viewed as a set of individual patches corresponding to a restricted host surface area that can be colonized by a single pathogen individual. Thus only indirect competition between pathogen strains for a shared resource is considered. Spores produced by all infectious tissues are assumed to mix uniformly in the air and then land on any host class according to the law of mass action, that is the probability of contact between a spore and host k is proportional to the total susceptible leaf surface area of this host. The density of airborne spores is denoted by A.

The parasite is assumed to reproduce clonally. Its population is made of a set of genetic variant termed thereafter strains. At each infection cycle (*i.e.* generation), mutations randomly displace strains into this phenotype space. Each

Category	Description	Unit
Notations		
$N_c \geq 2$	Total number of host classes	
$k \in 1, 2, \cdots, N_c$	Index on host class	
N	Dimension of the phenotype space	
$x \in \mathbb{R}^N$	Label on the pathogen strain.	
a	Time since infection	
States variables		
$S_k(t)$	Density of healthy tissue of host k at time t.	
$i_k(t, a, x)$	Density of infected tissue of host k at time t infected since time a by strain x	
$A(t, x)$	Density of airborne pathogen spores of strain x at time t.	
Parameters		
Λ	Birth rate of healthy host tissue	$\text{HTD} \cdot \text{Tu}^{-1}$
θ	Death rate of host tissue	Tu^{-1}
δ	Rate at which spore becomes unviable	Tu^{-1}
$d_k(a, x)$	Disease induced mortality of host k infected since a by strain x	Tu^{-1}
$\beta_k(x)$	Infection efficiency of pathogen strain x on host k	$\text{SD}^{-1} \cdot \text{Tu}^{-1}$
$p_k(x)$	Total number of spores produced by pathogen strain x on host k	$\text{SD} \cdot \text{HTD}^{-1}$
$\tau_k(x)$	Latent period of pathogen strain x on host k	Tu
$\lambda_k(x)$	Sporulation curve shape of strain x on host k : rate of sporulation events	Tu^{-1}
$n_k(x)$	Sporulation curve shape of strain x on host k : number of sporulation events	unitless
φ_k	Proportion of host k at the disease-free equilibrium	unitless
ε	Distance beyond which non-local mutations become "negligible"	unitless
$m_\varepsilon(x - y)$	Mutation probability from pathogen strain x to y	unitless

Tu= time unit; SD= spores density; HTD=host tissue density

Table 1: Main notations, state variables and parameters of the model.

strain with phenotype x is characterised, on each host class, by pathogenicity traits that describe the basic steps of the disease infection cycle : (i) infection efficiency $\beta_k(x)$, *i.e.* probability that a spore deposited on a receptive host surface produces a lesion, (ii) latent period $\tau_k(x)$ and (iii) shape of the sporulation curve. In line with the biology of plant fungi (van den Bosch et *al.*, 1988; Sache et *al.*, 1997; Kolnaar & Bosch, 2011; Segarra et *al.*, 2001), a gamma sporulation curve defined by three parameters is assumed : (i) total number of spores produced $p_k(x)$ during the infectious period, (ii) number of repeated sporulation events occurring on an individual foliar lesion $n_k(x)$ and (iii) rate of sporulation events $\lambda_k(x)$. Parameters n_k and λ_k defined the time shape of the sporulation curve (Figure 1A) by distributing the total amount of spores produced by a lesion (p_k) over its average infectious period (n_k/λ_k). Previous hypothesis lead to the following sporulation function :

$$r_k(a,x) = \begin{cases} p_k(x)\frac{\lambda_k^{n_k(x)}(a-\tau_k(x))^{n_k(x)-1}\exp[-\lambda_k(x)(a-\tau_k(x))]}{\Gamma[n_k(x)]} & \text{if } a > \tau_k(x), \\ 0 & \text{otherwise,} \end{cases} \tag{2.1}$$

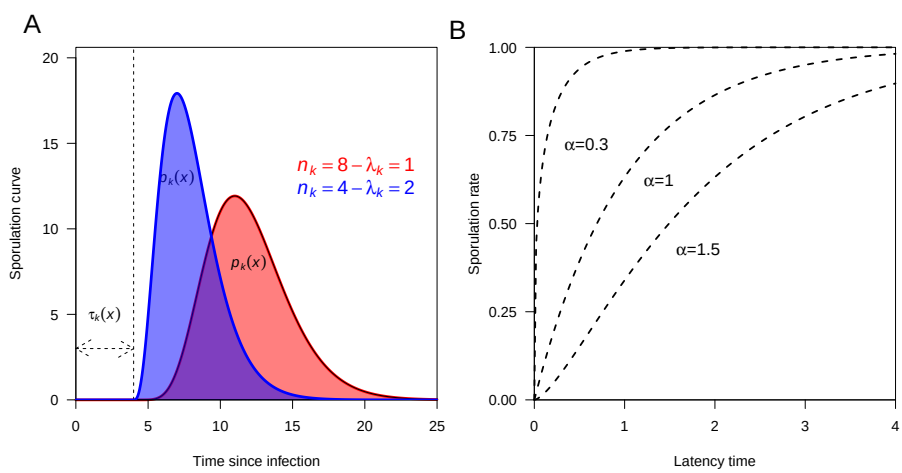

Figure 1: **A** Two gamma sporulation curves $r_k(a,x)$ with latent period $\tau_k = 4$ and total spore production $p_k = 80$. **B** Spores production capacity ($p_k/p_{k,\max}$) as a function of latency time (τ_k). The trade-off between the total number of spores produced (p_k) and the probability for an infected tissue to survive the latent period (s_k) is described by a power function. Its concavity is parametrized by α.

2.2 The model

We introduce a set of integro-differential equations modeling the epidemiological and the evolutionary dynamics of the host and pathogen populations just

described. The general formulation used encompasses several simpler models of the litterature (Appendix B). A key feature of the model is to explicitly track both the age of infection and the pathogen strain. This leads to a non-local age-structured system of equations posed for time $t > 0$, age since infection $a > 0$ and phenotype $x \in \mathbb{R}^N$,

$$\begin{cases} \partial_t S_k(t) = \varphi_k \Lambda - \theta S_k(t) - S_k(t) \displaystyle\int_{\mathbb{R}^N} \beta_k(y) A(t,y) \mathrm{d}y, \\ (\partial_t + \partial_a)\, i_k(t,a,x) = -\left(\theta + d_k(a,x)\right) i_k(t,a,x), \\ i_k(t,0,x) = \beta_k(x) S_k(t) A(t,x), \\ \partial_t A(t,x) = -\delta A(t,x) + \displaystyle\sum_{k=1}^{N_c} \int_{\mathbb{R}^N} \int_0^\infty m_\varepsilon(x-y) r_k(a,y) i_k(t,a,y) \mathrm{d}a \mathrm{d}y. \end{cases} \tag{2.2}$$

Table 1 lists the state variables and parameters of the model. $S_k(t)$ is the density of healthy tissue in host k at time t, $i_k(t,a,x)$ the density of tissue in host k that was infected at time $t-a$ by a pathogen with phenotype x, and $A(t,x)$ denotes the density of spores with phenotype x at time t. Without disease, susceptible hosts are produced at rate $\Lambda > 0$ and die at rate $\theta > 0$, regardless of their class. φ_k is the proportion of the host k at the disease-free equilibrium in the environment. With disease, susceptible hosts can become infected by airborne spores. The total force of infection on a host k is $h_k(t) = \int \beta_k(y) A(t,y) \mathrm{d}y$. Infected hosts die at rate $\theta + d_k(a,x)$ where $d_k(a,x)$ is the disease-induced mortality of infected tissue. Airborne spores produced by infected hosts become unviable at rate $\delta > 0$. Hosts infected by strain y produce airborne spores with phenotype x at a rate $m_\varepsilon(x-y) r_k(a,y)$, where $m_\varepsilon(x-y)$ is the probability of mutation from phenotype y to phenotype x and $r_k(a,y)$ is the sporulation function, which depends on host class, age of infection and parasite phenotype.

The kernel m_ε represents the effects of mutations that randomly displace phenotypes at each generation. It depends on a small parameter $\varepsilon > 0$ representing the mutation variance in the phenotypic space. To fix ideas, a multivariate Gaussian distribution $m = N(0,\Sigma)$ leads to $m_\varepsilon(x-y) = \frac{1}{\varepsilon^N} m\left(\frac{x-y}{\varepsilon}\right)$. The covariance terms of Σ can allow to take into account correlations between pathogen life-history traits (Martin & Lenormand, 2006; Gandon , 2004). The mutation kernel m is not restricted to Gaussian distributions, provided it satisfies some properties such as positivity and symmetry (Appendix A).

Further, a correlation between the time-lag to maturity and fecundity has been sometimes observed for plant fungi (Pariaud et *al.*, 2013). Here, the time-lag to maturity is measured by the probability for an infected host to survive the latent period $s_k(x) = e^{-\int_0^{\tau_k(x)} [\theta + d_k(\sigma,x)] \mathrm{d}\sigma}$, and fecundity by the total number of spores produced $p_k(x)$. This relationship describes a phenotypic trade-off because short latent period and high sporulation capacity represent fitness advantages. The model can handle such a trade-off using a power function $u(z) = \left(1 - z^{\frac{1}{\alpha}}\right)^\alpha$ defined for $z \in (0,1)$ and parametrized by $\alpha > 0$ which determines its global concavity (Egas et *al.*, 2004; Débarre & Gandon, 2010). The

within-host trade-off then writes (Figure 1B)

$$s_k(x) = u\left(\frac{p_k(x)}{p_{k,\max}}\right), \tag{2.3}$$

where $p_{k,\max}$ is the maximum of p_k.

3 Fitness function and evolutionary attractors

3.1 The fitness function

The basic reproduction number, usually denoted $\mathcal{R}_0$, is defined as the total number of infections arising from one newly infected individual introduced into a healthy (disease-free) host population (Diekmann et *al.*, 1990; Anderson, 1991). The disease-free equilibrium density of susceptible hosts in class k is $S_k^0 = \varphi_k \Lambda/\theta$. In an environment with N_c host classes, a pathogen with phenotype x will spread if $\mathcal{R}_0(x) > 1$, with

$$\mathcal{R}_0(x) = \frac{\Lambda}{\theta}\sum_{k=1}^{N_c}\varphi_k \Psi_k(x), \tag{3.4}$$

where the quantity $\mathcal{R}_0^k(x) = \frac{\Lambda}{\theta}\varphi_k\Psi_k(x)$, is the basic reproduction number of a pathogen with phenotype x in the host k, and the fitness function Ψ_k is given by

$$\Psi_k(x) = \frac{1}{\delta}\beta_k(x)\int_0^\infty r_k(a,x)\exp\left(-\theta a - \int_0^a d_k(\sigma,x)\mathrm{d}\sigma\right)\mathrm{d}a, \tag{3.5}$$

for all $k \in \{1,\ldots,N_c\}$. The quantity $\Psi_k(x)$ is the absolute fitness, or reproductive value, of a pathogen with phenotype x landing on host k (see Appendix C for details on calculations).

Assuming that d_k does not depend on the age of infection and a gamma sporulation function, we obtain the simpler expression

$$\Psi_k(x) = \frac{1}{\delta} \times \beta_k(x) \times e^{-(\theta+d_k(x))\tau_k(x)} \times p_k(x) \times \left(\frac{\lambda_k}{\lambda_k+\theta+d_k(x)}\right)^{n_k}. \tag{3.6}$$

The above equation means that, (i) during its life time $1/\delta$, (ii) a propagule infects a leaf area at rate β_k, (iii) this infected area survives the latent period with probability $e^{-(\theta+d_k)\tau_k}$, (iv) achieves n_k sporulation events with probability $\lambda_k/(\lambda_k+\theta+d_k)$ for each event and (v) produces a total number of spores p_k during the infection period. Equation (3.6) can also handle within-host trade-offs where terms (iii) and (v) are linked by (2.3).

Finally, if furthermore r_k is a constant (*i.e.* $r_k(a,x) = p_k(x)$ and $d_k(a,x) = d_k(x)$ for all a), we recover the classical expression of $\mathcal{R}_0$ for SIR models, with $\Psi_k(x) = \frac{\beta_k(x)p_k(x)}{\delta(\theta+d_k(x))}$ (Day, 2002).

3.2 Evolutionary Attractors

$\mathcal{R}_0$ can be used to study the spread of a pathogen strain x in an *uninfected* host population. To study the spread of a new mutant strain in a host population *already infected* by a resident strain x, and to characterize pathogen's evolutionary attractors among a large number of pathogen strains, we can use the adaptive dynamics methodology and calculate invasion fitness (Dieckmann, 2002; Diekmann et *al.*, 2005; Geritz et *al.*, 1997; Metz et *al.*, 1996).

Invasion fitness Here, we work in generation time and use the lifetime reproductive success of a rare mutant as a fitness proxy. Once the pathogen with phenotype x spreads, let us assume that the population reaches a monomorphic endemic equilibrium denoted by $E^x = (S_k^x, i_k^x(\cdot), A^x)_{k=1,\cdots N_c}$. Note that E^x is the environmental feedback of the resident x. Calculations are detailed in Appendix C along with the expression of S_k^x, $i_k^x(\cdot)$ and A^x.
A rare mutant with phenotype y will invade the resident population infected by the strain x if the invasion fitness $f_x(y)$ of y in the environment generated by x is such that

$$f_x(y) = \mathcal{R}(y, E^x) - 1 > 0,$$

where

$$\mathcal{R}(y, E^x) = \sum_{k=1}^{N_c} S_k^x \Psi_k(y). \tag{3.7}$$

Quantities $\mathcal{R}(y, E^x)$ and $\mathcal{R}_0(y)$, given by equations (3.4) and (3.7), have a strong analogy. Both expressions are basic reproduction numbers that measure the weighted contribution of the pathogen to the subsequent generations, but while $\mathcal{R}_0(y)$ is calculated in the disease-free environment $E^0 = \left(S_k^0, i_k^0(\cdot) = 0, A^0 = 0\right)_{k=1,\cdots N_c}$, $\mathcal{R}(y, E^x)$ is calculated in the environment set E^x by the resident strain x.

Noteworthy $\mathcal{R}(y, E^x)$ takes the form of a sum of the mutant pathogen's reproductive success in each host class as between-class transmission can be written as the product of host susceptibility times pathogen transmissibility. This is equivalent to the more general statement that pathogen propagules all pass through a common pool, as in our model in the compartment A (Rueffler & Metz (2013)). However, this property is not generally true as showed by Gandon (2004) in a two-class model.

$\mathcal{R}_0$ as proxy of invasion fitness In general, finding the evolutionary attractors of host-pathogen systems is mostly based on properties of the invasion fitness on an adaptive landscape (Diekmann et *al.*, 2005; Geritz et *al.*, 1997, 1998; Nowak & Sigmund, 2004). A Pairwise Invasibility Plot (PIP) must then be used to characterize evolutionary attractors. However, when infection efficiencies do not differ between host classes (*i.e.* $\beta_k = \beta, \forall k$), model (2.2) admits an optimisation principle (Mylius & Diekmann, 1995; Metz et *al.*, 2008; Lion & Metz, 2018; Metz & Geritz, 2016; Gyllenberg & Service, 2011). More precisely, the evolutionary attractors of the model coincide with the maxima of the $\mathcal{R}_0$. We prove in

Appendix E that the invasion fitness $f_x(y)$ of a rare mutant with y-phenotype in the resident x-population is such that $\text{sign}(f_x(y)) = \text{sign}\left(\mathcal{R}_0(y) - \mathcal{R}_0(x)\right)$. We emphasise again that this is not a general property of host-pathogen systems (see *e.g.* Lion & Metz (2018) for a more general discussion)

4 Differential effect of pathogenicity traits targeted by resistance genes on the evolutionary dynamics of fungal disease

In this section, we firstly characterize the evolutionary attractors of the coupled epidemiological and evolutionary dynamics described by model (2.2) by analysing the shape of the $\mathcal{R}_0$. Then, using simulations, we study how the population reaches this equilibrium state through a mutation-selection process and highlight how these transient dynamics may inform the sustainable management of resistance genes.

4.1 Case study : deployment of a plant resistant cultivar

We consider a monomorphic pathogen population resulting from the monoculture of a single plant cultivar, called susceptible (S), during a long-time. The S cultivar is infected by a pathogen density A_0 with Gaussian distributed phenotypes which is well adapted on the S cultivar. At $t = 0$, a fraction $\varphi \in (0, 1)$ of the S cultivar is replaced by a new cultivar bearing a quantitative resistance gene, called resistant cultivar (R). The resistance gene alters a single pathogenicity trait, characterized in both cultivars by normally distributed values with means $-\mu$ and μ on S and R cultivars, respectively. The inverse of their variance, $1/\sigma_S^2$, $1/\sigma_R^2$, define the selectivity of the S and R cultivars, respectively. Altogether, the parameters μ, σ_S^2 and σ_R^2 define the strength of the resistance gene efficiency by measuring to what extent the adaptation to one cultivar causes maladaptation to the other.

Two scenarios were considered: the resistance can either impose to the pathogen a trade-off on its total spore production (TSP scenario) or on its infection efficiency (TIE scenario). For each scenario, we illustrate how contrasted values of μ (a proxy of resistance efficiency) and φ (defining the deployment strategy) affect the evolutionary dynamics of the pathogen and the durability of the R cultivar. The durability was quantified by the time T_{inf} when at least 5% of the leaf area density of the R cultivar is infected (*i.e.* time t from which $\int I_R(t,x)\mathrm{d}x / \left(S_R(t) + \int I_R(t,x)\mathrm{d}x\right)$ is always $\geq 5\%$) (Rimbaud et *al.*, 2018). In practice this is the time where the erosion of the R gene become detectable in the field. All model parameters and initial conditions used for the simulations are summarized in Table 2.

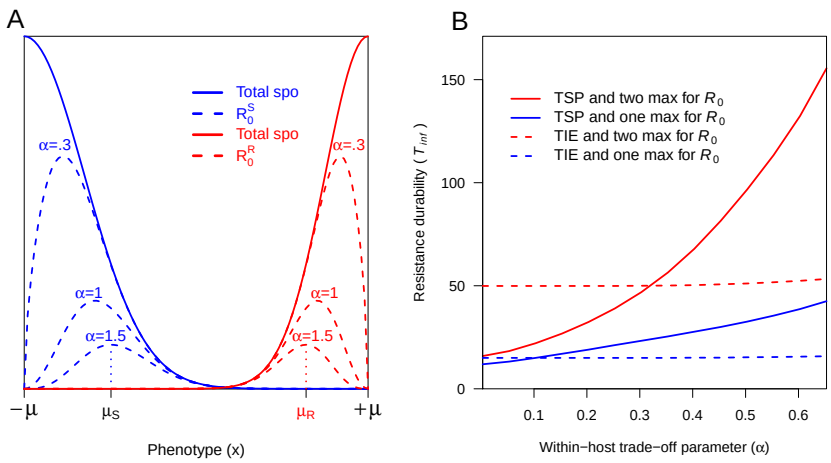

Figure 2: **A** Characterization of phenotypes μ_S and μ_R maximizing the $\mathcal{R}_0$ on S and R cultivars. The phenotypes with maximal spore production are located at $-\mu$ and $+\mu$ for the S and R cultivars respectively. But these are not the phenotypes with the maximal basic reproduction numbers $\mathcal{R}_0^k$ which are located at μ_k due to the within-host trade-off, parametrized by α, between spores production p_k and the probability for an infected host to survive the latent period s_k (with $k \in \{S, R\}$). **B** Impact of the within-host trade-off parameter (α) on the durability of the resistant cultivar (T_{inf}). Other parameters are the same as for Figures 3 and 4.

Parameters value		
ε	Mutation variance	0.01
$m_\varepsilon(x-y)$	Probability of mutation from x to y	$\varepsilon^{-1}\exp\left[-\lvert x-y\rvert/(2\varepsilon)\right]$
Λ	Birth rate of healthy host tissue	35
θ	Death rate of host tissue	1
δ	Rate at which spore becomes unviable	1
φ	Proportion of R cultivar	0 to 1
α	Within-host trade-off parameter	0.2
$n_S(x), \lambda_S(x)$	Shape of the gamma sporulation curve	$n_S = 8; \lambda_S = 1$
$n_R(x), \lambda_R(x)$	Shape of the gamma sporulation curve	$n_R = 8; \lambda_R = 1$
$d_S(a,x)$, $d_R(a,x)$	Disease induced mortality	0
$1/\sigma_S^2$	Selectivity of the S cultivar	$\sigma_S = 0.06$
$1/\sigma_R^2$	Selectivity of the R cultivar	$\sigma_R = 0.05$
$\tau_S(x)$	Pathogen's latent period on S cultivar	$-\theta^{-1}\log\left[u\left(p_S(x)/p_{S,\max}\right)\right]$
$\tau_R(x)$	Pathogen's latent period on R cultivar	$-\theta^{-1}\log\left[u\left(p_R(x)/p_{R,\max}\right)\right]$
TSP scenario		
μ	Phenotype with maximum sporulation	0.055; 0.1
$\beta_S(x)$, $\beta_R(x)$	Infection efficiency on S and R cultivars	0.3
$p_S(x)$	Total spore production on S cultivar	$94\cdot\exp(-(x+\mu)^2/(2\sigma_S^2))$
$p_R(x)$	Total spore production on R cultivar	$94\cdot\exp(-(x-\mu)^2/(2\sigma_R^2))$
TIE scenario		
μ	Phenotype with maximum infection efficiency	0.055; 0.1
$\beta_S(x)$	Infection efficiency on S cultivar	$0.3\cdot\exp(-(x+\mu)^2/(2\sigma_S^2))$
$\beta_R(x)$	Infection efficiency on R cultivar	$0.3\cdot\exp(-(x-\mu)^2/(2\sigma_R^2))$
$p_S(x)$, $p_R(x)$	Total spores on S and R cultivars	94
Initial conditions		
$S_S(0)$	Healthy S cultivar	$(1-\varphi)\Lambda/\theta$
$S_R(0)$	Healthy R cultivar	$\varphi\Lambda/\theta$
$i_S(0,a,x)$	Infected S cultivar	0
$i_R(0,a,x)$	Infected R cultivar	0
$A(0,x)$	Pathogen spores	$40 * \mathcal{N}(\mu_S, \sigma_S/5)(x)$

Table 2: Initial conditions and parameters used for the simulations with two host classes (S and R cultivars). Two scenarios were considered: the R cultivar can either alter the Infection Efficiency of the pathogen (TIE) or its total Spore Production (TSP). $\mathcal{N}$ stands for the density function of the normal distribution.

4.2 Evolutionary dynamics with resistance genes impacting sporulation

When the R gene impacts the total spore production of the pathogen, the maximum points of the $\mathcal{R}_0$ are given by $\mu_S = -\mu + \sigma_S\sqrt{2\alpha\log(2)}$ and $\mu_R = \mu - \sigma_R\sqrt{2\alpha\log(2)}$ (Figure 2 A, Appendix F). The $\mathcal{R}_0$ optimization principle holds here, and the population always becomes monomorphic around an evolutionary attractor characterized by the maximum of $\mathcal{R}_0$ (Section 3.2). We show how μ (a proxy of resistance efficiency) and φ (proportion of the R cultivar deployed) impact the shape of $\mathcal{R}_0$ (number of modes and their steepness) and the transient dynamics (Figure 3).

With a unique maximum of $\mathcal{R}_0$. This maximum point, located at $\mu^*(\mu_S < \mu^* < \mu_R)$, is the unique evolutionary attractor (Figure 3 A) which corresponds to a generalist pathogen. The fast transient dynamics observed on simulations, with a pathogen population rapidly concentrating around μ^* (Figure 3 B,C), corresponds to a fast erosion of the quantitative R (Figure 3 C).

With two local maxima of $\mathcal{R}_0$. $\mathcal{R}_0$ is maximized (globally) by a single phenotype around μ_R but a local maximum also exists around μ_S (Figure 3 D). The $\mathcal{R}_0$ maximization principle indicates that μ_R is the evolutionary attractor at equilibrium. This phenotype is a specialist of the R cultivar. The pathogen population lives for a relatively long time around the initially dominant phenotype μ_S and then shifts by mutation on μ_R (Figure 3 E,F). These dynamics occur simultaneously on the S and R cultivars. The durability of the R cultivar (as measured by T_{inf}) can be relatively long if the R cultivar remained firstly dimly (and decreasingly) infected. The choice of the proportion of R cultivar sown in the landscape is important for durability. Values of φ bringing closer the fitness peaks (in the sense $\mathcal{R}_0(\mu_S) \lessapprox \mathcal{R}_0(\mu_R)$) will lower the durability T_{inf} even if the shift toward the evolutionary attractor takes a longer time (Figure 3 G-I).

4.3 Evolutionary dynamics with resistance genes impacting infection efficiency

When the R gene impacts the infection efficiency of the pathogen, the within-host trade-off does not impact maximums points of the $\mathcal{R}_0$. We have $\mu_S = -\mu$ and $\mu_R = \mu$ (Appendix F). As the optimization principle does not hold, the shape of $\mathcal{R}_0$ function does not allow to characterize evolutionary attractors. PIP must be used instead (see Figure S1 for an illustration). In sharp contrast with the TSP scenario, two configurations - corresponding to monomorphic or dimorphic populations - are possible.

In the first configuration, the pathogen population is composed of a single generalist at equilibrium (Figure 4 A-C). In the second configuration, the

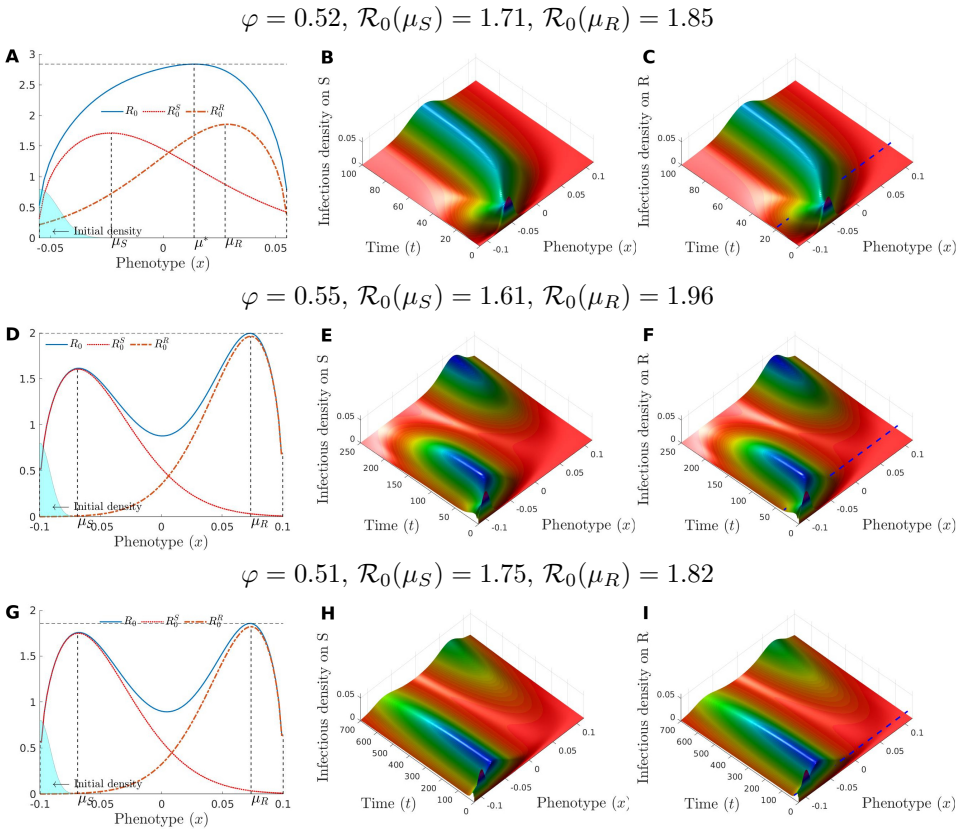

Figure 3: Evolutionary epidemiology dynamics when the resistance impacts the total spore production of the pathogen p_k for three configurations of the fitness function Ψ and with a within-host trade-off parameter $\alpha = 0.2$. **A-C** The fitness function is unimodal: $\mu = 0.055$; $\mu_S \simeq -0.023$; $\mu_R \simeq 0.023$. At $t = 0$, the pathogen population, essentially concentrated around the phenotype μ_S, is adapted on the S cultivar. The dynamics of the density of infected tissue and the phenotypic composition of the pathogen population in the S and R cultivars are display in B and C respectively, with $T_{\text{inf}} = 19$. Panels D-F and G-I are organized similarly with $T_{\text{inf}} = 32$ and 28 respectively. **D-F** and **G-I** The fitness function is bimodal with a unique global maximum μ_R ($\mu = 0.1$; $\mu_S \simeq -0.07$, $\mu_R \simeq 0.07$) but a local maximum also exists around μ_S. The value of $\varphi = 0.55$ in panels G-I implied that μ_S is closer to μ_R compared to panels D-F where $\varphi = 0.51$. In panels C,F,I the dash-blue line represents T_{inf}.

pathogen population is composed of two evolutionary attractors corresponding to specialists of each cultivars (Figure 4 panels D-F). Formally, dimorphism occurs if there exists two constants $a_S, a_R > 0$ defined by system (D.15), and typically quantifying weights of each strain μ_S and μ_R at the equilibrium (Appendix D). In practise, with a R gene targeting infection efficiency, each cultivar is infected by a specific strain. At equilibrium, the pathogen population is composed of different proportions of the two evolutionary attractors μ_S and μ_R (Figure 4 E-F). This is not the case for a R gene targeting sporulation where the S and R cultivars are *simultaneously* infected at a given time by the same pathogen strain (Figure 3 D-I).

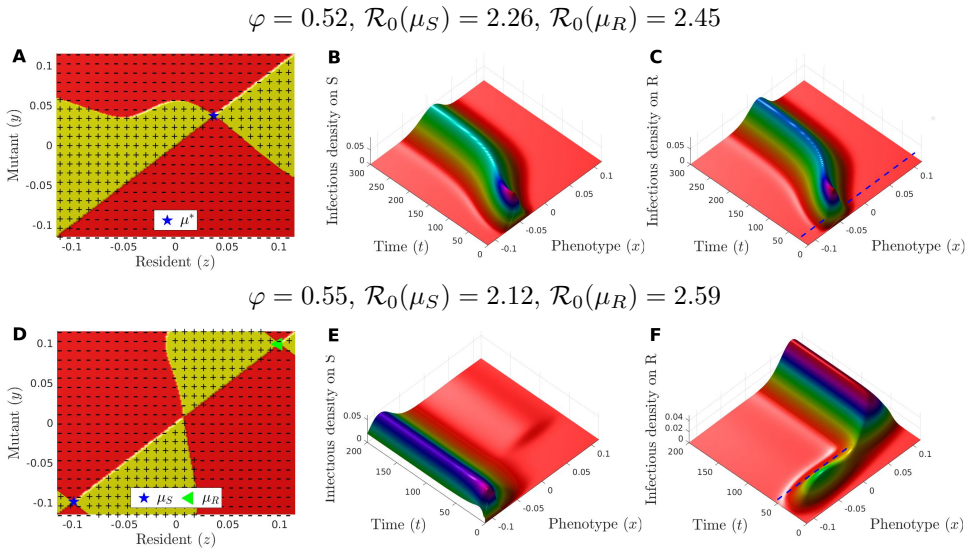

Figure 4: Evolutionary epidemiology dynamics when the resistance impacts the pathogen infection efficiency β_k for three configurations of the fitness function Ψ and with a within-host trade-off parameter $\alpha = 0.2$. **A-C** A unique evolutionary attractor μ^* for the PIP (sign of the invasion fitness $f_z(y)$): $\mu = 0.055$; $\mu_S = -0.0552$; $\mu_R = 0.0552$. At $t = 0$, the pathogen population, essentially concentrated around the phenotype μ_S, is adapted on the S cultivar. The dynamics of the density of infected tissue and the phenotypic composition of the pathogen population in the S and R cultivars are displayed in B and C respectively, with $T_{\text{inf}} = 17$. Panels D-F is organized similarly with $T_{\text{inf}} = 50$ and 44 respectively. **D-F** Two evolutionary attractors μ_S and μ_R for the PIP: $\mu = 0.1$; $\mu_S \simeq -0.0989$; $\mu_R \simeq 0.0989$. In panels C,F the dash-blue line represents T_{inf}. Here, singular strategies μ^*, μ_S and μ_R are evolutionarily stable (no nearby mutant can invade): in the PIP, the vertical line through μ^* (panel A), μ_S or μ_R (panels D) lies completely inside a region marked '$-$'.

5 Discussion

This work follows an ongoing trend aiming to jointly model the epidemiological and evolutionary dynamics of host-parasite interactions. Our theoretical framework, motivated by fungal infections in plants, allows us to tackle the question of the durability of plant quantitative resistance genes altering specific pathogen life-history traits. Many problems and questions are reminiscent of the literature on the epidemiological and evolutionary consequences of vaccination strategies. For instance, quantitative resistance traits against pathogen infection rate, latent period and sporulation rate are analogous to partially effective (imperfect) vaccines with anti-infection, anti-growth or anti-transmission modes of action, respectively (Gandon et *al.*, 2001). Similarly, the proportion of fields where a R cultivar is deployed is analogous to the vaccination coverage in the population (Gandon & Day, 2007).

Evolutionary outcomes with multimodal fitness functions. In line with early motivations for developing a theory in evolutionary epidemiology (Day & Proulx, 2004), we investigated both the short- and long-term epidemiological and evolutionary dynamics of the host-pathogen interaction. Although the short-term dynamics is investigated numerically, the long-term analysis is analytically tractable and allows us to predict the evolutionary outcome of pathogen evolution. In contrast with most studies in evolutionary epidemiology, the analysis proposed allows us to consider multimodal fitness functions, and to characterize evolutionary attractors at equilibrium through a detailed description of their shape (number of modes, steepness and any higher moments with even order). Similarly, our results are neither restricted to Gaussian mutation kernel m (see also Mirrahimi (2017)), provided that m is symmetric and positive (Appendix A), nor to rare mutations as in the classical adaptive dynamics approach.
In our work, the TSP model admits an optimisation principle and potential evolutionary attractors are located at the peaks $\mathcal{R}_0$. This is not always the case for the TIE model (except for some special configurations). An important consequence of the existence of an optimisation principle is that evolutionary branching (*i.e.* a situation leading to pathogen diversification and to long term coexistence of different pathogen strategies) is impossible.

$\mathcal{R}_0$ expression for fungal pathogens in heterogeneous host environment. Usually, the computation of $\mathcal{R}_0$ is based on the spectral radius of the next generation operator (NGO) (Diekmann et *al.*, 1990; Diekmann & Heesterbeek, 2000). The method was applied by van den Bosch et *al.* (2008) to calculate the $\mathcal{R}_0$ for lesion forming foliar pathogens in a setting with only two cultivars and no effect of the age of infection a on sporulation rate and disease-induced mortality. Here, we follow the methodology based on the generation evolution operator (Inaba, 2012) to derive an expression for the basic reproduction number $\mathcal{R}_0$ in heterogeneous host populations composed of N_c cultivars (Appendix

C).

Lannou (2012) pointed out the need for $\mathcal{R}_0(x)$ expressions allowing to compare the fitness of competing pathogen strains with different latent periods. We provide such an expression of $\mathcal{R}_0$ (3.4) for the classical gamma sporulation curve proposed by Segarra et *al.* (2001) and observed for several plant fungi (van den Bosch et *al.*, 1988; Sache et *al.*, 1997; Kolnaar & Bosch, 2011; van den Bosch et *al.*, 1988). This expression combine (i) the pathogenicity traits expressed at the scale of the plant during the basic infection steps (infection efficiency $\beta_k(x)$, latent period $\tau_k(x)$ and shape of the sporulation function $p_k(x)$, $n_k(x)$ and $\lambda_k(x)$) with (ii) the proportion of each cultivar k in the environment (φ_k). As these traits can be measured in the laboratory, $\mathcal{R}_0(x)$ bridges the gap between plant-scale and epidemiological studies, and between experimental and theoretical approaches. $\mathcal{R}_0$-based approach have been for example used to compare the fitness of a collection of isolates of potato light blight (Montarry et *al.*, 2010), to highlight the competition exclusion principle for multi-strains within-host malaria infections (Djidjou-Demasse & Ducrot, 2013) and to predict the community field structure of Lyme disease pathogen from laboratory measures of the three transmission traits (Durand et *al.*, 2017).

$\mathcal{R}_0$ as a proxy of invasion fitness for pathogenicity traits involved in infection cycle after spore germination. In the context of model (2.2), the function $\Psi(x)$, which is proportional to $\mathcal{R}_0(x)$, is an exact fitness proxy for competing strains differing potentially for the latent period and/or the shape of the sporulation function. The basic reproduction number $\mathcal{R}_0$ can thus be used to investigate how basic choices made when deploying a new resistance (resistance gene choice, proportion cultivated) impact resistance durability and the emergence of specialist or generalist pathogen. With a unique local maximum of $\mathcal{R}_0$, a generalist pathogen will selected while with two local maxima a specialist is selected. But, in any case, the pathogen population will become monomorphic at equilibrium after the deployment of a R cultivar impacting any pathogenicity traits expressed after spore germination (e.g. TSP scenario) as the optimization principle avoid evolutionary branching. However, more generally, a clear distinction between pathogen invasion fitness $\mathcal{R}(x, y)$ and epidemiological $\mathcal{R}_0(x)$ is necessary to properly discuss the adaptive evolution of pathogens (Lion & Metz, 2018). In our case study, the deployment of a R cultivar impacting infection efficiency (TIE scenario) can lead to the selection of either a monomorphic population with a generalist pathogen or a polymorphic population with two specialist pathogens (Figure 4). The occurrence of such evolutionary branching is of practical importance for management purposes as evidenced for example in the wheat rust fungal disease where disease prevalence varies with the frequencies of specialist genotypes in the rust population (Papaïx et *al.*, 2011).

Our results also highlight that a detailed knowledge of within-host pathogenicity trait correlations is required to manage resistance durability. Only few studies taking explicitly into account evolutionary principles compared how resistant cultivars targeting different aggressiveness components of fungal pathogens im-

pact durability (Iacono et *al.*, 2012; Bourget *al.*, 2015; Rimbaud et *al.*, 2018). These studies assumed that aggressiveness components are mutually independent while correlations have been sometimes identified between latent period and propagule production (Pariaud et *al.*, 2009; Lannou, 2012; Nidelet et *al.*, 2009; Pariaud et *al.*, 2013). We show that such correlations impact durability when quantitative resistance targets any traits involved in the infection cycle after spores germination on a receptive host leaf. In the TSP scenario, T_{inf} can increase substantially with the within-host trade-off parameter α (Figure 2 B), as a result of the term involving α in the equations of the maximum points μ_S and μ_R of the $\mathcal{R}_0$. Therefore, any guidelines aiming to help plant breeders to adequately choose resistance QTLs in breeding programs should consider these potential correlations, in particular for quantitative R gene targeting any traits involved in the infection cycle after spore germination on a receptive host leaf.

Notes on some model assumptions. The model assumes an infinitely large pathogen population. Demographic stochasticity is thus ignored while it can impact evolutionary dynamics (*e.g.*, lower probabilities of emergence and fixation of beneficial mutations, reduction of standing genetic variation (Kimura, 1962)). In particular, genetic drift is more likely to impact the maintenance of a neutral polymorphism rather than of a protected polymorphism where selection favors coexistence of different genotypes against invasions by mutant strategies (Geritz et *al.*, 1998). The effect of genetic drift depends on the stability properties of the model considered. As our model has a unique globally stable equilibrium, genetic drift is likely to play a much lesser role than with models characterized by unstable equilibrium. Moreover large N_e in the range $\simeq 10^3$ - 3.10^4 have been reported at field scale for several species of wind-dispersed, spore-producing plant pathogens (Ali et *al.*, 2016; Zhan et *al.*, 2001; Walker et *al.*, 2017), suggesting a weak effect of genetic drift for their evolution.

The model assumes a unique pool of propagules and spore dispersal disregard the location of healthy and infected hosts. This assumption is more likely when the extent of the field or landscape considered is not too large with respect to the dispersal function of airborne propagules. Airborne fungal spores often disperse over substantial distances with mean dispersal distance in the range 10^2 to 10^3 meters and, in most case, fat-tail dispersal kernels associated to substantial long-distance dispersal events (Fabre et *al.* (2020) for a review). Recently Mirrahimi (2017) used integro-differential equations to describe a phenotypically structured population subject to mutation, selection and migration between two habitats. Rimbaud et *al.* (2018) used a stochastic spatially-explicit model to assess the epidemiological and evolutionnary outcomes of resistant deployement. It would be interesting to draw on these examples and extend our approach to a spatially explicit environment. When dispersal decreases with distance, large homogeneous habitats promote diversification while smaller habitats, favoring migration between distinct patches, hamper diversification (Débarre & Gandon, 2010; Haller et *al.*, 2013; Papaïx et *al.*, 2013). Managing the resulting population polymorphisms, either for conservation purpose in order to preserve the

adpative potential of endangered species or for disease control purpose in order to hamper pest and pathogen adaptation should become a priority (Vale, 2013).

Acknowledgements

Authors thank Loup Rimbaud for comments and suggestions on the manuscript.

Code availability

The MATLAB codes used to simulate the model and generate the figures have been deposited in Dataverse at https://doi.org/10.15454/WAEIMA

References

Anderson, P.K., Cunningham, A.A., Patel, N.G., Morales, F.J., Epstein, P.R. and Daszak, P. 2004. Emerging infectious diseases of plants: pathogen pollution, climate change and agrotechnology drivers. Trends in Ecology & Evolution, 19, 535-544.

Ali, S., Soubeyrand, S., Gladieux, P., Giraud, T., Leconte, M., Gautier, A. Mboup, M., Chen, W., Vallavieille-Pope, C. and Enjalbert, J. 2016. clon-case: Estimation of sex frequency and effective population size by clonemate resampling in partially clonal organisms. Molecular Ecology Resources, 16, 845-861.

Anderson, R. M. 1991. Populations and Infectious Diseases: Ecology or Epidemiology? Journal of Animal Ecology, 60, 1-50.

Bourget, R., Chaumont, L., Durel, C-E. and Sapoukhina, N. 2008. Sustainable deployment of QTLs conferring quantitative resistance to crops: first lessons from a stochastic model. New Phytologist, 206(3), 1163–1171

Burie, J. B., Ducrot, A., Griette, Q., & Richard, Q. (2019). Concentration estimates in a multi-host epidemiological model structured by phenotypic traits. arXiv preprint arXiv:1910.09385.

Day, T. 2002. Virulence evolution via host exploitation and toxin production in spore-producing pathogens. Ecology Letters, 5(4), 471-476.

Day, T., and Proulx, S. R. 2000. A general theory for the evolutionary dynamics of virulence. The American Naturalist, 163(4), e40-63.

Day, T., Gandon, S. 2006. Insights from Price's equation into evolutionary. Disease evolution: models, concepts, and data analyses, 71, 23.

Débarre, F., and Gandon, S. 2010. Evolution of specialization in a spatially continuous environment. Journal of evolutionary biology, 23(5), 1090-1099.

Diekmann, O., Heesterbeek, J. A. P. and Metz, J. A. 1990. On the definition and the computation of the basic reproduction ratio R0 in models for infectious diseases in heterogeneous populations. Journal of mathematical biology, 28(4), 365-382.

Dieckmann, O. and Heesterbeek, J. P. 2000. Mathematical epidemiology of infectious diseases: Model building, Analysis and Interpretation, Wiley, Chichester, UK.

Diekmann, O., Jabin, P.E., Mischler, S. and Perthame, B. 2005. The dynamics of adaptation: an illuminating example and a Hamilton-Jacobi approach. Theoretical Population Biology, 67, 257-271.

Dieckmann, U. 2002. Adaptive dynamics of pathogen-host interactions. In U. Dieckmann, J. A. J. Metz, M. W. Sabelis et K. Sigmund (eds), Adaptive dynamics of infectious diseases: In pursuit of virulence management. Cambridge University Press, pp. 39-59.

Djidjou Demasse, R. and Ducrot, A. 2013. An age-structured within-host model for multistrain malaria infections. SIAM Journal of Applied Mathematics, 73, 572-593.

Djidjou-Demasse, R., Ducrot, A. and Fabre, F. 2017. Steady state concentration for a phenotypic structured problem modeling the evolutionary epidemiology of spore producing pathogens. Mathematical Models and Methods in Applied Sciences, 27(02), 385-426.

Durand, J., Jacquet, M., Rais, O., Gern, L., and Voordouw, M. J. 2017. Fitness estimates from experimental infections predict the long-term strain structure of a vector-borne pathogen in the field. Scientific reports, 7(1), 1851.

Egas, M., Dieckmann, U. & Sabelis, M.W. 2004. Evolution restricts the coexistence of specialists and generalists: the role of trade-off structure. Am. Nat. 163: 518-531.

Fabre, F., Coville, J. & Cunniffe, N. J. 2020. Optimising reactive disease management using spatially explicit models at the landscape scale. Preprint, https://hal.archives-ouvertes.fr/hal-02375867.

Gandon, S., Mackinnon, M.J., Nee, S. and Read, A.F. 2001. Imperfect vaccines and the evolution of pathogen virulence. Nature. 414(6865), 751–756.

Gandon, S. 2004. Evolution of Multihost Parasites. Evolution, 58(3), 455-469.

Gandon, S. and Day, T. 200). The evolutionary epidemiology of vaccination. Journal of the Royal Society Interface, 4(16), 803-817.

Geritz, S.A., Metz, J.A., Kisdi, É. and Meszéna, G. 1997. Dynamics of adaptation and evolutionary branching. Physical Review Letters, 78(10), 2024-2027.

Geritz, S.A.H., Kisdi, É., Meszéna, G. and Metz, J.A.J. 1998. Evolutionarily singular strategies and the adaptive growth and branching of the evolutionary tree. Evolutionary Ecology, 12, 35-57.

Gyllenberg, M., & Service, R. (2011). Necessary and sufficient conditions for the existence of an optimisation principle in evolution. Journal of Mathematical Biology, 62(3), 359-369.

Haller, B.C., Mazzuccco, R. and Dieckmann, U. 2013. evolutionary branching in complex landscape. American Naturalist, 184(4), e127-141.

Iacono, G.L., van den Bosch, F. and Paveley, N. 2012. The evolution of plant pathogens in response to host resistance: factors affecting the gain from deployment of qualitative and quantitative resistance. Journal of Theoretical Biology, 304, 152-163.

Inaba, H. 2012. On a new perspective of the basic reproduction number in heterogeneous environments. Journal of mathematical biology, 65(2), 309-348.

Kennelly, M. M., Gadoury, D. M., Wilcox, W. F., Magarey, P. A., & Seem, R. C. (2007). Primary infection, lesion productivity, and survival of sporangia in the grapevine downy mildew pathogen Plasmopara viticola. Phytopathology, 97(4), 512-522.

Kimura, M. 1962. On the probability of fixation of mutant genes in a population. Genetics, 47, 713-719.

Kolnaar, R.W. & Bosch, F.V.D. 2001. Effect of temperature on epidemiological parameters of *Puccinia lagenophorae*. Plant Pathology 50: 363–370.

Lannou, C. 2012. Variation and selection of quantitative traits in plant pathogens. Annual Review of Phytopathology, 50, 319-338.

Lion, S. and Metz, J. A. J. 2018. Beyond R_0 maximisation: on pathogen evolution and environmental dimensions. Trends In Ecology & Evolution, 33, 75-90.

Martin, G. and Lenormand, T. 2006. A general multivariate extension of Fisher's geometrical model and the distribution of mutation fitness effects across species. Evolution, 60, 893-907.

McDonald, B. A. and Linde, C. 2002. Pathogen population genetics, evolutionary potential, and durable resistance. Annual review of phytopathology, 40(1), 349-379.

Metz, J.A.J., Geritz, S.A.H., Meszéna, G., Jacobs, F.J.A. and van Heerwaarden, J.S. 1996. Adaptive dynamics, a geometrical study of the consequences of nearly faithful reproduction. In: van Strien, S.J., Verduyn Lunel, S.M. (Eds.), Stochastic and spatial Structures of Dynamical Systems. North-Holland, Amsterdam, pp. 183-231.

Metz, J. A., & Geritz, S. A. (2016). Frequency dependence 3.0: an attempt at codifying the evolutionary ecology perspective. Journal of mathematical biology, 72(4), 1011-1037.

Metz, J. A. J., Mylius, S. D., & Diekmann, O. (2008). When does evolution optimise? Evolutionary Ecology Research, 10: 629–654

Montarry, J., Hamelin, F.M., Glais, I., Corbière, R. and Andrivon, D. 2010. Fitness costs associated with unnecessary virulence factors and life history traits: evolutionary insights from the potato late blight pathogen Phytophthora infestans. BMC Evolutionary Biology, 10, 1-9.

Mirrahimi, S. 2017. A Hamilton–Jacobi approach to characterize the evolutionary equilibria in heterogeneous environments. Mathematical Models and Methods in Applied Sciences, 27(13), 2425-2460.

Mundt, C. 2014. Durable resistance: A key to sustainable management of pathogens and pests. Infection, Genetics and Evolution, 14, 446-455.

Mylius, S. D. and Diekmann, O. 1995. On evolutionarily stable life histories, optimization and the need to be specific about density dependence. Oikos, 218-224.

Nidelet, T., Koella, J. C., & Kaltz, O. (2009). Effects of shortened host life span on the evolution of parasite life history and virulence in a microbial host-parasite system. BMC Evolutionary Biology, 9(1), 65.

Niks, R. E., Qi, X. and Marcel, T.C. 2015. Quantitative Resistance to Biotrophic Filamentous Plant Pathogens: Concepts, Misconceptions, and Mechanisms. Annual Review of Phytopathology, 53, 444-470.

Nowak, M. A., & Sigmund, K. 2004. Evolutionary dynamics of biological games. science, 303(5659), 793-799.

Pariaud, B., Ravigné, V., Halkett, F., Goyeau, H., Carlier, J. and Lannou, C. 2009. Aggressiveness and its role in the adaptation of plant pathogens. Plant Pathology, 58(3), 409-424.

Pariaud, B., van den Berg, F., van den Bosc,h F., Powers, S.J., Kaltz, O. and Lannou, C. 2013. Shared influence of pathogen and host genetics on a trade-off between latent period and spore production capacity in the wheat pathogen, Puccinia triticina. Evolutionary Applications 6: 303–312.

Papaïx, J., Goyeau, H, Du Cheyron, P., Monod, H and Lannou, C. 2011. Dynamics of Adaptation in Spatially Heterogeneous Metapopulations. New Phytologist, 191(4), 1095-1107.

Papaïx, J., David, O., Lannou, C. and Monod, H. 2013. Dynamics of Adaptation in Spatially Heterogeneous Metapopulations. PLoS ONE, 8(2), e54697.

Poland, J. A., Balint-Kurti, P. J., Wisser, R. J., Pratt, R. C. and Nelson, R. J. 2009. Shades of gray: the world of quantitative disease resistance. Trends in Plant Science, 14, 21-29.

Parlevliet, J. E. 1986. Pleiotropic association of infection frequency and latent period of two barley cultivars partially resistant to barley leaf rust. Euphytica, 35, 267-272.

Pilet-Nayel, M.-L., Moury, B., Caffier, V., Montarry, J., Kerlan, M.-C., Fournet, S., Durel, C.-E. and Delourme, R. 2017. Quantitative Resistance to Plant Pathogens in Pyramiding Strategies for Durable Crop Protection. Frontiers in Plant Science, 8, 21-29.

Raberg, L., Graham, A. L. and Read, Andrew F. 2009. Decomposing health: tolerance and resistance to parasites in animals. Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences, 364, 37–49.

Restif, O. and Koella, J. C. 2004. Concurrent evolution of resistance and tolerance to pathogens. The American Naturalist 164, e90-102.

Richardson, K. L., Vales, M. I., Kling, J. G., Mundt, C. C. and Hayes, P. M. 2006. Pyramiding and dissecting disease resistance QTL to barley stripe rust.Theoretical and Applied Genetics, 113, 485–495.

Rimbaud, L., Papaïx, J., Rey, J. F., Barrett, L. G. and Thrall, P.H. 2018. Assessing the durability and efficiency of landscape-based strategies to deploy plant resistance to pathogens. Plos Computational Biology, 14(4), e1006067.

Rueffler, C. and Metz, J. A. 2013. Necessary and sufficient conditions for R_0 to be a sum of contributions of fertility loops. Journal of mathematical biology, 66(4-5), 1099-1122.

Sache, I. 1997. Effect of density and age of lesions on sporulation capacity and infection efficiency in wheat leaf rust (*Puccinia recondita* f.sp. tritici). Plant Pathology, 4, 581-589.

Segarra, J., Jeger, M. J. and Van den Bosch, F. 2001. Epidemic dynamics and patterns of plant diseases. Phytopathology, 91(10), 1001-1010.

St. Clair, D. A. 2010. Quantitative disease resistance and quantitative resistance loci in breeding. Annual Review of Phytopathology, 48, 247-268.

van den Driessche, P. and Watmough, J. 2008. Further notes on the basic reproduction number. Mathematical epidemiology, 159-178, Lecture Notes in Math., 1945, Springer, Berlin.

van Den Bosch, F., Frinking, H.D., Metz, J.A.J. and Zadoks, J.C. 1988. Focus expansion in plant disease. III: two experimental examples. Phytpathology 78: 919–925.

van den Bosch, F., McRoberts, N., Van den Berg, F. and Madden, L. V. 2008. The basic reproduction number of plant pathogens: matrix approaches to complex dynamics. Phytopathology, 98(2), 239-249.

Vale, P. F. 2013. Killing them softly: managing pathogen polymorphism and virulence in spatially variable environments. Trends in Parasitology, 29(9), 417-422.

Walker, A.-S., Ravigne, V., Rieux, A., Ali, S., Carpentier, F. and Fournier, E. 2017. Fungal adaptation to contemporary fungicide applications: the case of Botrytis cinerea populations from Champagne vineyards (France). Molecular Ecology, 26, 1919-1935.

Zhan, J., Mundt, C.C. and McDonald B.A. 2001. Using restriction fragment length polymorphisms to assess temporal variation and estimate the number of ascospores that initiate epidemics in field populations of Mycosphaerella graminicola. Phytopathology 91:1011-1017.

Zhan, J., Thrall, P. H., Papaïx, J., Xie, L. and Burdon, J. J. 2015. Playing on a pathogen's weakness: using evolution to guide sustainable plant disease control strategies. Annual Review of Phytopathology, 53, 19-43.

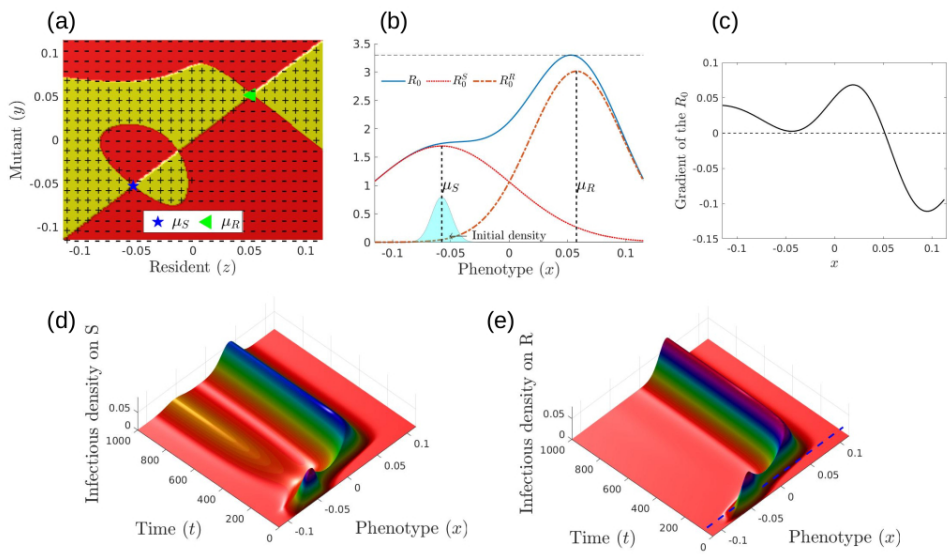

Figure S1: Here we have a polymorphic pathogen population at equilibrium in different proportions (panels d,e) but only one local maximum for the $\mathcal{R}_0$ as confirmed by the gradient (panels b,c). However, the PIP predicts a polymorphic population (panel a). Indeed, singular strategies, μ_S and μ_R, are respectively branching point and evolutionarily stable (no nearby mutant can invade). Here, we have fixed $\varphi = 0.64$, $\sigma_S = 0.06$, $\sigma_R = 0.04$ and $\mu_S = -\mu_R = -0.0579$.

A Properties of the mutation kernel m_ε

The kernel function m_ε arising in model (2.2) should satisfy the following properties:

(H1) The function m_ε is almost everywhere strictly positive on $\mathbb{R}^N$ and should be normalised such that,

$$\int_{\mathbb{R}^N} m_\varepsilon(x)\mathrm{d}x = 1.$$

This last condition expresses that all interactions generated on the phenotypic space of pathogens necessarily end up somewhere on that space.

(H2) Its variation should only depend on the distance separating the points between which the interactions are evaluated (*i.e.* $m_\varepsilon(x) = m_\varepsilon(-x)$, for all $x \in \mathbb{R}^N$).

(H3) It is highly concentrated and decays rather fast at infinity in the sens that $m_\varepsilon(x) = \varepsilon^{-N} m(x/\varepsilon)$ and $m(x) = O\left(\frac{1}{\|x\|^\infty}\right)$ as $\|x\| \to \infty$.

B Some special cases of the general model (2.2)

By omitting the age structure, we re-write model (2.2) as follows

$$\begin{cases} \partial_t S_k(t) = \varphi_k \Lambda - \theta S_k(t) - S_k(t) \displaystyle\int_{\mathbb{R}^N} \beta_k(y) A_k(t,y) \mathrm{d}y, \\ \partial_t i_k(t,x) = \beta_k(x) S_k(t) A(t,x) - \left(\theta + d_k(x) + \dfrac{1}{l_k(x)}\right) i_k(t,x), \\ \partial_t A(t,x) = -\delta A(t,x) + \displaystyle\sum_{k=1}^{N_c} \int_{\mathbb{R}^N} m_\varepsilon(x-y) p_k(y) i_k(t,y) \mathrm{d}y, \end{cases} \tag{B.1}$$

wherein we take into account the (host and strain-specific) duration of the sporulation period, denoted by $l_k(x)$.

Furthermore, if we assume that there are no "interactions" in the phenotypic space of pathogens, *i.e.* without mutations: $\varepsilon \to 0$, then the simplified model (B.1) rewrites

$$\begin{cases} \partial_t S_k(t) = \varphi_k \Lambda - \theta S_k(t) - S_k(t) \displaystyle\int_{\mathbb{R}^N} \beta_k(y) A_k(t,y) \mathrm{d}y, \\ \partial_t i_k(t,x) = \beta_k(x) S_k(t) A(t,x) - \left(\theta + d_k(x) + \dfrac{1}{l_k(x)}\right) i_k(t,x), \\ \partial_t A(t,x) = \displaystyle\sum_{k=1}^{N_c} p_k(x) i_k(t,x) - \delta A(t,x). \end{cases} \tag{B.2}$$

C The fitness function

In this appendix we explain how to compute the fitness function. To that aim, by formally taking the limit $\varepsilon \to 0$ into (2.2), this system becomes

$$\begin{cases} \partial_t S_k(t) = \varphi_k \Lambda - \theta S_k(t) - S_k(t) \displaystyle\int_{\mathbb{R}^N} \beta_k(y) A(t,y) \mathrm{d}y, \\ (\partial_t + \partial_a)\, i_k(t,a,x) = -\left(\theta + d_k(a,x)\right) i_k(t,a,x), \\ i_k(t,0,x) = \beta_k(x) S_k(t) A(t,x), \\ \partial_t A(t,x) = \displaystyle\sum_{k=1}^{N_c} \int_0^\infty r_k(a,x) i_k(t,a,x) \mathrm{d}a - \delta A(t,x). \end{cases} \tag{C.3}$$

Let us assume that system (C.3) reaches a monomorphic epidemiological equilibrium $E^z = (S_k^z, i_k^z(\cdot)\delta_z, A^z\delta_z)_{k=1,\cdots N_c}$, for some trait z, before a new mutation with trait value, say, y occurs. Note that E^z is the environmental feedback of the resident z. We introduce a small perturbation in (C.3) in the phenotype trait y, so that the evolution of the system reads as follows: $S_k(t) = S_k^z + u_k(t)$ and

$$i_k(t,a,x) = i_k^z(a)\delta_z(x) + j_k(t,a)\delta_y(x) \text{ and } A(t,x) = A^z\delta_z(x) + B(t)\delta_y(x),$$

and the small perturbations for the infection, j_k and B, are governed by the linearized system of equations around E^z. This reads as

$$\begin{cases} (\partial_t + \partial_a)\, j_k(t,a) = -\left(\theta + d_k(a,y)\right) j_k(t,a), \\ j_k(t,0) = \beta_k(y) S_k^z B(t), \\ B'(t) = \displaystyle\sum_{k=1}^{N_c} \int_0^\infty r_k(a,y) j_k(t,a) \mathrm{d}a - \delta B(t). \end{cases} \tag{C.4}$$

In order to study the evolution of this perturbation we will derive a renewal equation on $b^z(t,y)$, the density of newly produced spores at time t with phenotype y in the resident population with phenotype x. This term is more precisely defined by

$$b^z(t,y) = \sum_{k=1}^{N_c} \int_0^\infty r_k(a,y) j_k(t,a) \mathrm{d}a.$$

It then follows from the j_k-equation of the linear system (C.4), that

$$j_k(t,a) = \begin{cases} j_k(0,a-t) e^{-\theta t - \int_{a-t}^a d_k(\sigma,y)\mathrm{d}\sigma}, & a \geq t, \\ \beta_k(y) S_k^z B(t-a) e^{-\theta a - \int_0^a d_k(\sigma,y)\mathrm{d}\sigma}, & a < t, \end{cases}$$

while

$$B(t) = \int_0^t b^z(s,y) e^{-\delta(t-s)} \mathrm{d}s + B(0) e^{-\delta t}.$$

As a consequence, $b^z(t,y)$ satisfies the following renewal equation:

$$b^z(t,y) = \sum_{k=1}^{N_c} S_k^z \int_0^t r_k(a,y)\beta_k(y) \int_0^{t-a} b^z(s,y) e^{-\delta(t-a-s)} e^{-\theta a - \int_0^a d_k(\sigma,y)\mathrm{d}\sigma} \mathrm{d}s\mathrm{d}a + \mathcal{F}(t,y,z), \tag{C.5}$$

wherein we have set

$$\begin{aligned} \mathcal{F}(t,y,z) = &\sum_{k=1}^{N_c} \int_t^\infty r_k(a,y) j_k(0,a-t) e^{-\theta t - \int_{a-t}^a d_k(\sigma,y)\mathrm{d}\sigma} \mathrm{d}a \\ &+ B(0) \sum_{k=1}^{N_c} S_k^z \int_0^t r_k(a,y)\beta_k(y) e^{-\delta(t-a)} e^{-\theta a - \int_0^a d_k(\sigma,y)\mathrm{d}\sigma} \mathrm{d}a. \end{aligned}$$

Then (C.5) can be rewritten as

$$b^z(t,y) = \int_0^t B^z(a,y) b^z(t-a,y) \mathrm{d}a + \mathcal{F}(t,y,z),$$

where $B^z(a,y)$ is the expected number of new infections produced per unit time, in a resident host population with phenotype z, by an individual which was infected a units of time ago with the phenotype y, given by

$$B^z(a,y) = e^{-\delta a} \sum_{k=1}^{N_c} S_k^z \beta_k(y) \int_0^a r_k(s,y) e^{\delta s - \theta s - \int_0^s d_k(\sigma,y)\mathrm{d}\sigma} \mathrm{d}s.$$

Due to the above formulation, it follows from classical adaptive dynamics (Diekmann et *al.*, 2005; Geritz et *al.*, 1997; Metz et *al.*, 1996) that the spore numbers, $\mathcal{R}(y, E^z)$, of a rare mutant strategy, y, in the resident z-population is given by

$$\mathcal{R}(y, E^z) = \int_0^\infty B^z(a, y)\mathrm{d}a = \sum_{k=1}^{N_c} S_k^z \Psi_k(y),$$

wherein $\Psi_k(y) = \frac{1}{\delta}\beta_k(y)\int_0^\infty r_k(a, y)\exp\left(-\theta a - \int_0^a d_k(\sigma, y)\mathrm{d}\sigma\right)\mathrm{d}a$. Then, the invasion fitness $f_z(y)$ of a mutant strategy y in the resident z-population is given by

$$f_z(y) = \mathcal{R}(y, E^z) - 1 = \sum_{k=1}^{N_c} S_k^z \Psi_k(y) - 1. \tag{C.6}$$

Note that when the environmental feedback E^z is reduced to the disease-free environment, then S_k^z re-writes as $S_k^z = \frac{\Lambda\varphi_k}{\theta}$. And the epidemiological basic reproduction number of the pathogen with the phenotype y is calculated as

$$\mathcal{R}_0(y) = \frac{\Lambda}{\theta}\Psi(y), \quad \text{with} \quad \Psi = \sum_{k=1}^{N_c} \varphi_k \Psi_k.$$

Once the pathogen has spread and reached the monomorphic equilibrium, then the endemic feedback environment E^z becomes

$$S_k^z = \frac{\Lambda\varphi_k}{\theta + \beta_k(z)A^z}, \quad i_k^z(a) = \beta_k(z)A^z S_k^z \exp\left(-\theta a - \int_0^a d_k(\sigma, z)\mathrm{d}\sigma\right), \tag{C.7}$$

where $A^z > 0$ is the unique solution of the following equation (only defined when $\mathcal{R}_0(z) > 1$):

$$\sum_{k=1}^{N_c} \frac{\Lambda\varphi_k}{\theta + \beta_k(z)A^z}\Psi_k(z) = 1. \tag{C.8}$$

D Dimorphic or monomorphic equilibrium

To simplify the presentation, we consider system (2.2) with $N_c = 2$ corresponding to S and R cultivars. Denote by $(S_0, i_0(\cdot), A_0)$ the endemic equilibrium of system (2.2) as $\varepsilon \to 0$ and when only S is cultivated (*i.e.* when the proportion φ of R is zero). From results in (Djidjou-Demasse et *al.*, 2017) we have

$$S_0 = \frac{1}{\Psi_S(\mu_S)}. \tag{D.9}$$

Now, let $(S_S, S_R, i_S(\cdot), i_R(\cdot), A)$ be an equilibrium of system (2.2) when a proportion $\varphi > 0$ of R is cultivated. Next recall that, for $k \in \{S, R\}$,

$$S_k = \frac{\varphi_k\Lambda}{\theta + \int_{\mathbb{R}^N}\beta_k(z)A(z)\mathrm{d}z} \text{ and } i_k(x, a) = \beta_k(x)A(x)S_k\exp\left(-\theta a - \int_0^a d_k(\sigma, x)\mathrm{d}\sigma\right),$$

so that $A(\cdot)$ becomes a solution of the nonlinear equation:

$$\int_{\mathbb{R}^N} m_\varepsilon(x-y) \sum_{k\in\{S,R\}} \frac{\varphi_k \Psi_k(y)}{\theta + \int_{\mathbb{R}^N} \beta_k(z)A(z)\mathrm{d}z} A(y)\mathrm{d}y = \frac{1}{\Lambda} A(x). \tag{D.10}$$

Using this equation we heuristically explore conditions yielding to dimorphic or monomorphic equilibrium.

Resistant gene altering infection efficiencies β_S and β_R (TIE scenario). We formally assume that the population of spores writes $A(x) = a_S\delta_{\mu_S}(x) + a_R\delta_{\mu_R}(x)$, and we plug this ansatz into equation (D.10) above. This yields, for any x,

$$\begin{aligned}
&a_R \left[\frac{\varphi\Psi_R(\mu_R)}{\theta + a_R\beta_R(\mu_R) + a_S\beta_R(\mu_S)} + \frac{(1-\varphi)\Psi_S(\mu_R)}{\theta + a_R\beta_S(\mu_R) + a_S\beta_S(\mu_S)}\right] m_\varepsilon(x-\mu_R) \\
&+ a_S \left[\frac{\varphi\Psi_R(\mu_S)}{\theta + a_R\beta_R(\mu_R) + a_S\beta_R(\mu_S)} + \frac{(1-\varphi)\Psi_S(\mu_S)}{\theta + a_R\beta_S(\mu_R) + a_S\beta_S(\mu_S)}\right] m_\varepsilon(x-\mu_S) \\
&= \frac{1}{\Lambda}\left[a_R\delta_{\mu_R}(x) + a_S\delta_{\mu_S}(x)\right].
\end{aligned}$$

Letting $\varepsilon \to 0$ and recalling that $m_\varepsilon(x) \approx \delta_0(x)$, one obtains

$$\begin{aligned}
&a_R \left[\frac{\varphi\Psi_R(\mu_R)}{\theta + a_R\beta_R(\mu_R) + a_S\beta_R(\mu_S)} + \frac{(1-\varphi)\Psi_S(\mu_R)}{\theta + a_R\beta_S(\mu_R) + a_S\beta_S(\mu_S)}\right] \delta_{\mu_R}(x) \\
&+ a_S \left[\frac{\varphi\Psi_R(\mu_S)}{\theta + a_R\beta_R(\mu_R) + a_S\beta_R(\mu_S)} + \frac{(1-\varphi)\Psi_S(\mu_S)}{\theta + a_R\beta_S(\mu_R) + a_S\beta_S(\mu_S)}\right] \delta_{\mu_S}(x) \\
&= \frac{1}{\Lambda}\left[a_R\delta_{\mu_R}(x) + a_S\delta_{\mu_S}(x)\right],
\end{aligned}$$

that is

$$\begin{cases}
\dfrac{a_R\varphi\Psi_R(\mu_R)}{\theta + a_R\beta_R(\mu_R) + a_S\beta_R(\mu_S)} + \dfrac{a_R(1-\varphi)\Psi_S(\mu_R)}{\theta + a_R\beta_S(\mu_R) + a_S\beta_S(\mu_S)} = \dfrac{a_R}{\Lambda}, \\
\dfrac{a_S\varphi\Psi_R(\mu_S)}{\theta + a_R\beta_R(\mu_R) + a_S\beta_R(\mu_S)} + \dfrac{a_S(1-\varphi)\Psi_S(\mu_S)}{\theta + a_R\beta_S(\mu_R) + a_S\beta_S(\mu_S)} = \dfrac{a_S}{\Lambda}.
\end{cases}$$

As a consequence, for the equilibrium to be dimorphic, namely $a_R > 0$ and $a_S > 0$, it is necessary that there exist $a_R > 0$ and $a_S > 0$ satisfying the following system of equations:

$$\begin{cases}
\dfrac{\varphi\Psi_R(\mu_R)}{\theta + a_R\beta_R(\mu_R) + a_S\beta_R(\mu_S)} + \dfrac{(1-\varphi)\Psi_S(\mu_R)}{\theta + a_R\beta_S(\mu_R) + a_S\beta_S(\mu_S)} = \dfrac{1}{\Lambda}, \\
\dfrac{\varphi\Psi_R(\mu_S)}{\theta + a_R\beta_R(\mu_R) + a_S\beta_R(\mu_S)} + \dfrac{(1-\varphi)\Psi_S(\mu_S)}{\theta + a_R\beta_S(\mu_R) + a_S\beta_S(\mu_S)} = \dfrac{1}{\Lambda}.
\end{cases}$$

We set

$$\begin{cases}
X = X(a_S, a_R) = \left(\theta + a_R\beta_R(\mu_R) + a_S\beta_R(\mu_S)\right)^{-1}, \\
Y = Y(a_S, a_R) = \left(\theta + a_R\beta_S(\mu_R) + a_S\beta_S(\mu_S)\right)^{-1}.
\end{cases} \tag{D.11}$$

Recall that with the TIE scenario we have $r_S = r_R$ and $d_S = d_R$ such that the fitness function $\Psi_k(x) = \frac{1}{\delta}\beta_k(x)\int_0^\infty r_k(a,x)\exp\left(-\theta a - \int_0^a d_k(\sigma,x)\mathrm{d}\sigma\right)\mathrm{d}a$, takes the form $\Psi_k = c_0\beta_k$ for $k = S, R$ (where c_0 is the same positive funtional for S and R). Doing that, the above system rewrites

$$\mathcal{K}(X,Y)^T = \frac{1}{c_0\Lambda}(1,1)^T, \tag{D.12}$$

wherein $\mathcal{K} = \begin{pmatrix} \varphi\beta_R(\mu_R) & (1-\varphi)\beta_S(\mu_R) \\ \varphi\beta_R(\mu_S) & (1-\varphi)\beta_S(\mu_S) \end{pmatrix}$ and $c_0 = c_0(\mu_S) = c_0(\mu_R)$. With the TIE scenario (*i.e.* with trade-off on infection efficiency β_k), we reasonably have $\beta_R(\mu_R) > \beta_R(\mu_S)$ and $\beta_S(\mu_S) > \beta_S(\mu_R)$. Therefore, $\det(\mathcal{K}) = \varphi(1-\varphi)\left(\beta_R(\mu_R)\beta_S(\mu_S) - \beta_R(\mu_S)\beta_S(\mu_R)\right) > 0$. Then, solving system (D.12) for (X,Y) yields to

$$\begin{cases} X = \dfrac{\beta_S(\mu_S) - \beta_S(\mu_R)}{c_0\Lambda\varphi\left(\beta_R(\mu_R)\beta_S(\mu_S) - \beta_R(\mu_S)\beta_S(\mu_R)\right)} > 0, \\ Y = \dfrac{\beta_R(\mu_R) - \beta_R(\mu_S)}{c_0\Lambda(1-\varphi)\left(\beta_R(\mu_R)\beta_S(\mu_S) - \beta_R(\mu_S)\beta_S(\mu_R)\right)} > 0. \end{cases}$$

Since $\mathcal{R}_0^k(x) = \frac{\varphi_k\Lambda}{\theta}\Psi_k(x) = \frac{\varphi_k\Lambda c_0(x)}{\theta}\beta_k(x)$, the above system rewrites

$$\begin{cases} \theta X = \dfrac{\mathcal{R}_0^S(\mu_S) - \mathcal{R}_0^S(\mu_R)}{\mathcal{R}_0^R(\mu_R)\mathcal{R}_0^S(\mu_S) - \mathcal{R}_0^R(\mu_S)\mathcal{R}_0^S(\mu_R)} > 0, \\ \theta Y = \dfrac{\mathcal{R}_0^R(\mu_R) - \mathcal{R}_0^R(\mu_S)}{\mathcal{R}_0^R(\mu_R)\mathcal{R}_0^S(\mu_S) - \mathcal{R}_0^R(\mu_S)\mathcal{R}_0^S(\mu_R)} > 0. \end{cases}$$

Coming back to the definition of $X = X(a_S, a_R)$ and $Y = Y(a_S, a_R)$ provided by (D.11), we then find

$$\mathcal{G}(a_R, a_S)^T = \left(\frac{1}{X} - \theta, \frac{1}{Y} - \theta\right)^T, \tag{D.13}$$

with $\mathcal{G} = \begin{pmatrix} \beta_R(\mu_R) & \beta_R(\mu_S) \\ \beta_S(\mu_R) & \beta_S(\mu_S) \end{pmatrix}$. Because $\det(\mathcal{G}) = (\beta_R(\mu_R)\beta_S(\mu_S) - \beta_R(\mu_S)\beta_S(\mu_R)) > 0$, it comes that for the equilibrium to be dimorphic it is necessary that

$$\begin{cases} \theta X < 1, \\ \theta Y < 1, \\ \beta_S(\mu_S)\left(\dfrac{1}{\theta X} - 1\right) > \beta_R(\mu_S)\left(\dfrac{1}{\theta Y} - 1\right), \\ \beta_R(\mu_R)\left(\dfrac{1}{\theta Y} - 1\right) > \beta_S(\mu_R)\left(\dfrac{1}{\theta X} - 1\right). \end{cases} \tag{D.14}$$

This heuristic condition (D.14) is necessary (but not sufficient) for system (2.2) (here with $N_c = 2$) to admit an endemic dimorphic equilibrium. The

situation with a technical assumption on disjoint supports of β_k, is rigorously studied in Burie *al.* (2019).

But here, in order to go slightly further in our analysis, we assume a strong trade-off on infection efficiency, namely

$$\Psi_l(\mu_k) < 1 \text{ and } \beta_l(\mu_k) \ll 1 \text{ for } l, k = R, S \text{ and } l \neq k.$$

We deduce that the above system of equation roughly simplifies into

$$\begin{cases} \dfrac{\varphi \Psi_R(\mu_R)}{\theta + a_R \beta_R(\mu_R)} \approx \dfrac{1}{\Lambda}, \\ \dfrac{(1-\varphi)\Psi_S(\mu_S)}{\theta + a_S \beta_S(\mu_S)} \approx \dfrac{1}{\Lambda}. \end{cases}$$

Hence the proportions of each phenotype, μ_S and μ_R, can be calculated as

$$a_R \approx \frac{\varphi \Lambda \Psi_R(\mu_R) - \theta}{\beta_R(\mu_R)} \quad \text{and} \quad a_S \approx \frac{(1-\varphi)\Lambda \Psi_S(\mu_S) - \theta}{\beta_S(\mu_S)}, \tag{D.15}$$

provided the following threshold conditions in this strong trade-off framework

$$\varphi \frac{\Lambda}{\theta} \Psi_R(\mu_R) > 1 \text{ and } (1-\varphi)\frac{\Lambda}{\theta}\Psi_S(\mu_S) > 1.$$

As a consequence, the density of healthy hosts at equilibrium, when a proportion $\varphi > 0$ of R is cultivated, writes

$$S_S \approx \frac{1}{\Psi_S(\mu_S)} \quad \text{and} \quad S_R \approx \frac{1}{\Psi_R(\mu_R)}. \tag{D.16}$$

Therefore, (D.9)-(D.16) lead to $S_S + S_R = (1/\Psi_S(\mu_S) + 1/\Psi_R(\mu_R)) > S_0 = 1/\Psi_S(\mu_S)$ meaning that with a strong-trade off on infection efficiency, the time during which a proportion $\varphi > 0$ of R gene deployed remains beneficial (in terms of Healthy Area Duration gain) can be considered as large as possible.

Resistant gene altering total sporulation production p_S and p_R (TSP scenario). In this case, using the same argument as in (Djidjou-Demasse et *al.*, 2017) we can prove that the spore population is monomorphic at equilibrium such that $A(x) = a^* \delta_{\mu^*}(x)$; with $a^* > 0$, providing that we are not in a strict symmetric configuration of the fitness function. Moreover, with a strong trade-off on sporulation rate, it is well known that $\mu^* \in \{\mu_S, \mu_R\}$. Then, applying the same arguments as in the previous section lead to

$$\frac{a^*}{\theta + a^* \beta(\mu^*)} m_\varepsilon(x - \mu^*) \Psi(\mu^*) = \frac{a^*}{\Lambda} \delta_{\mu^*}(x).$$

Again with $\varepsilon \to 0$, it comes

$$a^* = \frac{\Lambda \Psi(\mu^*) - \theta}{\beta(\mu^*)} = \frac{\theta}{\beta(\mu^*)} \left[\mathcal{R}_0(\mu^*) - 1 \right],$$

with $\mathcal{R}_0(\mu^*) > 1$.

Therefore, the density of healthy hosts at equilibrium, when a proportion $\varphi > 0$ of R is cultivated, writes

$$S_S = \frac{1-\varphi}{\Psi(\mu^*)} \quad \text{and} \quad S_R = \frac{\varphi}{\Psi(\mu^*)}. \tag{D.17}$$

Therefore, (D.9)-(D.17) lead to $S_S + S_R > S_0$ if and only if $\Psi(\mu^*) < \Psi_S(\mu_S)$ meaning that with a strong-trade off on infection efficiency: (i) if $\Psi(\mu^*) < \Psi_S(\mu_S)$ the time during which a proportion $\varphi > 0$ of R gene deployed remains beneficial (in terms of Healthy Area Duration gain) can be consider larger as possible; (ii) else, this time is quantified by the unique time T such that $S_S(t) + S_R(t) \geq S_0(t)$ for all $0 < t \leq T$.

E $\mathcal{R}_0$ as the fitness proxy

By Equations (C.6) and (C.7), it comes

$$f_z(y) = \sum_{k=1}^{N_c} \frac{\Lambda \varphi_k \Psi_k(y)}{\theta + \beta_k(z) A^z} - 1. \tag{E.18}$$

Using Equation (C.8) defining the resident equilibrium, i.e. $\mathcal{R}(z, E^z) = 1$, (E.18) becomes

$$f_z(y) = \sum_{k=1}^{N_c} \frac{\Lambda \varphi_k}{\theta + \beta_k(z) A^z} \left(\Psi_k(y) - \Psi_k(z)\right). \tag{E.19}$$

When infection efficiencies do not differ between host classes (*i.e.* $\beta_k = \beta(x)$, for every k and every x). Then (E.19) gives

$$f_z(y) = \frac{\theta}{\theta + \beta(z) A^z} \left(\mathcal{R}_0(y) - \mathcal{R}_0(z)\right),$$

and then

$$\text{sign}(f_z(y)) = \text{sign}\left(\mathcal{R}_0(y) - \mathcal{R}_0(z)\right). \tag{E.20}$$

F Maximum points of the fitness function

Here we explicitly determine maxima of the fitness function (3.6) which writes:

$$\Psi_k(x) = \frac{1}{\delta} \frac{1}{\left[1 + \left(\theta + d_k(x)\right)/\lambda\right]^n} \beta_k(x) \times p_k(x) \times e^{-(\theta + d_k(x))\tau_k(x)}. \tag{F.21}$$

With the normally distributed function hypothesis, in the TSP scenario, the resistance imposes a trade-off on the total number of spores, such that

$$p_S(x) = p_0 \times \exp\left(-\frac{(x+\mu)^2}{2\sigma_S^2}\right),$$
$$p_R(x) = p_0 \times \exp\left(-\frac{(x-\mu)^2}{2\sigma_R^2}\right),$$

and infection efficiencies β_k,s are constants (*i.e.* $\beta_S(x) = \beta_R(x) = \beta_0$), wherein p_0, β_0 are positive constants. Since $d_k = 0$, (F.21) takes the form

$$\Psi_k(x) = C^{\text{te}} \times p_k(x) \times u\left(\frac{p_k(x)}{p_0}\right).$$

We then find that Ψ_k's maximum points are $-\mu + \sigma_S\sqrt{2\alpha\log(2)}$ and $\mu - \sigma_R\sqrt{2\alpha\log(2)}$ for S and R respectively.

In the TIE scenario, the resistance imposes a trade-off on the infection efficiency, such that

$$\beta_S(x) = \beta_0 \times \exp\left(-\frac{(x+\mu)^2}{2\sigma_S^2}\right),$$
$$\beta_R(x) = \beta_0 \times \exp\left(-\frac{(x-\mu)^2}{2\sigma_R^2}\right),$$

and the total spores produced p_k, are constants (*i.e.* $p_S(x) = p_R(x) = p_0$). Again, since $d_k = 0$, (F.21) takes the form

$$\Psi_k(x) = C^{\text{te}} \times \beta_k(x).$$

We then find that the maximum points of Ψ_k are $-\mu$ and μ for S and R respectively. Here, the within-host trade-off does not impact the optimal phenotype of the fitness function.