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High levels of auto-infection in plant pathogens favour short latent periods: a theoretical approach

F. van den Berg · S. Gaucel · C. Lannou · C. A. Gilligan ·
F. van den Bosch

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Abstract Auto-infection (infection arising from inoculum produced on the same host unit) is common in polycyclic plant pathogens, but often neglected in experimental and theoretical studies, which focus instead on infection of new hosts (allo-infection). Here we test the hypothesis that high auto-infection, as observed for leaf infecting fungal pathogens, could select for short latent periods. An individual-based simulation model keeps track of lesions, resulting from the spread of spores, between and within individual leaves. Linked to a trade-off between latent period and spore production capacity, as observed for *Puccinia triticina* on wheat, the adaptation of the latent period is analysed for different levels of auto-infection using the methods of pairwise invasibility plots. Results suggest that increased auto-infection selects for reduced latent periods. A reduction in leaf longevity also selects for reduced latent periods, which is most obvious for a relatively low ratio of auto- to allo-infection. This study is the first to consider the effect of auto-infection on the evolution of pathogen life history traits. The fact that auto-infection could drastically reduce pathogen latent periods highlights the need for more research in this area.

Keywords Auto-infection · Individual based model (IBM) · Latent period · Leaf level density dependence · *Puccinia triticina* (Brown rust) · Wheat

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F. van den Berg (✉) · F. van den Bosch
Department of Biomathematics and Bioinformatics, Rothamsted Research Harpenden,
Hertfordshire AL5 2JQ, UK
e-mail: Femke.vandenbergh@rothamsted.ac.uk

S. Gaucel · C. Lannou
INRA, UMR 1290 Bioger, 78850 Thiverval Grignon, France

C. A. Gilligan
Department of Plant Sciences, University of Cambridge, Downing Street, Cambridge CB2 3EA, UK

Introduction

Evolutionary models of parasites usually make a clear distinction between among-host transmission and within-host growth. Within-host growth allows the parasite to increase in size or number and ultimately to produce dispersal units for transmission. In such systems, within-host growth is damaging for the host and, since the parasite needs a living host for its own survival, it also has consequences for the parasite's fitness. This has classically been formalized as a virulence-transmission trade-off (Anderson and May 1982) and the evolutionary consequences of this trade-off have been investigated by many authors (e.g. Dieckmann et al. 2002). In most plant-parasite systems, however, within-host growth is very limited and a single infection or a few infections have no detectable effect on host fitness (Heraudet et al. 2008). In these systems, infections result in small localized lesions and disease transmission is realized by spores. A fraction of the spores produced by a parasite lesion is dispersed among the hosts and allows disease spread in the host population, but the remainder of the spores is dispersed over a very short distance away from the emitting lesion and thus re-infects the same leaf or plant. This process is referred to as auto-infection (Robinson 1976). Auto-infection thus considerably increases the disease level on a plant (Lannou et al. 2008) and allows the colonization of a host plant by the parasite.

Auto-infection has been measured for the rust pathogens (Lannou et al. 2008; Frezal et al. 2009) but is of epidemiological significance for any polycyclic air-borne pathogen (e.g. Robinson 1976; Schoeny et al. 2008). High levels of auto-infection lead to strong local density-dependence in the pathogen and are consequently likely to affect the spatial and temporal dynamics of epidemics and to increase local competition among pathogen genotypes and might even affect the genetic spatial structure of the pathogen population. Epidemiological implications of auto-infection have been discussed (Mundt 2002, 2009) but the evolutionary consequences of auto-infection in plant parasites remain largely unknown (Lannou 2012).

The effects of auto-infection on the evolution of plant pathogens have mainly been studied within the very specific context of varietal mixtures (Barrett 1980; Østergaard 1983; Lannou 2001) showing that in diversified host populations auto-infection dampens the evolution of the pathogen towards a higher complexity in terms of qualitative gene-for-gene virulence factors. In a different context, Tellier and Brown (2007) have shown that auto-infection helps to stabilise polymorphisms in gene-for-gene systems and is thus likely to have a large influence on plant pathogen evolution in general. However, the consequences of auto-infection on the evolution of pathogen life history traits have not yet been studied. In the present paper we investigate the effect of auto-infection on the evolution of an individual life history trait, the latent period.

The latent period is the time interval between infection and the onset of sporulation from the infection. It can be seen as analogous to “age at maturity” in other organisms (Nelson 1979; Heraudet et al. 2008) and determines, to a considerable extent, the pathogen's generation time (Sackett and Mundt 2005). It thus has a strong effect on epidemic velocity (Sackett and Mundt 2005) and severity (Lehman and Shaner 1996). It is well established that pathogens with a shorter latency outperform other slower parasites in the field, even if all of them have an equivalent propagation rate (Antonovics and Alexander 1989; Pringle and Taylor 2002; Lannou 2012). The latent period is thus expected to have a large influence on the rate at which pathogen strains are selected for. Note also that, in

pathogens such as rusts, spore emission follows a circadian periodicity (Pady et al. 1965) and even a small difference in latent period may result in a 1-day difference in spore release and leaf local invasion.

Evolution of the latent period in plant pathogens is not independent of other epidemiological traits. Increased evidence has come to light for the existence of a trade-off between latent period and spore production. This trade-off has been identified experimentally for the pathogen *Puccinia triticina* (Pariaud et al. 2012), as well as for several other patho-systems. Heraudet et al. (2008) identified a phenotypic trade-off between latent period and transmission success for the pathogen *Hyaloperonospora arabidopsis* on *Arabidopsis thaliana* and Andrivon et al. (2009) showed that in the potato pathogen *Phytophthora infestans* the latent period was linked to the total number of sporangia produced per lesion. Such a trade-off could result from the fact that shorter latent periods allow less time for mycelial structures to develop and thus allows for less resources to be taken up from the host, thereby resulting in the production of fewer spores.

In this paper, we test the hypothesis that in the presence of high levels of auto-infection, which results in strong local density-dependence, a pathogen will adapt to reduced latent periods because of the high level of competition for space on the infected leaves. When two infections simultaneously occur on the same leaf, the number of descendants resulting from auto-infection should be higher for the genotype with the shortest latent period, since the leaf area available for new infections is limited. However, despite the clear fitness advantage of a reduced latent period, there is an associated cost of a reduced spore production capacity due to the trade-off between latent period and spore production. We will thus investigate whether in the presence of a high level of auto-infection the benefits of a reduced latent period outweigh the associated costs of a reduced spore production capacity.

To investigate this question we develop an individual based simulation model (IBM) that keeps track of pathogen lesions resulting from the successful spread of individual spores both between and within individual leaf segments. Using the methods of pairwise invasibility plots we show that when this model is linked to a trade-off relationship between the latent period and spore production capacity, adaptation leads to intermediate latent periods known as continuously stable strategies (CSSs). We subsequently test the effect of the level of auto-infection on the location of this CSS.

Materials and methods

The *Puccinia triticina*–wheat pathosystem

This section provides a summary of the published experimental data used to inform the development of the population model and the trade-off relationship. The *P. triticina*–wheat pathosystem is used as a characteristic case study since for this system both a high level of auto-infection (Lannou et al. 2008; Frezal et al. 2009) and a trade-off between latent period and spore production capacity (Pariaud et al. 2012) have been identified experimentally. Furthermore, for this patho-system parameter values for all other life history traits are readily available.

Auto-infection

Rust species such as *P. triticina* are subject to relatively high levels of auto-infection. From Lannou et al. (2008) it can be calculated that about fifty percent of newly produced *P. triticina* spores remain on the parent leaf (see also Table 1).

Strain competition at the leaf level

The leaf tissue available for lesion development is limited and hence spores necessarily compete for space. Rust spores produced under different conditions have been shown to have the same nitrogen and carbon content (Robert et al. 2002). In the presence of stress it thus seems that the pathogen reduces the amount of spores produced rather than adjusting the nutritional and structural quality of the spore, thereby suggesting that individual spores do not differ in competitive capability due to density changes. In the presence of two pathogen strains, the probability that a newly arising lesion is of a given strain is assumed to be directly related to the relative spore density of that strain at that specific location on the leaf (see (1)). When auto-infection levels are relatively high, many spores remain on the parent leaf resulting in a relatively high spore density for that specific strain and this strain is thus more likely to win the local competition for space.

The trade-off relationship

A trade-off between a latent period and spore production capacity was identified experimentally for *P. triticina* infecting wheat leaves (Pariaud et al. 2012). The exact shape of the trade-off relationship is, however, hard to determine based on the data sets available. However, it is likely that spore production will become limited for large latent periods and we thus assume that the trade-off relationship can be mathematically represented by a Monod function (see (2)).

Trait selection

Lehman and Shaner (1996, 1997) showed that the latent period of *P. triticina* is under polygenic control and that there is heritable variation in the population for this trait. Similar results have been found for several other plant pathogens (Pariaud et al. 2009). The fact that there is selectable variation in the latent period makes this life-history trait a suitable candidate for evolutionary analysis.

Model development

A population model computes the progress of an invader pathogen strain in a resident pathogen population in the presence of leaf level density-dependence caused by auto-infection. This stochastic individual based population model is subsequently incorporated into an evolutionary model to study the evolutionary effect of auto-infection on the latent period of the pathogen. The main hypothesis in this paper is that in the presence of high levels of auto-infection a pathogen will adapt to reduced latent periods because of the high level of competition for space on the infected leaves. In the discussion we however consider an alternative hypothesis. See Online Appendix S1 for a more detailed description of the population model following the Overview, Design, Concepts, Details protocol (ODD) for individual-based models (Grimm et al. 2006).

Table 1 Model variables and default model parameters based on *P. triticina* on wheat

Symbol	Description	Value	Unit	Literature source and additional information
Variables				
S	Number of healthy sites			
$E_r (E_m)$	Number of sites containing a latent resident (invader) lesion			
$I_r (I_m)$	Number of sites containing an infectious resident (invader) lesion			
R	Number of removed sites			
P	Probability that the resident strain wins the competition for space			See (1)
$U_r (U_m)$	Number of resident (invader) spores deposited on a single site			The relative density of resident spores on the site determines the probability that the resident strain wins the competition for space. See also (1)
γ_{CSS} Parameters				
N	Evolutionary stable latent period			
M	Number of leaves in the population	1,000	–	Chosen arbitrarily
	Number of sites per leaf	500	–	Area directly under influence of auto-infection is 9 cm ² and at 100 % disease saturation contains 165 lesions/cm ² . We assume that density dependence reduces this number by a factor of 3
l/ω	Wheat leaf life span	48	Days	van den Berg et al. (2007) and Milne et al. (2003)
$\gamma_r (r_m)$	Latent period of resident (invader) lesion	11–17	Days	Field: 11–17 days (Lannou et al. 2008)
$1/\mu$	Infectious period	12	Days	Controlled environment: 18–20 days (Rime et al. 2005) Field: 11–18 days (observations by C. Lannou)
ψ	Infection efficiency	0.02	–	Adhesive strips with 0.8–1 spores/mm ² were used to inoculate leaves whereby a total strip area of 20 cm ² resulted in 2–73 lesions (Lannou et al. 2008)
δ	Probability of dispersal death	0.1	–	Chosen arbitrarily
φ	Auto-infection fraction	0.5	–	Fig. 2a of Lannou et al. (2008): 150 lesions produced around mother lesion due to auto-infection; 50 lesions on rest of leaf; 10 lesions on 10 neighbouring leaves, so 50 % of all lesions due to auto-infection

Table 1 continued

Symbol	Description	Value	Unit	Literature source and additional information
σ_r (σ_m)	Number of resident (invader) spores produced per lesion per day	67	Day ⁻¹	At intermediate latent periods <i>P. triticina</i> produces 30 μg spores/ mm^2 between day 21 and 23 after inoculation (Pariaud et al. 2012). Given, infectious period is 12 days, lesion size is 1.8 mm^2 and 1 mg spores gives around 200,000 spores, this gives around 40,000 spores per generation. Divide by 5 for conversion from CE to field data. Divide by 10 to represent initial spore loss (e.g. blown out of the system). Divide by infectious period, $1/\mu$, to derive the number of spores produced per lesion per day
ρ	Shape parameter	0.13	–	Defines the steepness of trade-off relationship
η/ρ	Maximum spore production	1,154	–	Chosen such that the resulting CSS latent period falls within the range of latent periods found under field conditions
B	Healthy site generation rate		Day ⁻¹	The generation rate does not need to be quantified as it does not affect the CSS latent period (see “ODE model”)
β	Transmission rate		Day ⁻¹	See comments for B

Host structure

The plant population is represented by a fixed number of individual leaf units, N , whereby each leaf unit contains a fixed number of, M , sites (an area of leaf that can contain one lesion). In the model presented in this paper we assume that a leaf is represented by a number of sites that is under the direct influence of auto-infection. We use an SEIR (Anderson and May 1991) model framework where each site on a leaf belongs to one of four classes: healthy (S), exposed (E) containing a single latent lesion, infectious (I) containing a single sporulating lesion or removed (R) containing a single dead/necrotic lesion. Leaves have a fixed probability per time unit, ω , to die due to natural causes other than the pathogen (Fig. 1). In order to study the equilibrium properties of the system we assume that a dead leaf is replaced by a completely healthy leaf, leading to a continuous supply of host tissue.

Dynamics of the resident pathogen strain

Figure 1 gives a schematic representation of the dynamics of the resident pathogen strain. Healthy sites become exposed (latent) upon infection by an effective pathogen spore. These lesions have a fixed probability per unit time, $1/\gamma_r$, to leave the latent stage and to become infectious (sporulating), whereas sporulating lesions have a fixed probability per unit time, μ , to be moved to the removed class. The total number of new infections depends upon the number of effective pathogen spores that land on healthy sites within the host population. This number is determined by the following processes:

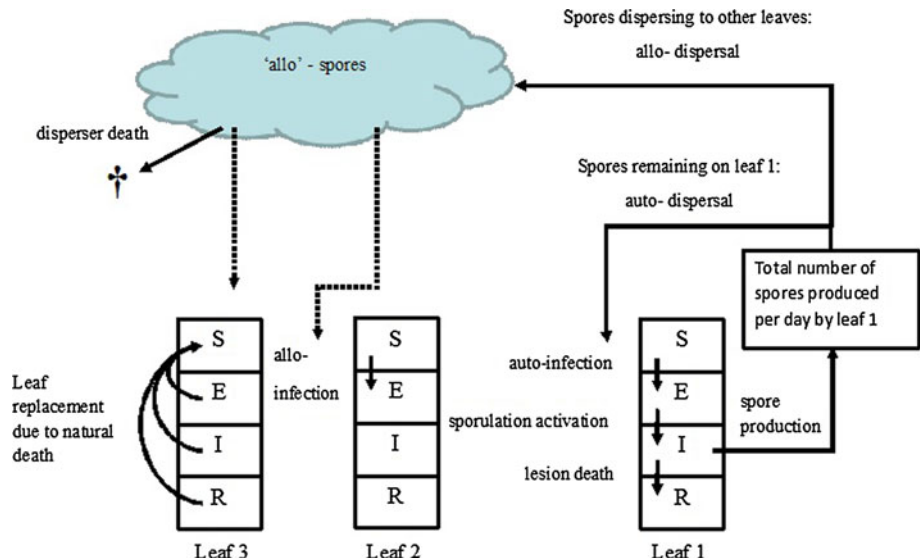


Fig. 1 Schematic overview of the resident pathogen strain dynamics. The boxes labelled S, E, I and R represent the total number of healthy, exposed (latent), infectious (sporulating) and removed sites on the leaf of interest, respectively and together make up the total number of sites on a leaf. The arrows between boxes indicate the processes driving the change in state of leaf sites

Sporulation Each sporulating resident lesion produces a fixed number of spores per unit time, σ_r , which is linked to its latent period through the trade-off (see ‘[Evolutionary dynamics](#)’ for details of the trade-off relationship).

Dispersal Of the newly produced spores a fixed fraction, ϕ , remains on the parent leaf (auto-infection), whereas all other spores, $1 - \phi$, disperse to other leaves within the host population (allo-infection). There is a fixed probability per unit time, δ , for spores to leave the system due to spore death, deposition on the ground or leaving the canopy boundary layer.

Spore deposition An allo-infecting spore is deposited on a randomly selected leaf. All auto- and allo-infecting spores either land on a healthy site with the potential of causing infection or on an occupied site which leads to spore death.

Infection success Whether a spore that lands on a healthy site results in infection depends on the pathogen’s infection efficiency, ψ . Upon successful infection, the healthy site develops a latent lesion and thus moves to the exposed class.

Dynamics of the invader pathogen strain in the resident pathogen population

An invader pathogen strain can arise through a mutation in the resident strain. Invader lesions differ from lesions of the resident strain in their latent period and their associated spore production, whereas all other life-history traits, such as the infection efficiency, remain unchanged. This means that in the presence of the invader strain each site on a leaf belongs to one of six rather than four classes: healthy (S), exposed (E_r) containing a single latent lesion of the resident type, exposed (E_m) containing a single latent lesion of the invader type, infectious (I_r) containing a single sporulating lesion of the resident type, infectious (I_m) containing a sporulating lesion of the invader type or removed (R) containing a dead/necrotic lesion (cf. Fig. 1). Because we investigate the success of a newly arisen invader strain in an existing resident population we assume that mutation occurs in one direction only.

Infection success If all spores deposited on a healthy site are of the resident/invader strain only, the site will develop into an exposed site of the resident/invader type. If a mixture of resident and invader spores is deposited on a healthy site competition for space takes place, whereby the relative density of resident spores determines the probability, P , that the resident strain wins the competition, i.e.

$$P = \frac{U_r}{U_r + U_m} \quad (1)$$

where U_r and U_m denote the number of resident and invader spores, respectively. If the resident strain wins the competition the latent lesion that develops on the exposed site will be of the resident type, otherwise the latent lesion will be of the invader type.

Initial conditions, updating procedures and output

The parameter values of the population model are based on the *P. triticina*—wheat pathosystem and can be found in Table 1. At the start of a simulation all leaves are entirely

healthy, with the exception of one randomly assigned leaf that contains a single latent lesion of the resident strain. All processes described above take place each time step, which is represented by 1 day. At the end of each time step the means of the number of sites of each type on an individual leaf are calculated. These means give a clear overview of infection and hence disease progress over time (See results and Fig. 3 for an example) and are used in the evolutionary algorithm to decide whether invasion is successful or not.

Because the model is designed to study the fate of a newly emerging strain in the resident pathogen population, the population model is first run in the absence of the invader until the resident population has reached equilibrium. For each parameter combination used to create the results presented in this paper we initially ran fifty simulations in which only the resident strain was present. For all these simulations the mean number of sites on a leaf within each class roughly converged to a constant value well within 3 years (*cf.* Fig. 3). In all further simulations we thus assumed that in the absence of the invader, the resident population has reached equilibrium after 3 years. The invader strain is introduced after 3 years, i.e. at equilibrium, by adding one infectious site of the invader type to ten randomly selected leaves and subsequently determining the fate of the invader strain. Invasion is assumed successful if the resident population dies out and unsuccessful when the invader population dies out. Typically one of the strains dies out within a few years to several decades after the introduction of the invader strain. There are however some rare cases where complete strain replacement by the invader strain takes more than a hundred years. In these extreme and rare cases we adopt a much longer invasion criterion which states that if after 250 years the mean number of sporulating lesions per leaf that are of the invader type (meSPM) is still smaller than 1, we consider the invasion to be unsuccessful. If this number exceeds 1 we consider that the invader has established and that invasion is successful. As commonly assumed in this kind of an approach, phenotypic changes are assumed to be small and to occur rarely enough for the system to have converged to equilibrium before the next mutation occurs.

Evolutionary dynamics

The population model is used to study the effect of auto-infection on the selection of a pathogen's latent period by using pair-wise invasibility plots (PIPs; Fig. 3; Geritz et al. 1998) (Fig. 4). The PIPs show for each resident latent period value, γ_r , all invader latent period values, γ_m , for which an initially rare invader either invades the environment set by the resident and replaces the resident population (the invader has a positive population growth rate) or dies out (the invader has a negative population growth rate). In PIPs, the fitness environment as experienced by a rare invader corresponds to the vertical lines (*cf.* Fig. 4) where the resident trait value, γ_r , is constant. Neutrality curves separate areas of successful invasion of the initially rare invader from those of unsuccessful invasion. Since the resident phenotype value is neutral in its own environment the neutrality curves always include the main diagonal, i.e. for $\gamma_m = \gamma_r$ the invader's population growth rate is zero (Fig. 4).

Latent periods for which the neutrality curves intersect are the evolutionarily singular strategies and denote potential evolutionary endpoints. The singular strategies can subsequently be classified visually from the PIP as discussed in Geritz et al. (1998). See also Waxman and Gavrillets (2005) for a more population geneticist's interpretation of adaptive dynamics. The singular strategy is an evolutionary stable strategy (ESS) if the singularity is uninvadable and if this ESS is also an attractor whereby evolution is towards the singular strategy the strategy is said to be a convergence stable strategy (CSS). On the other hand, when evolution is away from the singular strategy the singularity is an evolutionary

repeller. Finally, when evolution is initially towards the singular strategy but once reached the population branches into two coexisting strains the singularity is called an evolutionary branching point.

Extensive numerical studies suggest that in our model all singular strategies are of the ESS type. Further interpretation of the PIPs shows that in our case all ESSs are also convergence stable and thus all singular strategies discussed in this paper are continuously stable strategies (CSSs). The invasion success indicated in the final PIPs is based on up to 100 replicates. When none of the hundred replicates record invasion the final PIP point is scored as unsuccessful invasion whereas as soon as one of the hundred replicates finds successful invasion the final PIP point is scored as successful invasion. This whole process is repeated three times for each point within the PIP and the final result, i.e. successful or unsuccessful invasion, determined according to a majority rule. Once the CSS latent period is determined for the default fraction of auto-infection, the fraction of auto-infection is altered to study its effect on the location of the CSS.

Trade-off relationship The trade-off relationship is modelled as a Monod function leading to

$$\sigma_i = \mu \left(\frac{\eta \gamma_i}{1 + \rho \gamma_i} \right) \quad \text{with } i = \{r, m\} \quad (2)$$

with σ_i the strain specific total number of spores produced per lesion per day given that the lesion is alive, γ_i the strain specific latent period, η/ρ the maximum number of spores produced over the life time of a lesion and ρ an indication for the steepness of the trade-off and whereby spore production is maximised for infinite values of γ_i . The values for η and ρ were chosen such that the resulting CSS latent period falls within the range of *P. tritici* latent periods found under field conditions (Table 1; Fig. 4a).

See Fig. 2 for a schematic overview of the full conceptual model.

Results

Population dynamics

Successful invasion by an invader strain tends to be characterised by a series of small local epidemic outbreaks of which one eventually manages to spread globally through spore dispersal to neighbouring leaves (Fig. 3a). Through this global spread the invader strain eventually replaces the resident strain in the population. When invasion by an invader strain is classed as unsuccessful, local small scale epidemic outbreaks might still occur when the newly arising invader spores by chance give rise to lesions on a leaf with a relatively high number of healthy sites. However, these local epidemic outbreaks are never able to spread globally and the resident strain thus remains the dominant strain in the population (Fig. 3b). The occurrence of local epidemic outbreaks increases with the ratio of auto- to allo-infection.

Effect of auto-infection level on the CSS latent period

In the PIPs, the intersection point of the neutrality curves separating the areas of successful and unsuccessful invasion by an invader strategy represents the continuously stable

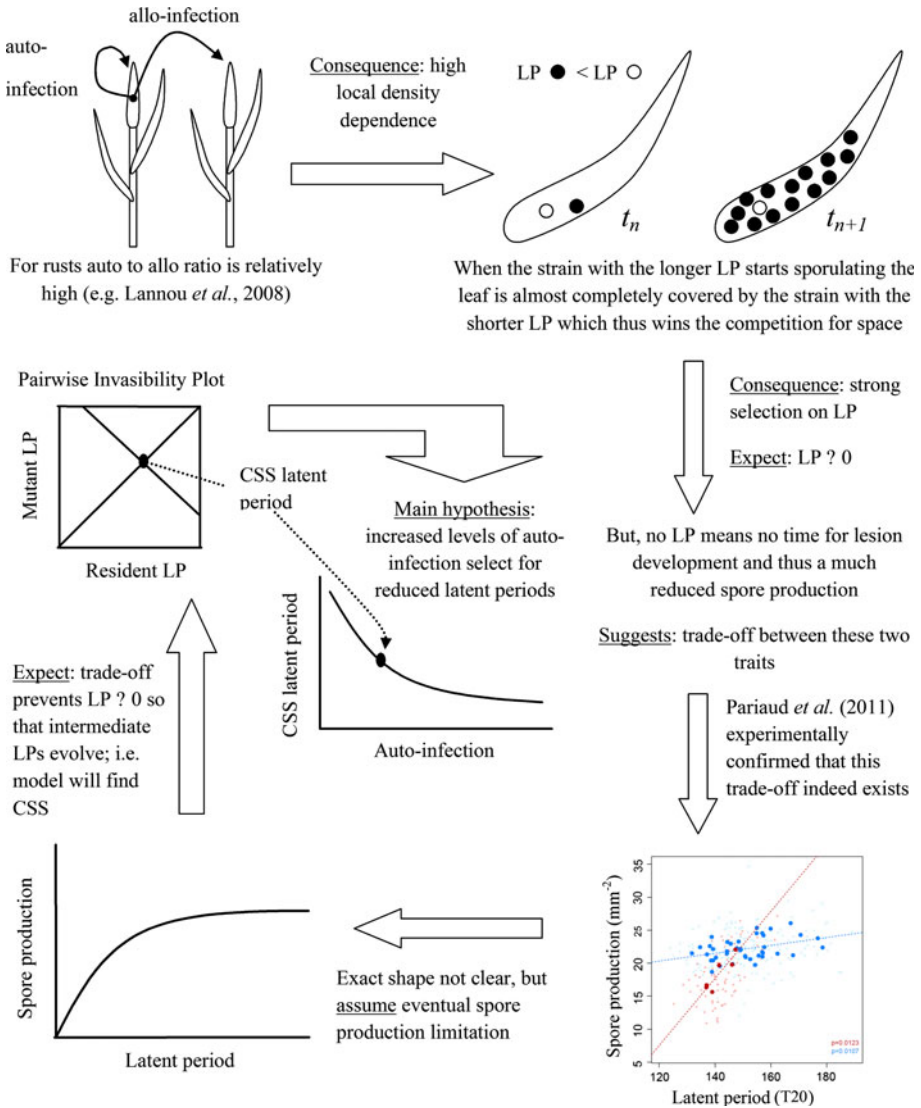


Fig. 2 Schematic overview of the conceptual model

strategy, i.e. the CSS latent period (Fig. 4). The CSS latent period decreases with increased levels of auto-infection (Figs. 4, 5).

Effect of other life-cycle parameters

Shorter leaf longevity selects for a reduced latent period, but these effects decrease with an increasing ratio of auto- to allo-infection (Fig. 5a). Changes in the infection efficiency of the pathogen do not put a selection pressure on the evolution of the pathogen’s latent period (Fig. 6a) whereas changes in the shape of the LP trade-off do (Fig. 6b). A trade-off

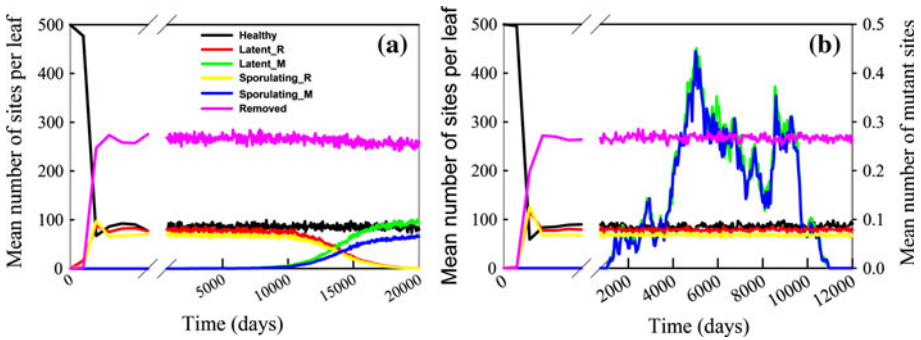


Fig. 3 Dynamics of the mean number of each type of sites per leaf for an invader strain being introduced at time $t = 1,095$ days. The resident population has a latent period of 11 days, whereas the invader population has a latent period of either 14 days (a) or 10 days (b), leading to successful and unsuccessful invasion, respectively. Note that in a the scale of the y-axis is identical for the resident and the invader, but not in b

with a larger maximum number of spores produced per time unit (lower ρ value) results in the selection of an increased latent period (Fig. 6b).

Comparison with a classical ODE model

In the absence of auto-infection newly produced spores spread homogenously over the host population, i.e. there is no local density-dependence. In this case, on average, each spore has the same probability to land on a particular healthy site and thus each spore has the same probability to result in infection. In the absence of auto-infection our individual based model thus becomes a stochastic version of the ordinary differential equation (ODE) system:

$$\begin{aligned}
 dS/dt &= B - \beta IS - \omega S \\
 dE/dt &= \beta IS - E/\gamma - \omega E \\
 dI/dt &= E/\gamma - \mu I - \omega I \\
 dR/dt &= \mu I - \omega R
 \end{aligned}
 \quad \text{with} \quad
 \begin{cases}
 B = \omega(S + E + I + R) = \omega M \\
 \beta = \frac{\eta\gamma}{1 + \rho\gamma}
 \end{cases}
 \quad (3)$$

where B is the healthy tissue generation rate, β the transmission rate, ω the leaf death rate, γ the latent period and $1/\mu$ the infectious period. As in our individual-based model there is a trade-off between infection success and latent period. The basic reproduction number, R_0 , defined as the total number of infections arising from one newly infected individual introduced into a healthy population is for this system given by

$$R_0 = \frac{\beta \bar{S}_0}{\omega + \mu} \frac{1}{1 + \gamma\omega} = \frac{\eta\gamma B}{\omega(1 + \rho\gamma)(\omega + \mu)(1 + \gamma\omega)} \quad (4)$$

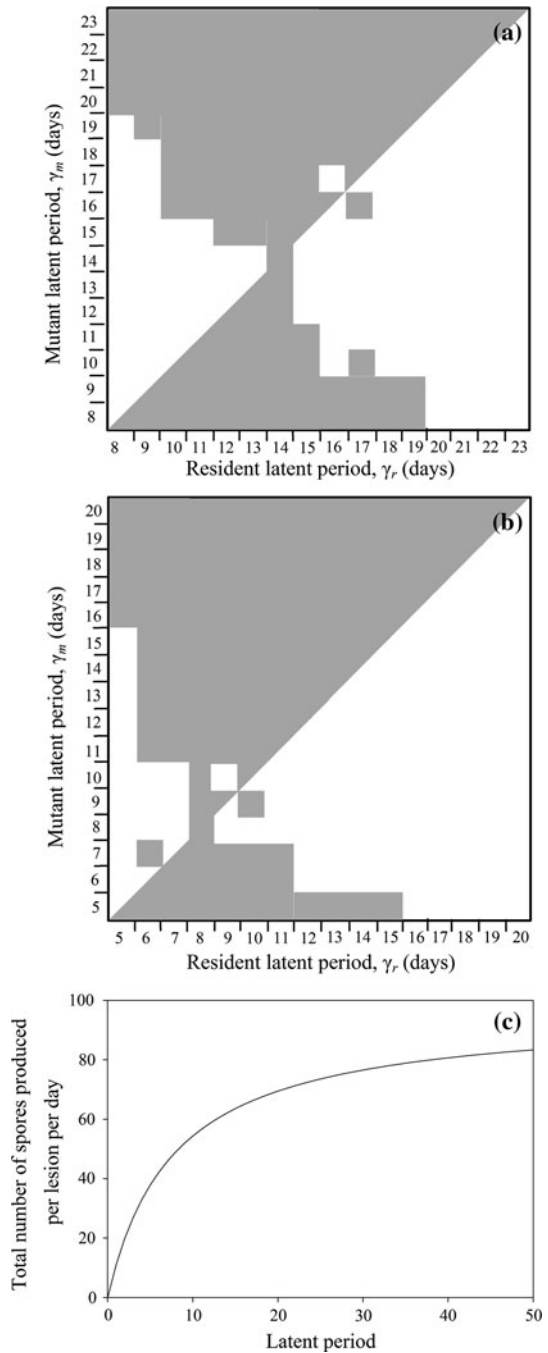
with \bar{S}_0 the disease free host equilibrium.

For this simple ODE model excluding auto-infection, solving $dR_0/d\gamma = 0$ for γ , leading to

$$\gamma_{\text{singular}} = 1/\sqrt{\rho\omega} \quad (5)$$

gives the singular strategies of the system. In our system, where the pathogen competes for a single resource, i.e. healthy sites, the second derivatives indicate that these singular

Fig. 4 Examples of a pairwise invasibility plot (PIP) for **a** the default scenario with an auto-infection fraction of 0.5 and **b** an auto-infection fraction of 0.9. The *white areas* represent strategies for which the invader strain can invade the resident population, whereas the *grey areas* represent strategies for which the invader strain cannot invade. The latent period at which the lines separating the areas of opposing colour intersect denotes the pathogen’s evolutionary stable state. **c** The trade-off relationship between latent period and spore production



strategies are both uninvadable and convergence stable (see e.g. Geritz et al. 1998), i.e. $\gamma_{\text{singular}} = \gamma_{\text{CSS}}$.

As for the stochastic individual based model the ODE model reveals that shorter leaf longevities select for reduced latent periods (Fig. 5b). Although such an ODE system

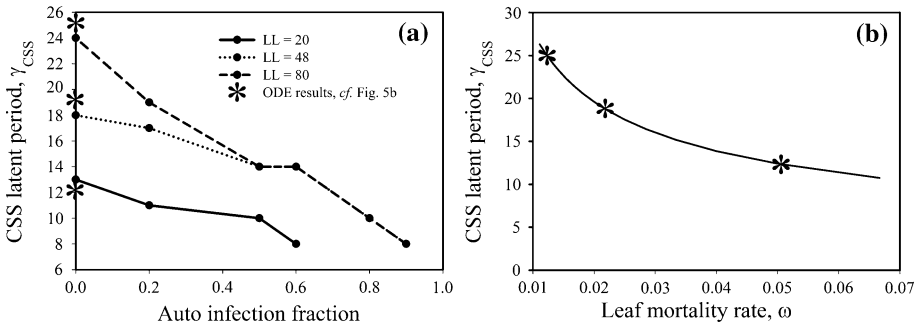


Fig. 5 **a** Effect of auto-infection (i.e. leaf level density dependence) on the evolutionary stable latent period strategy (CSS) for different leaf longevities (LL) and as calculated with the IBM model. *Solid line* leaf longevity = 20, *dotted line* leaf longevity = 48 and *dashed line* leaf longevity = 80. *Solid circles* represent the CSS values as derived from the simulated PIPs, whereas *lines* represent the trends across these points. *Stars* indicate CSS latent period values as calculated analytically with the ODE model (cf. Fig. 5b). **b** Effect of leaf longevity on the evolutionary stable latent period as calculated with the ODE model

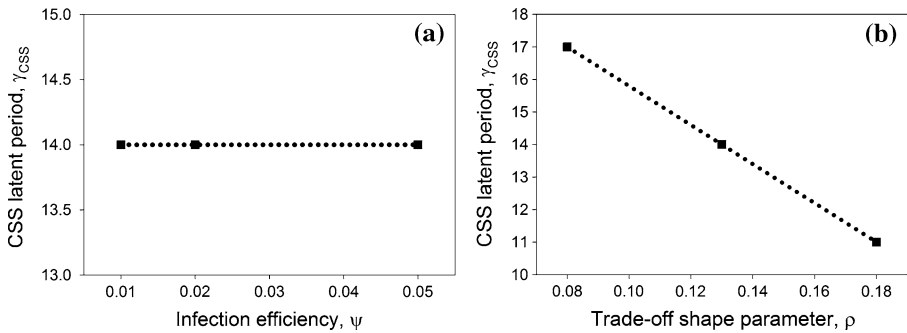


Fig. 6 Effect of **a** infection efficiency and **b** trade-off shape parameter ρ on the CSS latent period under the default level of auto-infection. The fraction of auto-to allo-infection is 0.5. Increasing ρ reduces the maximum number of spores produced over the life-time of a lesion

cannot generate predictions for the effect of auto-infection on the evolution of the latent period, it provides a model validation by comparing the ODE analysis results (stars in Fig. 5a, b) with those found by our model for the scenario of no auto-infection (Fig. 5a). This comparison reveals that both models find very similar CSS latent periods.

Discussion

Polycyclic foliar plant pathogens tend to be subject to relatively high levels of auto-infection (Lannou et al. 2008; Frezal et al. 2009) yet few studies investigate the epidemiological and evolutionary consequences of the presence of auto-infection. Tellier and Brown (2007) have shown that auto-infection helps stabilise polymorphisms in gene-for-gene systems, but don't consider auto-infection as a selection pressure itself. Furthermore, current models incorporating auto-infection do not consider local leaf level density-dependence effected by local space limitation (van den Berg and van den Bosch 2004;

Tellier and Brown 2007). The methods described in Metz and Gyllenberg (2001) allow our model system to be expressed analytically whereby differential equations track the fraction of leaves with various numbers of sites (n) in the different infection states together with a spore disperser density. However, considering that each site on a leaf can be in one of 4 infection states (healthy, latent, infectious or removed) and that each leaf contains 500 sites it was proven computationally impossible to model the required number of sites per leaf with this analytical approach (this would require several million differential equations to be solved simultaneously). The hypothesis was therefore tested with a numerical approach and the resultant model suggests that the presence of auto-infection could potentially have significant evolutionary consequences.

High levels of auto-infection lead to a strong local increase in pathogen density. It is already well known that differences in lesion density lead to a plastic response in pathogen development, resulting in reduced lesion sizes, shorter latent periods and a reduced spore production (Robert et al. 2004; Rime et al. 2005; Cooke et al. 2006). Here we show that auto-infection might also result in selective effects in favour of genotypes with shorter latent periods.

The model study suggests that a high level of auto-infection and its associated local density dependence selects for strains adopting a fast colonising strategy, which is represented by a short latent period (Fig. 5). Shorter leaf longevities might also pose a selection pressure on the pathogen leading to shorter latent periods (Fig. 5). This makes intuitive sense since biotrophic pathogens require live plant tissue to survive and sporulate and a reduced leaf longevity thus increases the chance that a lesion will die before sporulation has taken place. These effects decrease with an increasing ratio of auto- to allo-infection, suggesting that ignoring auto-infection will overestimate the selection pressure of reduced leaf longevities. De Jong et al. (2000) showed that local density-dependence has similar evolutionary consequences for generation times in monocarpic (semelparous) plants, whereby increasing within-patch seed dispersal as compared with the between-patch seed dispersal selects for shorter generation times. Furthermore, similar to us, they find that when the patch survival increases there is selection for longer generation times. The advantages of early plant reproduction have been extensively explored by plant ecologists (Begon et al. 1990), but the current study is the first to make such inferences about plant pathogen dynamics. In the absence of auto-infection the results from the stochastic IBM model compare well with those from its equivalent non-stochastic ODE model (Fig. 5). This suggests that our IBM model compares well with the classical mean-field models but also reinforces the idea that auto-infection should be considered in plant pathogen models.

The CSS latent period is not affected by the infection efficiency (Fig. 6a). Reducing the infection efficiency increases the time it takes for a leaf to become saturated but, with our approach, at the point of invasion the resident population is at equilibrium, which means that there is already a very high density of spores in the air. Reducing the infection efficiency is thus very unlikely to relax the local density effect and the infection efficiency does thus not select for changes in the CSS latent period.

A central assumption in pathogen evolution models is that trait adaptation is limited by the existence of trade-offs between individual life history traits. For fungal plant pathogens, trade-offs have been suggested between survival and transmission (Montarry et al. 2007) and latent period and transmission success (Heraudet et al. 2008) and a trade-off has been demonstrated between latent period and spore production capacity (Pariaud et al. 2012). Nevertheless, experimental evidence for the existence of trade-offs remains limited for fungal plant pathogens (Sacristan and Garcia-Arenal 2008) and the few studies

exploring the existence of trade-offs between quantitative traits of the plant-pathogen interaction have so far not been able to establish the shape of these trade-offs. In our study, the CSS latent period is strongly affected by trade-off shape (Fig. 6b). We studied the effect of the trade-off shape on the CSS latent period by varying ρ . When this parameter is reduced, the maximum number of spores produced over the life-span of a lesion (i.e. η/ρ , cf. (2)) increases whereas the initial growth rate of the curve remains unchanged. The fact that a trade-off with an increased maximum number of spores produced results in weaker selection for shorter latent periods seems logical since under these conditions longer latent periods have the clear benefit of higher spore production whereas the relative cost of shorter latent periods (the trade-off steepness) remains unchanged. These results highlight the importance of obtaining more experimental data, especially field based data, to establish the exact shape of pathogen trade-off relationships.

Although parameter changes within realistic ranges do not seem to affect the qualitative nature of the results (Figs. 5, 6) there is always the possibility that more realistic expressions of certain life-cycle traits might have an effect on the model results. For example, for simplicity and as is custom in mathematical models, we assumed that the number of spores produced per day is constant during the infectious period. However, it has been shown for *P. triticina* and other similar pathogens that, after the latent period, sporulation rapidly increases to a peak and then tapers off slowly until the host tissue necroses. With a more realistic spore production curve the spore production would be relatively more intense early on during the infectious period. We expect that this would lead to an even stronger density dependent competition for available healthy leaf tissue and it is thus likely that a more realistic spore production curve would reinforce the selection for shorter latent periods, although we expect the difference to be of a purely quantitative nature.

The model suggests that the potentially large local epidemic outbreaks resulting from high levels of auto-infection might have strong disease management implications. Consider two neighbouring fields, one containing a susceptible cultivar and the other a qualitatively resistant cultivar (here, resistance confers immunity as often the case in an agricultural context). In such a system pathogen mutation allowing infection of the resident cultivar occurs only within the field with the susceptible cultivar, since the resistant field is free of disease. Even though the invaders that occur in the susceptible field will generally get overwhelmed by the resident strain, local success (as shown in Fig. 3b) might lead to an inoculum build-up sufficient for spread to the neighbouring resistant fields. Since the invader is able to break the crop resistance, this might subsequently lead to successful invasion. This would mean that local inoculum build-up due to auto-infection could lead to resistance breakdown, at a multi-plot scale, even if the new invader only builds up transient and undetectable populations in the susceptible fields. The durability of resistance to disease in crops is often directly attributed to the number of resistance genes in the host. However, conclusions about durability should be based not only on host resistance but also on pathogen epidemiology and the ability of pathogen invaders to overcome host resistance. Taking into account the combined effects of evolutionary constraints (trade-offs) and dispersal patterns (auto-infection and spore exchange between plots with different cultivars), would thus lead to a more realistic approach for investigating resistance durability.

Auto-infection is difficult to measure directly (Lannou et al. 2008) and it would be even more challenging, if not impossible, to manipulate auto-infection levels experimentally within a patho-system in order to study the evolutionary consequences of changes in auto-infection. However, as an alternative, published data could be used to test whether high

levels of auto-infection are generally correlated with relatively short latent periods. Unfortunately, as of yet, there are too few patho-systems for which auto-infection estimates are available to allow for such comparison. Further experimental work with respect to auto-infection thus seems crucial, even though modelling approaches as developed in this paper can effectively be used to complement the few existing experimental data.

Despite the relatively high number of replicates, some false positive and false negative results occurred in the simulations (see Fig. 4a, b), especially close to the neutrality curves where resident and invader strategies are similar. False negative results occur because of a lack of replicates or, in very rare cases, when invasion is successful but the invasion threshold is not reached within the allowed 250 years of invader presence. Such false negatives are most frequent when the ratio of auto-to allo-infection is small. False positive results occur when, due to stochasticity, the conditions for the resident strain are temporarily sub-optimal giving the invader an otherwise unavailable advantage and are most frequent when the ratio of auto- to allo-infection is high. Because the simulations are stopped as soon as invasion has occurred, the risk of false positive results increases with the number of replicates. Besides stochasticity, the discrete time step in latent period and spore densities also contribute to these irregularities around the neutrality curves and are typical for stochastic, individual-based models (Pels et al. 2002; Salathé et al. 2007). Despite these minor irregularities, the general patterns can readily be recognised.

In this paper we test the initial hypothesis that the presence of high levels of auto-infection results in strong local density dependent competition for space between pathogen strains, leading the pathogen to adapt to reduced latent periods. However, an alternative hypothesis that deserves future attention is that the patterns observed are not simply a result of increased density dependent competition, but instead the result of increased relatedness (kin selection). In the presence of high levels of auto-infection the majority of offspring remains close to the original lesion, which means that increased levels of auto-infection are likely to result in an increased relatedness between individuals infecting the same plant. Day and Taylor (2000) for example showed that in competing plant populations increased relatedness results in the plants to adapt to switch from pure growth to pure reproduction earlier during the growing season. Moreover, they find that evolution optimises the life time reproductive output (R_0) when all individuals are related. In our case we expect R_0 to be optimal for relatively high levels of auto-infection, but R_0 cannot be optimal for an auto-infection fraction of 1, since when all spores land locally the epidemic cannot sustain itself. It is important to note though that in this paper auto-infection is expressed at the leaf level, not the plant level. Since leaves are relatively small and allow only a limited number of infections to occur, once infected, they tend to become rapidly saturated with disease (Fig. 2). The leaves then die and get replaced with completely healthy new leaves. Colonisation of these leaves results from spores originating from other previously infected leaves whereby the dispersing spores are randomly mixed at each generation before infecting new healthy leaves. In our model, as well as in the corresponding biological system, auto-infection is thus likely to increase relatedness at the leaf level but, due to the relatively short life expectancy of the leaves, this is only a transient effect. So, at the leaf level auto-infection favours strains with a shorter latent period since leaves co-infected with mutants and residents tend to produce more mutants, whereas the pathogen is unlikely to produce enough generations on the same leaf for a kin selection effect to occur. However, in systems with much longer lived patches that allow for multiple pathogen generations, increased auto-infection might lead to substantial kin selection. In fact, when all infections on a leaf are of the same genotype evolution is likely to select for strains that maximise spore production and hence increased latent periods (Alizon and Taylor 2008).

Although there seem to be clear parallels between the original and alternative hypothesis in this specific case we believe that auto-infection selects for reduced latent periods due to increased local density dependent competition.

To facilitate interpretation and analysis, the model does not currently incorporate seasonality. This poses the question of the potential elimination of the invading strain at the end of the epidemic season via genetic drift when the pathogen population goes through its annual bottleneck. Although the larger resident population densities, when faced with a bottleneck, are beneficial in that they increase the pathogen's probability to survive between seasons, the invaders that do survive until the onset of the following season have the clear advantage of a reduced latent period providing them with a head start in this new season. Interestingly, it has been shown that bottlenecks do not necessarily lead to extinction of the less frequent invader strain even when the dilution effect between seasons is quite severe (Wahl et al. 2002; Escarmis et al. 2006). The inclusion of seasonality and the consequential bottlenecks are likely to have a considerable effect on the short term population dynamics, but it is not immediately clear how this would affect the long term dynamics. Furthermore, in seasonal systems whereby spores need to survive a period of host absence the trade-off relationships may vary from the "classical" relationships generally defined for non-seasonal SIR models with direct contact between individuals (see e.g. Caraco and Wang 2008). In future studies it is thus essential to test how the results are affected by different trade-off relationships since the authors have previously shown that different trade-off relationships can lead to opposing selection pressures (van den Berg et al. 2011).

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