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Lay summary.

Powdery mildew is a relatively new yet already common foliar disease of European oak trees, caused by a complex of fungal species that coevolved with Asian oaks and were introduced to Europe last century. To explore its eco-evolutionary dynamics, we developed a semi-discrete model combining a SIR model in the epidemic phase and a discrete-time model between years. This model, based on a within year - between year transmission trade-off, adequately described two main features of the disease: seasonality and the occurrence of a pathogen complex. We discuss refinement of this model and other modelling approaches for the evolution of virulence and resistance in a context of changing environment.

Abstract.

Oak powdery mildew in Europe is an example of disease in a wild perennial plant which has displayed dramatic changes over the course of a century; from typical invasion dynamics after pathogen introduction into a new area, characterized by severe damage, to a new equilibrium with moderate damage. Several non-mutually exclusive hypotheses could account for this, including pathogen evolution towards lower virulence, a reciprocal increase in oak population resistance, and both environmental biotic (phyllosphere microbes) and abiotic (climate) factors. We show that understanding the pathosystem requires the accounting of both seasonality (i.e. succession of epidemic and inter-epidemic phases linked to availability of susceptible leaves) and the occurrence of a pathogen complex with several cryptic fungal species differing in their life history traits. Observational data suggests that the severity of annual epidemics is linked to inter-annual pathogen transmission, including winter survival and the infection success of the primary inoculum in spring. Climate-driven phenological synchrony between host and pathogen in spring thus appears to be a critical factor. Several cryptic *Erysiphe* species are associated with the disease and co-occur at multiple spatial scales from individual leaves to continent. A semi-discrete model combining a SIR model in the epidemic phase and a discrete-time model between years, based on a within season (intra-epidemic) - between season (inter-epidemic) transmission trade-off, adequately describes seasonality and the coexistence of pathogen species. We discuss the refinement of this model, through the introduction of age classes in the host population in particular, and other modelling approaches for the evolution of pathogen virulence and host resistance in a context of changing environment.

Figure 15.1 Oak powdery mildew symptoms. Clockwise from upper left corner: (1) first symptoms visible in spring, the flag shoots, corresponding to heavily infected shoots (=covered in mycelium and spores giving a white, cottony appearance) developing from buds infected in the previous season; (2) primary infections (white spots) corresponding to ascospore-derived colonies; (3) severe infection on oak seedlings; (4) infection on leaves of the first flush in a mature oak tree; (5) infection of the second flush is generally much more severe than that of the first flush; (6) severe infection leads to necrosis, distortion, early senescence of leaves and, finally, defoliation.

15.1 Introduction.

All plants interact with a diversity of pathogens, increasingly recognized as playing major roles in population and community ecology and evolutionary dynamics (e.g. Mordecai, 2011; Bever *et al.*, 2015). Although by definition pathogens inflict fitness costs to the individuals they infect, their effects in natural plant communities may be subtle, often passing unnoticed. Indeed, disease impact is rarely catastrophic over large spatial scales in co-evolved systems. Disease prevalence may be high at the meta-population level, but epidemics in wild plant - pathogen systems ('pathosystems', *sensu* Robinson, 1976) are often limited in time and space and have a low to moderate impact (Burdon *et al.,* 2013; Jousimo *et al.,* 2014). By contrast, plant diseases may have catastrophic effects in agricultural ecosystems or when new (non-native) pathogens are introduced into plant communities (Pautasso *et al.,* 2005). Agricultural ecosystems are characterized by high environmental and genetic uniformity,

2

favouring pathogen transmission and leading to the emergence of highly virulent host-specialized plant pathogens (Stukenbrock & McDonald, 2008). Conversely, wild plant communities are much more diverse but can be severely affected by introduced non-co-evolved pathogens (Pautasso *et al.,* 2005; Desprez-Loustau *et al.,* 2007).

Despite the contrasting features of different plant–pathogen associations (i.e. wild versus cultivated ecosystems, co-evolved versus non-coevolved interactions), Burdon *et al.* (2013) suggested they could be placed on the same continuum. Trajectories along this continuum are driven by ecological and genetic changes which contribute to the dynamic stability/instability of host-pathogen associations at different times. Oak powdery mildew in Europe illustrates this concept well. This foliar disease (Figure 15.1) is now one of the most common in European forests. It generally has moderate impact with highly variable prevalence over space and time, as typical of native plant-pathogen associations (Marçais & Desprez-Loustau, 2014). However very severe damage, including high local mortality rates, was reported when the disease suddenly appeared and spread throughout Europe at the start of the twentieth century (Mougou *et al.,* 2008; Figure 15.2). This raised fears that European oaks might disappear, just as current pathogen invasions are considered a threat to indigenous forest species (e.g. ash dieback caused by *Hymenoscyphus fraxineus*; Pautasso *et al.,* 2013). The invasion of Europe by oak powdery mildew thus provides a case study for investigating the mechanisms underlying the epidemiological and evolutionary trajectory from a typical invasion pattern, towards the establishment of a new pathosystem in which the pathogen is integrated into its new environment.
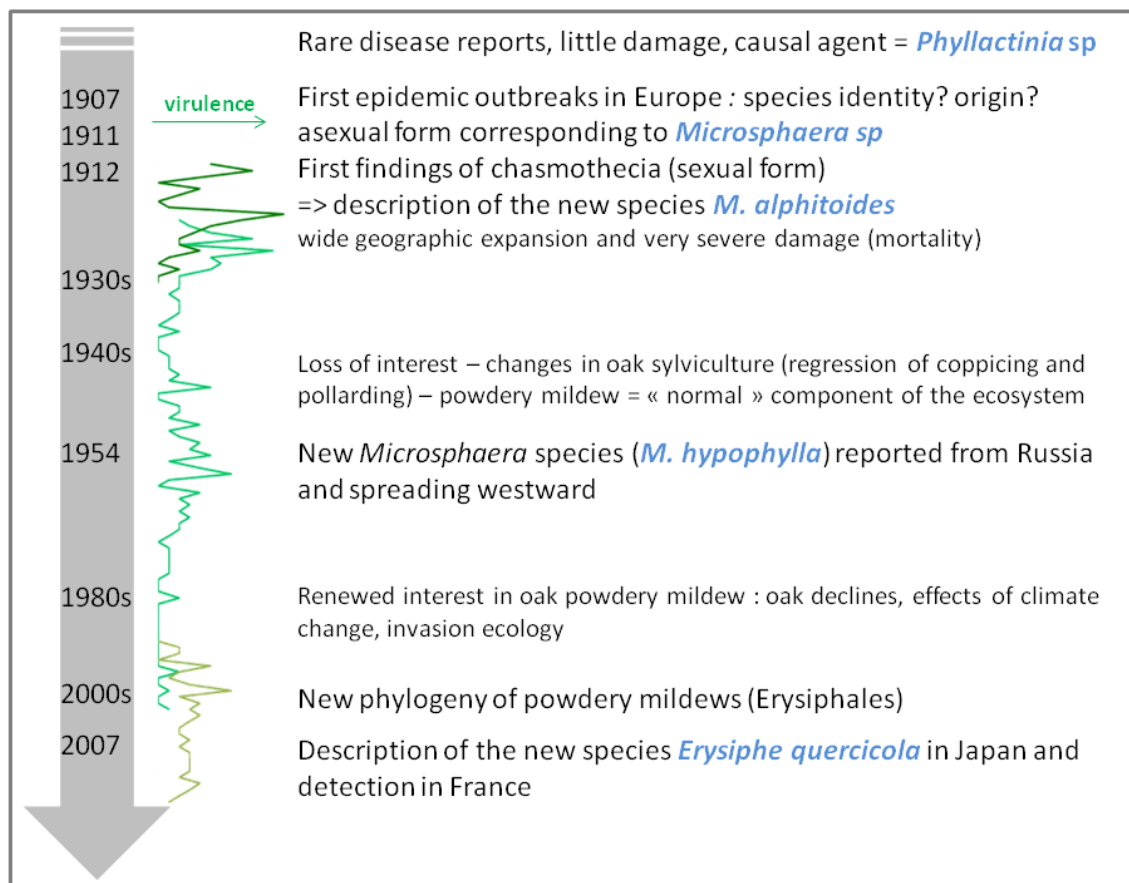

Figure 15.2 Short history of oak powdery mildew disease in Europe, showing the successive invasions (and descriptions) of several fungal pathogen species. Temporal trends of virulence, defined as the damage caused by disease in oak stands, were reconstructed from an analysis of the literature (represented as green lines on the left). Three proxies for virulence (represented with different shades) were extracted from: (1) 1912-1931, Annales des Epiphyties (France) - number of expressions related to oak powdery mildew damage in "Annual phytopathological reports"; (2) Review of Applied Mycology (1922 à 1970) and WoS (1970-2000) - number of publications dedicated to oak powdery mildew; (3) 1989-2015, French National Health Service (DSF) - index of disease severity.

Several non-mutually exclusive hypotheses may explain the observed trajectory of the oak powdery mildew pathosystem. Evolution of the pathogen towards lower virulence might be expected (Sacristan & Garcia-Arenal, 2008). Models predict evolution of virulence to intermediate levels when very high virulence is associated with lower pathogen fitness due to host death, i.e. when the positive relationship between transmission and virulence saturates and becomes a trade-off (Bull, 1994; Lenski & May, 1994). Furthermore, theory predicts that, early in emergence before an evolutionary equilibrium is reached, epidemic conditions (particularly the availability of large populations of susceptible hosts) can impose a transient selection pressure leading to high virulence. This pressure subsequently decreases as the epidemic depletes the pool of susceptible hosts (Bull & Ebert, 2008; Berngruber *et al.,* 2013). There are very few examples of plant pathosystems supporting these theoretical predictions (Jarosz & Davelos, 1995; but see Escriu *et al.,* 2003). However, what is known of the history of oak powdery mildew in Europe (Mougou *et al.,* 2008) suggests that this system may follow this pattern (Figure 15.2). Unfortunately, experimental support through comparative inoculation studies is not possible in the absence of a historical strain collection.

Jarosz & Davelos (1995) suggested that important characteristics of many plant pathosystems challenge the pivotal assumptions of simple adaptive models of virulence. First, although classical epidemiological models developed for animal and human populations assume that host availability ultimately limits pathogen populations, the suitability of environmental conditions may also be a critical factor for plant pathogens, as illustrated by the disease triangle (i.e. plant, pathogen and environment) widely used by plant pathologists (Francl, 2001). In particular, for a biotrophic foliar pathogen of a broadleaf tree like oak powdery mildew, climate-driven seasonality is expected to have very strong direct and indirect effects (Penczykowski *et al.,* 2015; Tack & Laine, 2014). Second, multiple infections of one or several pathogens on the same host is the rule rather than the exception in plants, even if a single disease is considered. The use of advanced molecular techniques has revealed a huge previously undescribed fungal diversity (e.g. Tedersoo *et al.,* 2014), leading to the suggestion that many plant pathogens represent several closely related sibling or cryptic species (Crous & Groenewald, 2005; Feau *et al.,* 2011). Many plant diseases are therefore caused by a complex of different pathogens, as was recently shown for oak powdery mildew (Takamatsu *et al.,* 2007).

In this chapter, we provide an overview of the available empirical data for the oak powdery mildew pathosystem, showing how these data support and call into question evolutionary epidemiology theory, in the context of a novel interaction following the introduction of the pathogen. We first explore the potential effects of seasonality and the occurrence of a pathogen complex on theoretical predictions of the evolution of virulence, and more generally the eco-evolutionary dynamics of the pathosystem. We then consider the evolution of oak resistance, including the evolutionary potential of oak populations under powdery mildew pressure and the possible role of the biotic environment of the pathogen in the phyllosphere.

15.2 Climate-driven seasonality: inter-annual disease transmission.

Evolution of virulence has classically been explored through SIR epidemic models in which the host population is continuously present (Anderson & May, 1982; Alizon *et al.*, 2009). Models of epidemic disease in animals generally take seasonality into account through fluctuations in the disease transmission rate (Keeling & Rohani, 2008). In contrast, for many plant diseases (e.g. of annual plants, or foliar diseases of deciduous trees), the host is present during only a fraction of the year (referred to hereafter as the 'season'). At the end of the season, infected material is removed (e.g. dead plants or leaves) and the parasite switches to survival forms (e.g. overwintering in leaf debris in the soil litter, or in dormant buds of perennial hosts). At the beginning of the next growth period, the survival forms of the parasite generate primary infections in the host population, initiating a new epidemic cycle. Secondary host-to-host infections then take over from primary infections.

Plant disease dynamics over several seasons have therefore been explored through models combining discrete-time events (including periodic demographic crashes in the host and pathogen populations) with continuous-time epidemiological dynamics over the season (Madden *et al.,* 2007; Van den Berg *et al.*, 2011). Models combining continuous- and discrete-time dynamics are widely used in biomathematics and are sometimes termed semi-discrete models (Mailleret & Lemesle, 2009). Such a model accounting for effects of seasonality on the evolution of pathogen virulence is presented in Box

15.1. In this context, the duration of host absence becomes a key parameter. Exploring the effects of seasonality, Van den Berg *et al.* (2011) suggested, in addition to the virulence-transmission trade-off, a second trade-off may occur between pathogen transmission during the season and pathogen survival outside it. The virulence outcome depends on which trade-off is most relevant. If the virulence-transmission trade-off prevails, pathogen transmission and virulence are predicted to decrease with decreasing off-season duration. In contrast, if the transmission-survival trade-off prevails, pathogen transmission (and possibly virulence) is predicted to increase with decreasing off-season duration. Relevant to oak powdery mildew, records of winter temperature in Europe show a long-term warming trend. Tree phenology has already changed significantly during the last century with both earlier bud-burst in spring and later leaf fall in autumn (Sparks & Carey, 1995; Menzel 2000). For oak, this earlier budburst may account for a 10% increase in the duration of leaf presence since the 1950s (Sparks *et al.*, 1997).

It remains difficult to attribute changes in oak powdery mildew virulence to past effects of climate, as it is unclear which of the two trade-offs (virulence-transmission or transmission-survival) prevails in this system. Decreasing virulence during the twentieth century implies that the virulence-transmission trade-off prevails. However, aerially dispersed plant pathogens are potentially subject to both trade-offs (Van den Berg *et al.*, 2011). In oak powdery mildew, premature leaf shedding observed in response to high levels of infection (Hajji *et al.*, 2009) may underlie both trade-offs by immediately decreasing the pool of spores available for secondary infections (i.e. within season transmission) and preventing the fungus from forming its resting structures (for overwintering) in autumn on senescent leaves (see below).
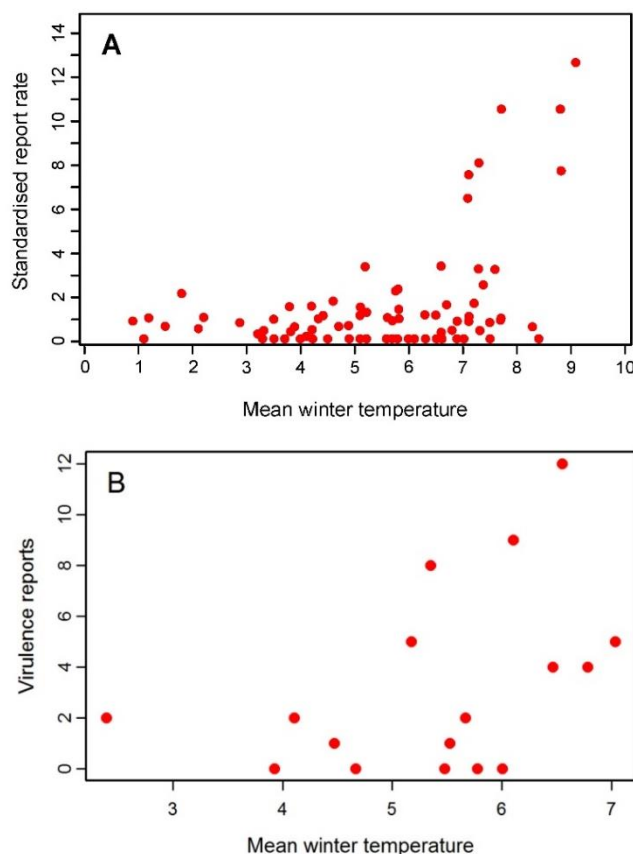

Figure 15.3 Winter temperature and oak powdery mildew disease in France. Disease data from two periods: (A) 1912-1931 (Annual phytopathological reports of "Annales des Epiphyties") and (B) 1989-2006 (Disease reports in the DSF database see Marçais & Desprez-Loustau, 2014) - Meteorological data from Meteo France.

Environmental conditions during the off-season are very important for oak powdery mildew epidemiology, as highlighted for another powdery mildew disease on a wild herbaceous plant (Penczykowski *et al.,* 2015; Tack *et al.,* 2014) and other tree diseases (e.g. Aguayo *et al.,* 2014). The analysis of climatic variables related to between-year variation in oak powdery mildew severity showed unexpectedly that off-season variables (such as winter temperature in particular), rather than climatic

variables during the season, had significant effects with severe epidemics occurring only after mild winters (Marçais & Desprez-Loustau, 2014). Interestingly, the role of warm winters in the severity of epidemics in the early twentieth century was emphasized by some authors (Vuillemin, 1910a). Colder winters in the following decades (http://www.meteofrance.fr/documents/10192/35608/25066-43.gif/) may partly account for the reported decrease in disease severity after the 1920s (Figure 15.2).

Off-season environmental conditions may affect between-season disease transmission through different mechanisms. Cold winters may decrease pathogen survival. Powdery mildews overwinter in two forms (Figure 15.4), mycelium and spores persisting on leaf primordia within dormant buds protected by bud scales, and specialised resting structures called chasmothecia (the sexual fruiting bodies of the fungus, with thick melanised walls) which form on infected leaves in the autumn (Glawe, 2008). Chasmothecia may remain on dead leaves in the litter or may detach from the leaves and come to rest in bark crevices and leaf scars on the trunk, which may provide the best sites for overwintering (Pearson & Gadoury, 1987). For overwintering in dormant buds, primary inoculum consists of the highly infected shoots emerging from infected buds at budburst, called "flag shoots". For overwintering as chasmothecia, the primary inoculum consists of ascospores, generated in these fruiting bodies once dormancy has been released. Several cycles of secondary infections occur over the season in both cases, mediated by conidia (asexually produced spores; Figure. 15.4).

Winter climatic conditions may be a major factor determining which overwintering mode prevails, as observed for other plant parasites (Halkett *et al.,* 2004). Most tropical powdery mildew species lack chasmothecia (Piepenbring *et al.,* 2011). Conversely, for hop and apple powdery mildews, very low temperatures have been shown to have a deleterious effect on fungal survival in buds (Liyanage & Royle, 1976; Spotts & Chen, 1984), and there is also evidence of better oak powdery mildew survival in buds during mild winters (Marçais, *et al.* 2017). Despite this sensitivity, pathogen hibernation in buds has the advantage of providing a "green bridge" between two growing seasons in temperate climates; the pathogen experiences no discontinuity in host availability and can resume its development in perfect synchrony with that of the host as soon as weather conditions are favorable for leaf development.

Between-season transmission may also be affected by off-season temperature through effects on synchrony between bud burst and ascospore release from chasmothecia. Oak leaves display ontogenic resistance, i.e. they are susceptible to powdery mildew only a short period after their emergence (Edwards & Ayres, 1982). The temporal coincidence of ascospore primary inoculum production and susceptible leaf tissue emergence in spring is thus critical in this pathosystem, conditioning the initiation of epidemics each year. Oak-fungus phenological synchrony clearly illustrates the 'encounter filter' of host-parasite interactions (sensu Combes, 2001; Figure.15.4). By using an altitudinal temperature gradient, we have shown that (1) both fungus (ascospore release) and oak (budburst) phenologies respond to temperature; (2) their responses are different, leading to differences in the phenological match between budburst and the presence of ascospores across altitudes; (3) oak phenology is a potential determinant of disease severity at the end of the growing season, in particular with early flushing trees at low altitudes likely to escape infections whereas late trees had a significantly higher percentage of their leaf area infected (Desprez-Loustau *et al.,* 2010; Dantec *et al.*, 2015).

Unlike oaks, which display local adaptation for phenology within Europe (Ducousso *et al.*, 1996), no differentiation between European populations of *Erysiphe alphitoides* was detected in terms of the phenology of ascospore production (Marçais *et al.,* 2009). It is possible that the fungus has not had time to adapt to the local climate as it has only been present in Europe for a century. However, the pathogen was found to show patterns of local adaptation at individual host tree level in terms of infection success over the same period (Roslin *et al.*, 2007; Desprez-Loustau *et al.,* 2011). The plasticity in powdery mildew phenology and the high local diversity of oak phenology may account for a relatively weak selection pressure on fungus phenology.

Figure 15.4 Oak powdery mildew life cycle. Powdery mildews are obligate biotrophic parasites, i.e. they cannot live without their host and they derive their energy from living cells. Most of the fungal development is epiphyllous, the only structures within plant tissues being the intra-cellular haustoria which absorb nutrients from the host. Left, complete life-cycle with sexual reproduction: in autumn (lower left), sexual fruiting bodies (chasmothecia) are formed on infected leaves; during winter, the chasmothecia remain dormant; in spring, the ascospores within the chasmothecia are released and airborne; primary infections result from the germination of ascospores on young susceptible leaves which produce colonies of epiphyllous mycelium bearing conidia (asexual spores); during the growing season (spring-summer), several cycles of secondary infections are produced by conidia; Right, alternative cycle without sexual reproduction: mycelium and conidia overwinter in dormant buds (under bud scales), infected buds produce "flag shoots" and conidia produce secondary infections.

15.3 Epidemiological implications of a pathogen complex.

The oak powdery mildew pathosystem has an additional layer of complexity, in that the disease is not caused by a single pathogen species but by a complex of closely related species (Figure 15.2).

Using the nuclear ribosomal DNA sequence (a region used as barcode for fungi; Schoch *et al.,* 2012), Takamatsu (2013) and Takamatsu *et al.* (2015) thoroughly revised the phylogeny of powdery mildews. They showed that at least seven closely related species in the *Erysiphe* genus, with a common ancestor probably of Asian origin, affect Asian oaks (Limkaisang, *et al.* 2006; Takamatsu *et al.,* 2007). At the time of oak powdery mildew invasion in Europe, these species were unknown and mycologists initially thought that the pathogen had been introduced from North America, as for grapevine powdery mildew a few decades earlier. However, the morphology of the invasive pathogen differentiated it from all described species known to infect oak, and the fungus was therefore described as the new species *E. alphitoides.* One of the other species in the clade described by Takamatsu *et al.* (2007)*, E. hypophylla,* was later shown to have spread westwards in Europe in the 1950s-60s (Viennot-Bourgin, 1968, Figure 15.2).

The recently described *E. quercicola* has been shown to occur together with *E. alphitoides* and *E. hypophylla* in France, in addition to *Phyllactinia* spp which may be an endemic powdery mildew species (Mougou, *et al.,* 2008; Mougou-Hamdane *et al.,* 2010; Figure 15.2). A recent survey showed that *E. alphitoides* predominates in most of Europe, with *E. quercicola* and *E. hypophylla* having much lower frequencies and more restricted distributions, towards the south for *E. quercicola* and the north-east for *E. hypophylla*. However, the different species can co-occur in a single region, stand, tree, leaf and even lesion (Mougou-Hamdane, *et al.* 2010; Marçais, *et al.,* 2017).

Box 15.1: Seasonality, semi-discrete epidemic models, and the evolution of virulence in plant parasites

We introduce a simple semi-discrete model accounting for seasonality with two types of infected individuals which we then use in two different but related contexts. (i) The two types correspond to different strains of the same species. Under certain conditions, evolution tends to select the strain with the largest reproductive number, and we discuss the implications of climate change (e.g. increasing season length) for the evolution of virulence in plant parasites. Under broader conditions, evolutionary branching may occur, leading to dimorphism in the parasite population. (ii) The two types are then assumed to correspond to different parasite species. We show that the two species can coexist in the long run while exploiting the same resource, contradicting the competitive exclusion principle (Armstrong & McGehee, 1980).

Model

For simplicity, we assume that total host density is constant throughout the season. Let S, I, and R be the densities of susceptible, infected, and removed (e.g. defoliated) hosts, respectively. In addition, let $I = I_1 + I_2$ with I_1 and I_2 representing hosts infected with type 1 and by type 2 parasites, respectively (for simplicity, we ignore multiple infections at the host scale chosen, e.g. the leaf). Let T be the duration of an annual cycle (one year), and k be a cycle index. Also, let τ be the length of the season. Let β_1 and β_2 be the secondary infection rates associated with type 1 and type 2 parasites, respectively. Similarly, let α_1 and α_2 be the disease-induced removal rate (virulence) associated with type 1 and type 2 parasites, respectively.

During the season, i.e. for all t between kT and $kT + \tau$, the epidemiological dynamics are described by an SIR model (Kermack & McKendrick, 1927; Segarra et al., 2001). For $i = 1, 2$, the model reads

$$\frac{dS}{dt} = -S(\beta_1 I_1 + \beta_2 I_2),$$

$$\frac{dI_i}{dt} = I_i(\beta_i S - \alpha_i). \tag{15.1}$$

From season to season, i.e. from $kT + \tau$ to $(k + 1)T$, the dynamics are described by a discrete-time model. Let S_0 be the initial susceptible host density (which is assumed to be renewed each year regardless of disease incidence) and χ be a composite parameter aggregating survival forms production per infected leaf, survival probability, and primary infection rate (Mailleret et al., 2012). This parameter is specific to each type of parasite, and χ_i will be referred to as the between-season transmission

Box 15.1: (cont.)

parameter associated with type i. Assuming that primary infections occur over a shorter timescale than secondary infections, we consider: for $i = 1, 2$,

$$S((k+1)T) = S_0 \exp\left(-\sum_{j=1}^{2} \chi_j I_j (kT + \tau)\right),$$

$$I_i((k+1)T) = S_0 \left(1 - \exp\left(-\sum_{j=1}^{2} \chi_j I_j (kT + \tau)\right)\right) \times \frac{\chi_i I_i (kT + \tau)}{\sum_{j=1}^{2} \chi_j I_j (kT + \tau)}.$$

$$(15.2)$$

The exponential term represents the probability of a susceptible leaf escaping primary infection. The fraction represents the probability of infection with species i given that infection occurred (Hamelin et al., 2011). The annual cycle repeats. Figure B15.1.1 illustrates the model. Table B.15.1.1 provides a list of the parameters and variables for equations (15.1) and (15.2).

Evolutionary invasion analysis

Let I_1 be a resident monomorphic population challenged by a small mutant subpopulation I_2. Assuming that the resident population is at ecological
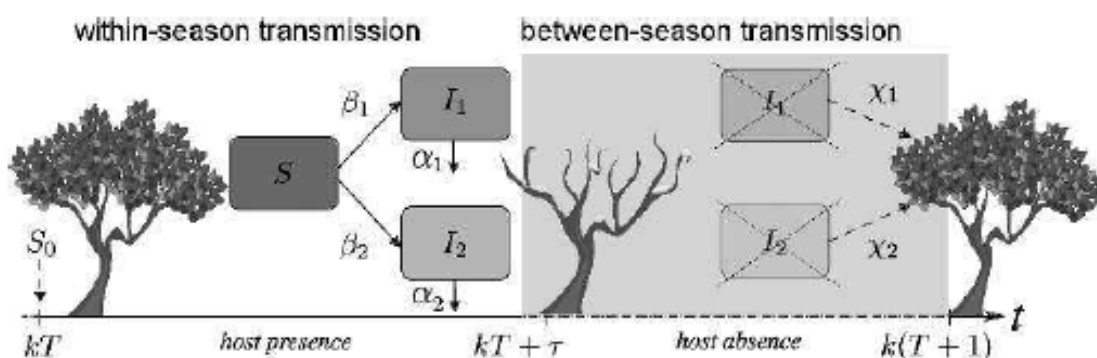

Figure B15.1.1 Flow-chart of the model associated with equations (15.1) and (15.2). At the beginning of the season ($t = kT$), a density S_0 of susceptible hosts (e.g. green leaves) is made available to the parasites. Susceptible hosts can be infected by type 1 or type 2 parasites. The within-season transmission rates of type 1 and type 2 parasites are β_1 and β_2, respectively. The hosts infected by type 1 and type 2 are continuously removed (e.g. defoliated) from the system at rates α_1 and α_2, respectively. At the end of the season (time $t = kT + \tau$), both susceptible and infected hosts are removed (e.g. leaves fall to the ground) and the parasites switch to survival forms (e.g. free-living spores). At the beginning of the next season (time $t = k(T + 1)$), survival forms generate new infections. The between-season transmission rates of type 1 and type 2 parasites are χ_1 and χ_2, respectively. Solid and dashed lines correspond to discrete- and continuous-time processes in the model, respectively.

Box 15.1: (cont.)

Table B15.1.1 *Model parameters and variables*

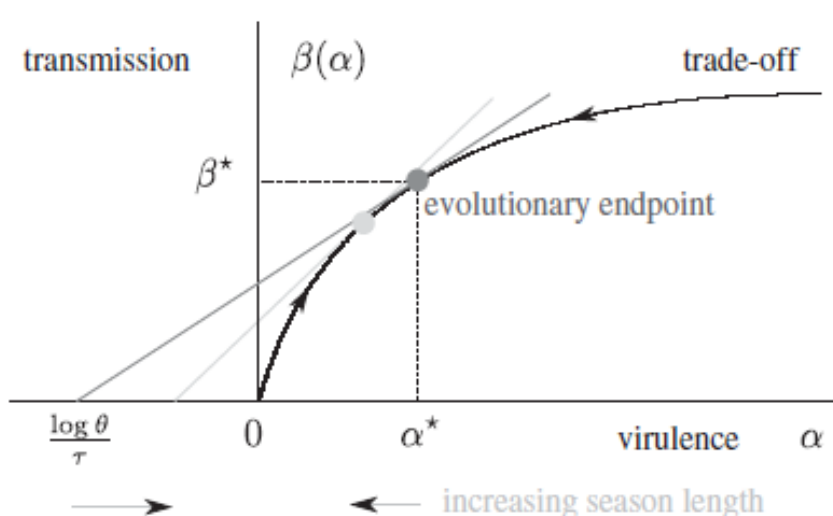| Parameter	Variable	Units
Length of the season	τ	[time] ($\leq 1a$)
Length of the off-season	$T - \tau$	[time] ($\leq 1a$)
Within-season transmission rates	β_1, β_2	[space/time]
Between-season transmission parameters	χ_1, χ_2	[space]
Infected leaf removal rate	α_1, α_2	[1/time]
Initial and maximum host density	S_0	[1/space]

Figure B15.1.2 Classical graphical solution of the optimal virulence strategy, maximising the basic reproductive number, for a possible trade-off between transmission and virulence (black solid curve). The differentiation of R_0 with respect to alpha indicates that the optimum is the point at which the dark grey tangent line passes through the point $(\log(\theta)/\tau,0)$ (Alizon et al., 2009; van den Berg et al., 2011). The originality here is that $\theta = \chi S_0 \ll 1$ is a season-to-season transmission parameter, and τ is the length of the season. Hence, increasing the length of the season decreases the evolutionarily stable level of virulence (light grey tangent line).

equilibrium when the mutant is introduced, it can be shown (Hamelin et al., 2011) that the mutant can invade if

$$\chi_2 \exp([\beta_2 \overline{S_1} - \alpha_2]\tau) > \chi_1 \exp([\beta_1 \overline{S_1} - {}_1]\tau), \tag{15.3}$$

where $\overline{S_1}$ is the mean healthy host density at the equilibrium corresponding to the resident parasite population. This quantity depends on $(\alpha_1, \beta_1, \chi_1)$, but no explicit expression of $\overline{S_1}$ is known.

Box 15.1: (cont.)
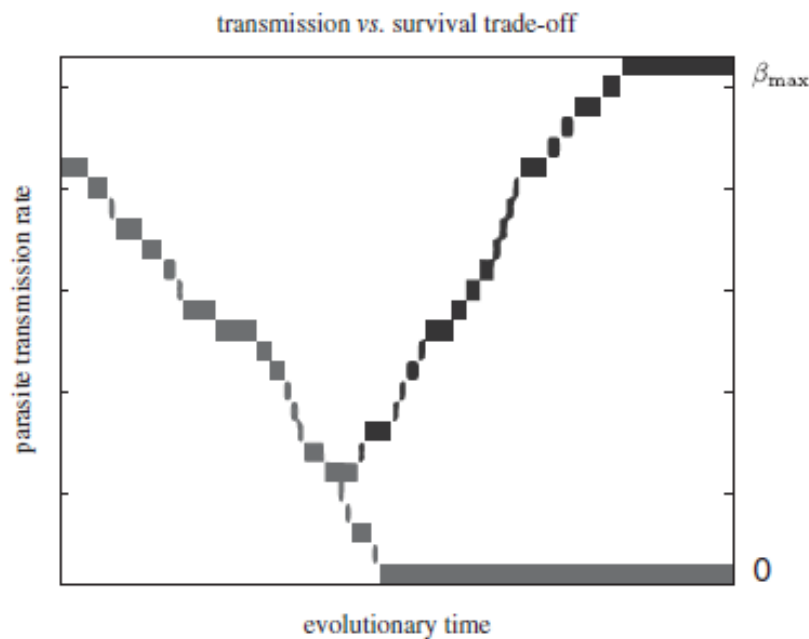
transmission *vs.* survival trade-off

Figure B15.1.3 Evolutionary dynamics associated with model (1–2) assuming a trade-off between within-season and between-season transmission (adapted from figure 2 in Hamelin et al., 2011). There is initially one ancestral parasite type. The mutation-selection process first selects for decreasing within-season transmission (thus increasing between-season survival), and subsequently splits the parasite population into two types, one specialising in within-season transmission, and the other in between-season transmission. The ecological dynamics and the parameter values corresponding to this dimorphic evolutionary endpoint are shown in Figure B15.1.4. (A black and white version of this figure will appear in some formats. For the colour version, please refer to the plate section.)

Considering a trade-off between transmission and virulence (β versus α), a simplification occurs for small χ values. Let $\beta(\alpha)$ represent the trade-off function, which is increasing and concave (Figure B15.1.2). In this case, it can be shown (van den Berg et al., 2011; Mailleret et al., 2012) that evolution selects the value of α maximising the basic reproduction number of the parasite:

$$R_0 = \frac{\beta(\alpha)S_0}{\alpha - \frac{\log(\theta)}{\tau}}, \tag{15.4}$$

where $= \chi S_0 \ll 1$. Interestingly, increasing the length of the growing season τ decreases the evolutionarily stable virulence, maximising R_0 (Figure B15.1.2). This is because increasing the season length increases the possible gain of parasite fitness associated with host longevity.
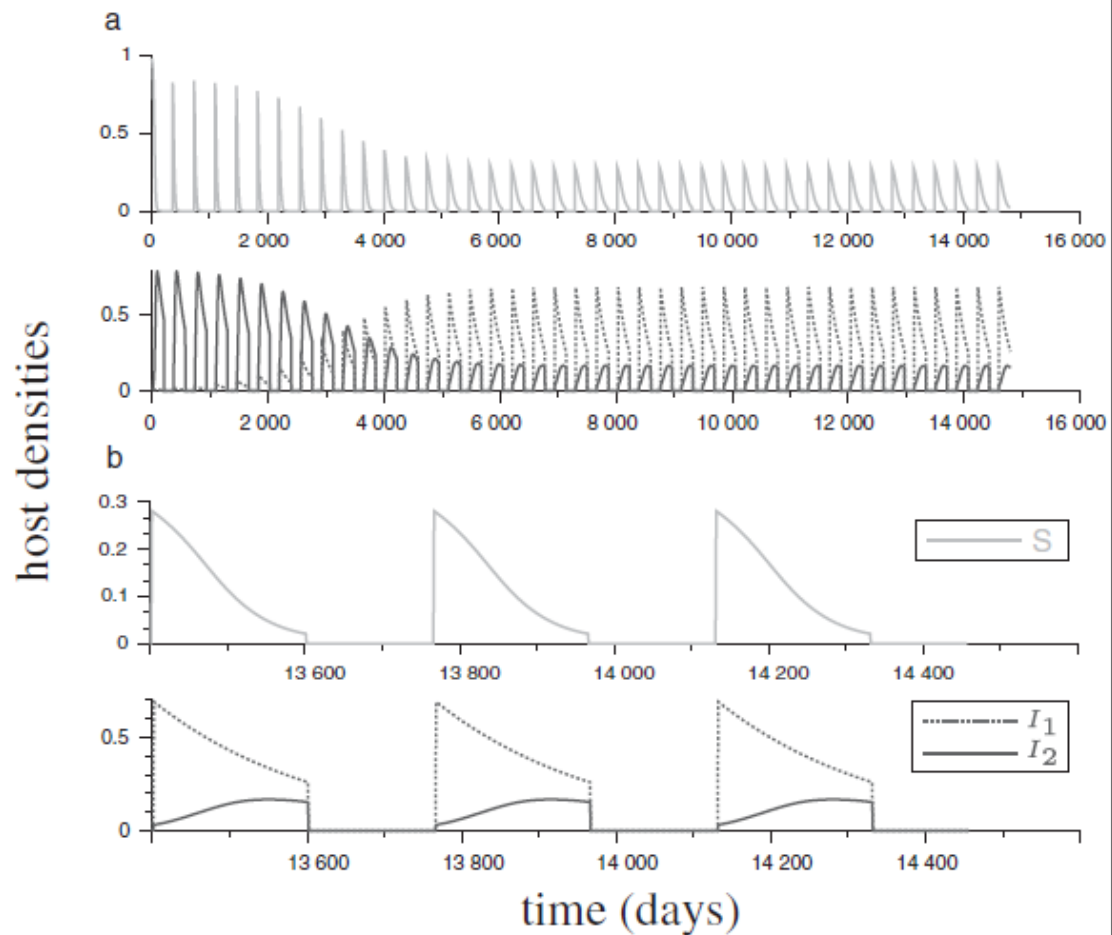
a

b

host densities

time (days)

Figure B15.1.4 Long-term coexistence of two parasite species subject to periodic absence of the host plant (adapted from figure 1 in Hamelin et al., 2016). (a) Infected plant densities I_1 and I_2 as a function of time, for $k = 40$ cycles (years). (b) Zoom on the last three cycles. Parameter values: $\alpha_1 = \alpha_2 = 0.005$, $\beta_1 = 0.1$, $\beta_2 = 0.001$, $\chi_1 = 0.369$, $\chi_2 = 4.68$, $T = 365$, $\tau = 200$, and $S_0 = 1$ (without loss of generality). (A black and white version of this figure will appear in some formats. For the colour version, please refer to the plate section.)

Considering a trade-off between in-season and between-season transmission (β versus χ) yields different evolutionary outcomes. Starting from a monomorphic population, evolutionary branching may lead to a stable dimorphism in the population: one type specialises on within-season transmission whereas the other type specialises on between-season transmission (Hamelin et al., 2011; Figure B15.1.3).

Long-term coexistence of two parasites exploiting the same plant host
A trade-off between within-season and between-season transmission can thus lead to long-term coexistence of two parasite species. Moreover, the two species may significantly overlap in time without compromising their coexistence

(Kisdi, 2012). For instance, Figure B15.1.4 shows model dynamics for a parameter set enabling the two species to coexist (Mailleret et al., 2012; Hamelin et al., 2016). A fast outbreak of type 1 at the beginning of the season leaves enough susceptible hosts for a second outbreak of type 2 because type 2 has a greater within-season transmission rate than type 1. However, type 2 has a lower between-season transmission rate than type 1, which is at an advantage during the primary infection phase at the beginning of the next season. Thus, type 2 does not interfere with the early outbreak of type 1, and both parasite species succeed and coexist on a single host plant.

The existence of pathogen complexes in both the putative region of origin and the invaded area raises several questions. The co-occurrence of closely related pathogen species exploiting the same host plant apparently challenges the competitive-exclusion principle (Amarasekare, 2003). Can time-partitioning account for this co-existence (Loreau, 1992; Chesson, 2000)? From an epidemiological perspective, could temporal differences between the pathogens result in greater host damage due to more complete resource exploitation? Such a complementarity effect between species has rarely been considered for pathogens but is one of the mechanisms underlying the well-established positive relationship between plant species richness and ecosystem productivity (Loreau & Hector, 2001).

From mathematical analysis and numerical simulation of semi-discrete models including seasonality, van der Berg *et al.* (2010, 2011) concluded that a trade-off between pathogen transmission rate and survival between cropping seasons could not account for the evolutionary branching observed in many plant pathogens. However, Hamelin *et al.* (2011) and Mailleret *et al.* (2012), revisiting this issue with the same type of model and further analysis, showed that evolutionary branching and coexistence through temporal niche partitioning might be biologically possible. Moreover, Hamelin *et al.* (2016) showed that coexistence may not be only possible but also, plausible as it can occur in a significant part of the parameter space of the model. Models also predict that the most frequent species at the beginning of the season may become the least frequent by the endwithout compromising the long-term coexistence of the two species. Hence, the existence of a trade-off between in-season and off-season transmission may allow sibling plant pathogens to coexist, with some species performing mainly as primary infectors (with high levels of inter season transmission) and others mainly as secondary infectors (with a large capacity to generate secondary cycles of infection within a season).

This generic model nicely fits several plant pathosystems in which pathogens belong to a complex of cryptic species (or lineages) with various modes of overwintering and differing in temporal dynamics (Fitt *et al.,* 2006; Montarry *et al.,* 2008). A similar situation applies to oak powdery mildew for which the two most frequent species in France, *E. alphitoides* and *E. quercicola*, produce similar symptoms on leaves but overwinter in different ways. Up to now, chasmothecia have been strictly associated with *E. alphitoides.* Conversely, recent collections of flag shoots (presumably associated with hibernating colonies of oak powdery mildew in buds) yielded only *E. quercicola* (Feau *et al.,* 2012), although flag shoots were commonly reported in the years following invasion by *E. alphitoides* (Woodward, 1929; Kerling, 1966). Similar differences in the mode of overwintering have been reported in the putative native area in Asia, with *E. alphitoides* often forming chasmothecia whereas *E. quercicola* seems to overwinter preferentially in buds, although this species has occasionally been reported to form chasmothecia in this region (Takamatsu *et al.,* 2007). The difference in the mode of winter survival between *E. alphitoides* and *E. quercicola* results in different temporal dynamics in spring at a given site: *E. quercicola* appears first in the season (in the form of flag shoots just after budburst), but its relative frequency decreases over time, and *E. alphitoides* is dominant at most sites by the end of the season (Feau *et al.,* 2012). The generic seasonal model of Hamelin *et al.* (2011) provides a satisfactory

fit to the joint dynamics of the two oak powdery mildew cryptic species (Figure 15.5); parameter estimation suggests that *E. alphitoides* has a higher secondary infection rate and lower between-season transmission rate than *E. quercicola* (Hamelin *et al.,* 2016).
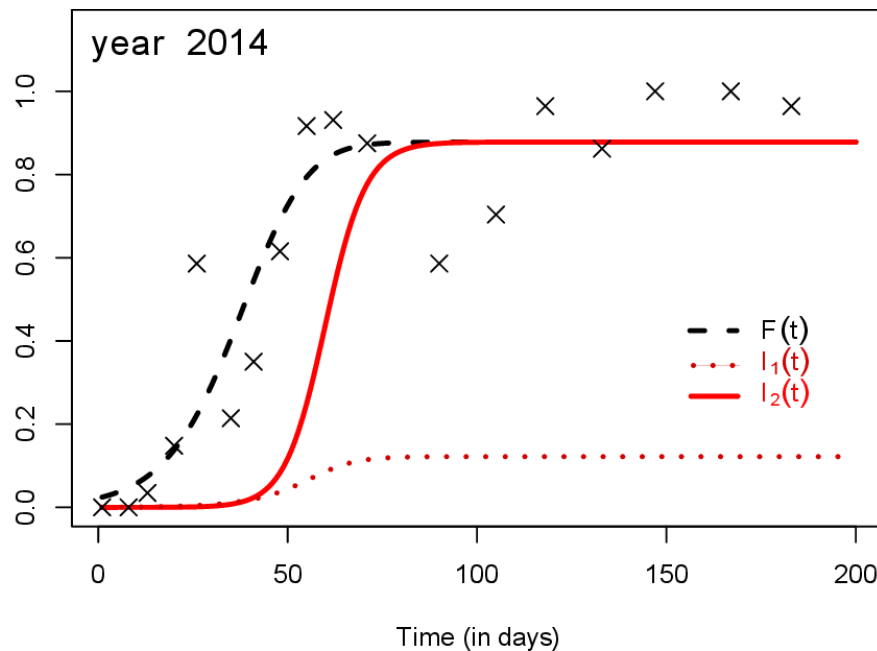

Figure 15.5 Fitting of a semi-discrete epidemiological model with seasonality to empirical data for *Erysiphe alphitoides* and *E. quercicola* temporal dynamics, through a maximum-likelihood method (see Hamelin *et al.,* 2016). The dashed curve represents the frequency of species 2 (*E. alphitoides*) relative to that of species 1 (*E. quercicola*), i.e. F = I2 / (I1 + I2), as fitted to the data (represented by crosses). The dotted and solid curves represent the associated (inferred) densities of species 1 (*E. quercicola*) and species 2 (*E. alphitoides*), respectively.

The possible effects of co-infection on disease dynamics and impact, and on pathogen evolution, have recently attracted attention (e.g. Alizon *et al.,* 2013), including for plant pathosystems. However, the effects of multiple infections on disease severity outcome and pathogen transmission are difficult to predict because mechanisms of interaction between pathogenic strains may be direct or indirect (acting through the host), and may act in opposite directions: synergistic or antagonistic interactions, complementarity effects, cross protection, etc. (Susi *et al.,* 2015; Tollenaere *et al.,* 2016). Moreover, the severity and impact of co-infections may be context-dependent, varying with the effects of environmental conditions on each pathogen (Bearchell *et al.,* 2005; Fitt *et al.,* 2006). In a large survey across France, we tested the hypothesis that *E. alphitoides* and *E. quercicola* occurrence in the same plot would cause greater disease severity, due to temporal complementarity with *E. quercicola* principally affecting the first flush of oak leaves and *E. alphitoides* the second. However, no such effect was shown at the host population scale, with disease severity being primarily explained by the prevalence of the most virulent species *E. alphitoides* (Marçais *et al.,* 2017).

15.4 Intrinsic resistance and phyllosphere microbial interactions.

In the dynamic interplay between hosts and parasites, not only virulence levels change, but resistance would be expected to evolve in the host population. However, genetic changes in long-lived species such as trees are expected to be slow, extending over long evolutionary time scales incompatible with responses to invading pathogens. Nevertheless, large populations of forest trees often display considerable variation in disease susceptibility, even to pathogens that they have not coevolved with. For most epidemics, a small percentage of trees display significant levels of resistance (Ennos, 2015; Budde *et al.,* 2016). In the current epidemic of ash dieback in Europe, 1-5 % of trees in all populations studied display high levels of genetic resistance, indicating that natural (or artificial) selection for much higher levels of resistance should be possible (Budde *et al.,* 2016). Such pre-existing or "serendipitous

14

resistance" (Burdon *et al.,* 2013) may result from evolution under the influence of other selective pressures, i.e. exapted resistance. For example, disease resistance may be related to phenological traits selected under abiotic pressure or may have evolved in response to native pathogens resembling the introduced one (Newcombe, 1998; Budde *et al.,* 2016).

The oak powdery mildew pathosystem has several characteristics that might favour evolution of resistance in oak populations, particularly during the period following the introduction of this pathogen into Europe. First, like many forest trees, oaks produce a large number of offspring (at least in mast years), and disease impact is highest at the seedling stage. Disease resistance is thus expected to be an important determinant of fitness at a stage when competition among individuals is strong. Several authors in the early twentieth century reported very high seedling mortality rates in areas invaded by the pathogen (Marçais & Desprez-Loustau, 2014). Recent studies based on exclusion experiments (using fungicides) and dendrochronological approaches demonstrated fitness costs of infection in the form of growth loss or mortality (Desprez-Loustau *et al.,* 2014; Marcais & Desprez-Loustau, 2014; Bert *et al.,* 2016). Second, pathogen pressure acts on populations displaying high levels of individual variation in disease-related traits (Desprez-Loustau *et al.,* 2014; Bert *et al.,* 2016). Moreover, this variation is genetically determined (Desprez-Loustau, *et al.* 2014) with moderate to high heritability estimates (ranging from 0.38 to 0.66) when comparing descendants in a single pedigree (Bartholomé *et al.*, unpublished). QTL analyses have identified several candidate disease resistance loci in *Q. robur* (Bartolomé *et al.*, unpublished).

The evolution of disease resistance is also dependent on phenotypic and genetic correlations between traits which will ultimately determine the resistance-fitness relationship. For example, Dantec *et al.* (2015) showed that the phenology-fitness relationship was opposite under exposure to powdery mildew or frost. Furthermore, the evolution of disease resistance may interact with disease tolerance, i.e. mechanisms that do not limit infection, but reduce its negative consequences on host fitness (Roy & Kirchner, 2000). Tolerance to damage is related to plant vigour (Weis *et al.,* 2000) and may play a key role in the outcome of infections, as long recognized for plant-herbivore interactions (Baucom & de Roode, 2011). Our results suggest that tolerance, positively correlated with growth potential, might overcome resistance effects on fitness, assessed by oak seedling survival under natural infection (Desprez-Loustau *et al.,* 2014). Testing for an increase in resistance in oak populations since the introduction of powdery mildew would require comparing levels in pre- and post-invasion oak populations. Very old trees that are still alive and were already mature when invasion occurred in the early twentieth century (i.e. older than 150 years) may be considered representative of pre-epidemic populations, since mortality at the time of invasion was mostly reported for seedlings and young trees, and not for mature trees in high forests (Viney, 1970). Comparisons of the susceptibility to disease of the offspring of these trees, to that of trees from younger cohorts (subject to pathogen selection pressure as juveniles), may provide an indication of the selective forces at work.

The microbial community living in association with trees, particularly in the phyllosphere, may also influence the potential of tree populations to cope with emerging diseases (Budde *et al.,* 2016); there is increasing evidence for its potential role in mediating susceptibility or resistance to disease (e.g. Berendsen *et al.,* 2012; Busby *et al.,* 2016). Moreover, as microbial communities are highly dynamic over time, they may supply the plant with a defence arsenal evolving at the same pace as pathogens. This could play a critical role in long-lived species such as trees, which are exposed to a great diversity of pathogens during their life-time (Lively *et al.,* 2014; Budde *et al.,* 2016). Jakuschkin *et al.* (2016) have shown that *E. alphitoides* is involved in a complex network of interactions in the phyllosphere. Their study, combining metabarcoding and network inference methods, demonstrated that infection with *E. alphitoides* was accompanied by significant changes in the composition of the foliar fungal and bacterial communities. Several potential bacterial and fungal antagonists to *E. alphitoides* were identified.

Interestingly, the involvement of an antagonist in the decline of the disease was first suggested early in the years following the oak powdery mildew invasion in Europe. Vuillemin (1910b) observed that the powdery mildew fungus was itself parasitised by another fungus, from the genus *Cicinnobolus*, and he suggested that this hyperparasite might be acting as a natural regulatory agent of the disease. These observations are consistent with the "pathogen accumulation hypothesis" proposed for long-term decline in the density and distribution of some invasive species (generally plants; Flory & Clay, 2013).

Ampelomyces quisqualis, previously known as *Cicinnobolus cesatii*, was described from infected grapevine leaves a few years after the appearance of grapevine powdery mildew in Europe in the 1850s (Emmons, 1930; Kiss *et al.,* 2004). We have detected *A. quisqualis* in oak powdery mildew lesions all over Europe but its impact on disease epidemiology remains to be investigated.

15.5 Future prospects.

Several developments are likely to increase our understanding of the pathosystem and help predict its future trajectory, involving the combination of various modelling approaches and the acquisition of empirical data guided by theory.

15.5.1 Disease modelling over multiple growing seasons, including climate effects.

The development of models capturing the long-term behaviour of pathosystems over multiple growing seasons, including temporal changes in host availability and pathogen overwintering (particularly for perennial hosts), has been identified as a key challenge in plant epidemiology (Cunniffe *et al.,* 2015). Our semi-discrete model provides a generic approach to this issue. Its application to oak powdery mildew highlights the need to explore transmission-virulence and transmission-survival trade-offs to improve predictions of the effects of climate change, through increases in growing season duration, on the pathosystem.

Virulence-transmission trade-offs have rarely been estimated for plant pathogens (Doumayrou *et al.,* 2013; Pasco *et al.,* 2016); an alternative could be to study fitness as a function of virulence (Alizon & Michalakis, 2015). Assessing pathogen fitness and virulence is not straightforward (Gilchrist *et al.,* 2006; Alizon *et al.,* 2009), but they could be measured at leaf level for oak powdery mildew. We may consider fitness as the total production of spores (i.e. the product of leaf life-span and spore production per day), and virulence as the decrease in leaf life-span. Several isolates should then be compared to determine whether the fitness-virulence function peaks at an intermediate virulence level. Furthermore, a possible partial virulence-overwintering trade-off could be investigated by quantifying the production of chasmothecia by isolates from different climates. However, assessing the between-season transmission parameter (Chi in Box 15.1) would also require the quantification of pathogen winter survival, primary inoculum production in spring and the success of primary infections.

As described above, primary infection success is governed by good phenological synchrony between host and pathogen, determined largely by the plastic response of both pathogen and host to environmental cues (especially temperature; Desprez-Loustau *et al.,* 2010; Altizer *et al.,* 2013). Available data for fungal ascospore and oak budburst timings (Marcais *et al.,* 2009; Vitasse *et al.,* 2011) should make it possible to adjust semi-mechanistic models of phenology, based on chilling and forcing phases driven by temperature (Chuine *et al.,* 2013), to simulate phenological synchrony over space and time (including for climate change scenarios). Disease data from the Forest Health Service database (Marçais & Desprez-Loustau, 2014) could be used to validate this synchrony index as a predictor of disease severity. Climate change is also likely to affect disease dynamics within the growing season, through effects on parasite performance and host immunity. Linking epidemiological models with the metabolic theory of ecology (Brown *et al.,* 2004) is a promising approach to addressing this question (Altizer *et al.,* 2013); applying this theory to the oak powdery mildew system provides an exciting framework for empirical studies.

15.5.2 Integrating tree population dynamics through age-structured modelling.

Our semi-discrete model (Box 15.1) includes the default assumption of constant host population size within and between seasons. An obvious improvement would be to incorporate host growth dynamics (Van den Berg *et al.,* 2011; Cunniffe *et al.,* 2015). In oaks, which display polycyclic shoot growth, within-season growth dynamics are characterised by the occurrence of successive flushes of new shoots separated by resting phases within the same vegetative period (Verdu & Climent, 2007). The continuous phase of our model could, therefore be split into several phases. However, most mature trees have only two flushes. The first flush is mostly infected by the primary inoculum whereas subsequent cycles of secondary inoculum infect the second flush. Thus, our model with two different transmission parameters for primary and secondary inoculum captures the within-season dynamics to some extent.

Future models could include oak demography by distinguishing between juvenile and mature stages. Indeed, seedlings and trees differ in many traits likely to affect disease dynamics, such as: phenology (Vitasse, 2013); polycyclism, which is more marked in seedlings, with up to four or five flushes (Desprez-Loustau *et al.,* 2014); height, which has been shown to have a strong influence over the likelihood of flag shoots being produced, and thus between-season transmission (Marçais *et al.,* 2017); and possibly leaf traits that could affect within-season transmission. Spatial structure also differs considerably between the juvenile and mature stages (with very high densities at the seedling stage) and this will likely affect dispersal-transmission. In particular, auto-infection (i.e. caused by inoculum produced on the same plant) would be expected to increase strongly between the seedling and mature stages, with increasing host genotype area and decreasing host density. This prediction is consistent with observed patterns of oak powdery mildew adaptation at tree level (Roslin *et al.,* 2007), and similar observations for oak insect herbivores supporting the adaptive deme formation hypothesis (Zandt & Mopper, 1998).

15.5.3 From a simple binary interaction to a network of interacting species.

The questions of evolutionary branching and the coexistence of cryptic pathogen species could also be explored with this new seasonal model including oak population dynamics (juvenile and mature oaks) and transmission-survival trade-off, and also with the virulence-transmission trade-off which was not considered previously (Hamelin *et al.,* 2011). Available data strongly suggest differences in the distribution patterns of *E. alphitoides* and *E. quercicola* between seedlings and trees in the same stand (unpublished data). Differences between seedlings and trees may also influence the infection of oak powdery mildew fungi with the mycoparasite *A. quisqualis* (e.g. through dispersal and microclimate), to which *E. alphitoides* and *E. quercicola* may not be equally susceptible. Incorporating the tritrophic interaction into the host structured semi-discrete model could be easily tested with observational data.

Our model can currently simulate several pathogen species but it includes only one host species. However, like many plant pathogens, *E. alphitoides* and *E. quercicola* can infect several species (including *Q. petraea* and *Q robur,* the most common oaks in Europe). Potential differences in virulence and transmission according to host and pathogen species, as well as relative host densities, are critical for eco-evolutionary disease dynamics (Cunniffe *et al.,* 2015). Species diversity in both hosts and pathogens is likely to affect competition relationships at both levels and the evolution of pathogen virulence and host resistance. Plant pathologists have shown great interest in these questions at the infra-specific level, focusing on the evolution of pathogen populations in host cultivar mixtures, mostly with a gene-for-gene model underlying strict host specificity (Jeger, 2000). Much less attention has been paid to this issue in diverse wild plant communities (Bever *et al.*, 2015). Differences in susceptibility to powdery mildew between oak species have been reported. In particular, *Q. pyrenaica* has been reported to suffer the highest mortality in early epidemics, and *Q. robur* appears to be slightly more susceptible than *Q. petraea* (Marçais & Desprez-Loustau, 2014*)*. Reciprocally, *E. alphitoides* and *E. quercicola* seem to display some differences in *Quercus* host species preference (Takamatsu *et al.,* 2007), including in Europe (Marçais *et al.*, 2017; unpublished data). Oak powdery mildew may therefore be an important driver of the joint dynamics of the different oak species occurring together in mixed stands in many areas across Europe, and may affect the many ecosystem services they provide.

15.5.4 Evolution of oak resistance and tolerance: growth-defence relationships.

A key concept in plant defence theory, based on considerations of the cost of resistance, is the growth-defence trade-off hypothesis (Brown, 2003; Huot *et al.,* 2014). However, its generality still requires empirical support. An immuno-ecological approach, with experiments using oak genotypes under various levels of resource supply and pathogen pressure, could inform on phenotypic plasticity of defence investments and on relationships between defence and growth in the oak powdery mildew pathosystem. However, no oak material is yet available for direct estimation of the cost of single genes, as was done in *Arabidopsis* using isogenic lines (Tian *et al.,* 2003). Modelling the evolution of host resistance through a growth-defence trade-off, either in the short term (same temporal scale as the pathogen cycle, with resistance mediated by the microbiota) or in the longer term (adaptive evolution of the host through an increase in intrinsic resistance) would be novel in the framework of semi-discrete models.

An alternative or complementary approach would be to use a stochastic individual-based, genetically explicit simulation framework such as Nemo (Guillaume & Rougemont, 2006) or Metapop (Soularue & Kremer, 2012). For example, disease and resistance evolution could be simulated on landscapes heterogeneous for climate (temperature) and resource availability. Environmental factors would condition tree fitness through a survival-defence trade-off associated with phenology (Dantec *et al.,* 2015) and a growth-defence trade-off. In contrast to defence, growth rate can be positively related to tolerance, with very different epidemiological and evolutionary outcomes (Roy & Kirchner, 2000; Best *et al.,* 2014; Cronin *et al.,* 2014). Exploring how these two strategies have evolved in the oak powdery mildew pathosystem, both from observations and modelling, is a very interesting avenue of research.

Rapid progress in the acquisition of genomic resources for both oaks (Plomion *et al.,* 2016) and powdery mildew should soon facilitate investigations of co-evolutionary and co-adaptation dynamics in this pathosystem. In particular, the recent release of a draft genome sequence of *E. alphitoides* (Dutech *et al.*, unpublished) provides valuable genomic resources to identify molecular markers for population genetic and phylogeographic studies. Studies based on living and herbarium specimens and Bayesian analyses will make it possible to reconstruct the invasion history of the three *Erysiphe* species, in particular to give further support or not to the hypothesis of an introduction from Asia. Whole-genome approaches in both powdery mildew and oak will also make it possible to study selection patterns at gene level and to disentangle adaptation processes in the host-pathogen interaction. Population genomic studies of powdery mildew on different hosts and at different geographic locations, and reciprocally of oaks in different regions or at different times (historical samples) likely to be subject to different disease pressures, may lead to the identification of 'hot' spots and 'cold' spots of co-evolution in the native and introduced areas.

15.6 Conclusions.

The oak powdery mildew pathosystem has displayed dramatic changes over the last century in Europe, from being an emerging disease with pathogen invasion dynamics, causing high damage, towards a new equilibrium with lower levels of damage. Several non-mutually exclusive hypotheses potentially account for the trajectory followed, including a decrease in the virulence of introduced pathogens, a reciprocal increase in the resistance of oak populations, and also effects of biotic (phyllosphere microbes) and abiotic (climate) environmental factors. Understanding the pathosystem requires two important characteristics to be accounted for: seasonality and the occurrence of a pathogen complex with several cryptic species. Observational data strongly suggest that the severity of annual epidemics is linked to between-season transmission of the pathogen, including off-season survival and primary inoculum success in spring. Climate-driven phenological synchrony between host and pathogen thus appears to be crucial. A semi-discrete model accounting for seasonality in the pathosystem can explain the coexistence of cryptic pathogen species with differing within-season and between-season transmission rates.

While emerging diseases caused by invasive pathogens are increasingly frequent in wild populations (e.g. Fisher *et al.*, 2012), mobilizing much research on the outbreak phase, understanding mechanisms explaining long term dynamics of such diseases is also critical. Oak powdery mildew, is a powerful case-study for exploring many questions in theoretical and applied plant epidemiology (Jeger, 2000; Cunniffe *et al.,* 2015) in the wider context of the evolutionary ecology of invasion and disease (Lively *et al.,* 2014).

15.7 Acknowledgements.

15.8 References

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