PURE

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Summary

Durable resistance to plant pathogens is highly desired but hard to achieve because the use of plant resistance selects for pathogen genotypes that break resistance. The effectiveness of resistance genes is therefore often short-lived, and breeders have to continually adapt varieties to challenges by novel genotypes of pathogens. We explore the effect of resistance gene deployment strategies and pathogen life-cycle components on the useful life of resistance genes, and search of management strategies that can prolong the useful life of plant resistance. Gene deployment strategies include sequential use of varieties with single resistance genes, stacking of resistance genes within one variety, simultaneous planting of multiple varieties with a single resistance gene, and concurrent use, where a variety with stacked resistance genes are planted together with varieties with single resistance genes. We developed two models at two scales: a regional scale (see deliverable D8.2 Blueprints for field level IPM strategies and spatial designs for resistant genotype deployment) and a national scale. In this deliverable we further explore the effect of resistance gene deployment on a national scale. We adapted the original model for spread of genotypes of yellow rust in France over time, to be able to also test the durability of resistance gene deployment when virulence has to emerge by mutation. To make this possible we had to add two things in the model: a limitation on the number of lesions per field (carrying capacity) and stochasticity in population size after each dispersal step to refelect that population is not equally distributed in each direction after dispersal but local variation is likely to occur (random walk process). The model was used to develop blueprints for spatial strategies of resistance gene deployment. These blueprints consist of variety choice and characteristics of spatial deployment, i.e. fraction of resistant fields and degree of clustering of wheat fields. We also explored the effect of crop rotation on the useful life of resistance genes.

2. Objectives

The objective of this work is to develop blueprints for spatial designs of resistant genotype deployment in space to find a management strategy that deploys plant resistance genes in the most durable way. This management strategy consists of two "levers" or management options. The first lever is variety choice; choosing between 1) single gene resistant varieties, 2) varieties with stacked resistance, 3) multiple single gene resistant varieties, or 4) concurrent use of single resistant and double resistant varieties. The second lever is deployment of varieties; choosing the fraction of fields grown with resistant varieties, whether the crop (e.g. wheat) is grown together over vast areas or more fragmented in the landscape and whether to apply crop rotation or not. We define a blueprint as a set of characteristics for spatial deployment of resistant varieties in combination with variety choice. Selection of resistant varieties and spatial deployment of varieties both are at the basis of integrated pest management strategies (IPM). The basis of IPM consists of cultural measures that can be taken to prevent the occurance of pest and diseases wherever possible, sanitation measures and crop rotation are two other management practises that are used to reduce the chance that disease occurs. Should prevention not be sufficient, and pests or disease reach a unacceptable mechanical measures or biological control are the first choice of action. Pesticide use is reduced and pesticides are only used when needed.

Spatial deployment of susceptible and resistant hosts affects the loss of spores between fields and therefore can potentially affect the spread of a new pathotype. The effect of spatial patterns of variety deployment has been studied on a small scale (ranging from tens of meters to several kilometres) (Saphoukina et al, 2009; Saphoukina et al., 2010; Skelsey et al., 2010), but has not been studied before considering a realistic landscape at a national scale.

Wind dispersed pathogen spores can travel long distances of several hundreds of kilometres (Zadoks, 1961; Hovmøller et al., 2002). Therefore we test the effect of spatial deployment and variety choice on the evolution and spread of an airborne resistance breaking pathogen genotype at a large spatial scale (980 km x 970 km). The management strategy scenarios were tested in a realistic spatial setting. The goal was to develop a model for spatial spread and population dynamics that is simple, fast running and that can easily be adjusted for other pathogens with different life history traits and that can be used at a national level or after adjustment of scale even at a level of several nations. The current scenario testing was done for France and parameterized for the pathogen *Puccinia striiformis* f.sp. *tritici* causing yellow rust in wheat. For derivation of parameter values, we had multiple interviews with Claude de Vallavieille-Pope and Marc Leconte, who are gratefully acknowledged for sharing their knowledge and experience with us.

3. Model for invasion of pathogen races at a national level for France

3.1 Population genetic model

As in the regional model (introduced in deliverable D8.2), we model a gene-for-gene relationship in which a pathogen can only infect a resistant host when the pathogen has lost its avirulence gene for that specific resistance. We developed a spatio-temporal population model for the dispersal and reproduction of avirulent and virulent pathogens in a landscape of susceptible and resistant hosts, over g growing seasons. In the landscape a fraction r of the host fields are planted with a resistant genotype of the host ("resistant fields", denoted by R) and the remaining fraction of the host fields is planted with a susceptible genotype of the host ("susceptible fields", denoted by S). In the model at national level host fields are interspersed by non-host fields in a realistic pattern. We assume that a fraction θ of the pathogen population P is virulent and that the remaining fraction is avirulent. The virulent genotype of the pathogen ("virulent pathotype", denoted by V) can infect both hosts in the susceptible fields and hosts in the resistant fields, and thus reproduce in all host fields, whereas the avirulent genotype of the pathogen ("avirulent pathotype", denoted by A) can infect only the hosts in the susceptible fields, and thus only reproduce in fields containing the susceptible host. There are τ generations of the pathogen in one growing season of the host. Each pathogen generation, the pathogen reproduces asexually. There is a carrying capacity, K, for the number of lesions per wheat field, this is a combination of both sporulating lesions and dead lesions. Therefore, we also keep track of the total number of lesions per plant (denoted by L_{tot}).

Presence of the susceptible host fields and the resistant host fields are flagged by the indicator variables $S(x,y,g)$, respectively $R(x,y,g)$, which are given for each spatial coordinate (x,y) and vary between growing season g.

$$S(x,y,g) = \begin{cases} 0 & \text{susceptible host absent} \\ 1 & \text{susceptible host present} \end{cases} \quad (1)$$

$$R(x,y,g) = \begin{cases} 0 & \text{resistant host absent} \\ 1 & \text{resistant host present} \end{cases} \quad (2)$$

Non-host fields are fields where both susceptible host and resistant host are 0. One pathogen generation is modelled in three steps, step I) dispersal, step II) formation of lesions, step III) production of new spores. The dispersal process is modelled with dispersal kernels, i.e. spatial probability distributions of the number of deposited spores per unit area at distance from the source. To calculate spore dispersal, the dispersing fraction q of the newly produced pathogen population at each location is integrated with the dispersal between locations as specified by the dispersal kernel (equation 3 and 4), resulting in an integro-difference equation. The three steps of the spatio-temporal dynamics of the avirulent pathogen population (A), the virulent pathogen population (V) and total number of lesions (L_{tot}) at location (x,y) and time t in generation g, are denoted below.

A new pathogen generation starts with the dispersal of spores from the lesions that were formed in the previous generation (step I), this is given by

$$A(x,y,g,t+\Delta\tilde{t}) = \int_{x'} \int_{y'} qA(x,y,g,t)K_{2Dt}(x-x',y-y')dx'dy' + (1-q)A(x,y,g,t) \quad (3)$$

$$V(x,y,g,t+\Delta\tilde{t}) = \int_{x'} \int_{y'} qV(x,y,g,t)K_{2Dt}(x-x',y-y')dx'dy' + (1-q)V(x,y,g,t) \quad (4)$$

where *x*' and *y*' denote all source locations contributing to the deposition of propagules at target location (*x*,*y*), and *x* and *y* are the target locations. The time step $\Delta\tilde{t}$ is shorter than one pathogen generation. The avirulent and virulent pathogen population density, *A* respectively *V*, are given in lesions per field. The spatial probability density kernel, K_{2Dt}, specifies where spores that are produced in pathogen generation *t* are deposited. As a dispersal model we use a 2Dt-distribution with two parameters, a length scale *u* in km, and a shape parameter ν (Clark et al., 1999; Robinet et al, 2012)

$$K_{2Dt}(x,y) = \frac{1}{u^2\pi\nu}\frac{\Gamma\left(\frac{\nu+1}{2}\right)}{\Gamma\left(\frac{\nu-1}{2}\right)}\left(1+\frac{1}{\nu}\frac{x^2+y^2}{u^2}\right)^{-\frac{\nu+1}{2}} \quad (12)$$

The 2Dt-distribution is a flexible dispersal model which can represent both a normal distribution, which has thin tails and is the analytical solution to a random walk process, and distributions with progressively wider tails, which mimic the outcome of biological dispersal processes that combine processes at multiple scales. Depending on the "degrees of freedom" parameter ν ("nu") parameterisation this model can approach a thin tailed normal distribution (ν→∞) or approach a fat tailed Cauchy distribution (ν→1) enabling long distance dispersal. Changing the length scale *u* reflects smaller or longer dispersal distances, the majority of the probability mass is within 2*u* from the source, and changing ν changes the frequency of long distance dispersal (Robinet et al, 2012).

We assume that the actual population size in a field after a dispersal round is a realisation from a Poisson process with mean equal to the population size after dispersal,

$$A(x,y,g,t+\Delta\tilde{t}) \sim Pois\left(A(x,y,g,t+\Delta\tilde{t})\right) \quad (5)$$

$$V(x,y,g,t+\Delta\tilde{t}) \sim Pois\left(V(x,y,g,t+\Delta\tilde{t})\right) \quad (6)$$

After dispersal new lesions are formed (step II). When the total number of lesions in a field approach the carrying capacity the formation of new lesions is reduced. The newly formed avirulent and virulent lesions and the total number of lesions are given by

$$A(x,y,g,t+\Delta\hat{t}) = S(x,y,g)A(x,y,g,t+\Delta\tilde{t})\left(1-\frac{A(x,y,g,t+\Delta\tilde{t})+V(x,y,g,t+\Delta\tilde{t})+L_{tot}(x,y,g,t)}{K}\right) \quad (7)$$

$$V(x,y,g,t+\Delta\hat{t}) = S(x,y,\mathrm{g})V(x,y,g,t+\Delta\tilde{t})\left(1-\frac{A(x,y,g,t+\Delta\tilde{t})+V(x,y,g,t+\Delta\tilde{t})+L_{tot}(x,y,g,t)}{K}\right)+$$
$$R(x,y,g)V(x,y,g,t+\Delta\tilde{t})\left(1-\frac{V(x,y,g,t+\Delta\tilde{t})+L_{tot}(x,y,g,t)}{K}\right) \quad (8)$$

$$L_{tot}(x,y,g,t+\Delta t) = L_{tot}(x,y,g,t)+V(x,y,g,t+\Delta\hat{t})+A(x,y,g,t+\Delta\hat{t}) \quad (9)$$

Where $\Delta\hat{t}$ is another intermediate time step, shorter than the pathogen generation time but bigger than $\Delta\tilde{t}$. At the end of the pathogen generation new spores are produced with factor λ (step III),

$$A(x,y,g,t+\Delta\mathrm{t}) = \lambda S(x,y,\mathrm{g})A(x,y,g,\hat{t}) \quad (10a)$$

$$V(x,y,g,t+\Delta\mathrm{t}) = \lambda\{S(x,y,\mathrm{g})+R(x,y,g)\}V(x,y,g,\hat{t}) \quad (11a)$$

When virulence has to emerge by mutation above the set of equations becomes

$$A(x,y,g,t+\Delta\mathrm{t}) = \lambda S(x,y,\mathrm{g})A(x,y,g,\hat{t}) - Pois\big(mi\lambda S(x,y,\mathrm{g})A(x,y,g,\hat{t})\big) \quad (10b)$$

$$V(x,y,g,t+\Delta\mathrm{t}) = \lambda\{S(x,y,\mathrm{g})+R(x,y,g)\}V(x,y,g,\hat{t}) + Pois\big(mi\lambda S(x,y,\mathrm{g})A(x,y,g,\hat{t})\big) \quad (11b)$$

Where during the production of new spores by an avirulent genotype by chance can mutate into a virulent genotype.

The model framework includes all parameters included in the model at regional level (deliverable D8.2) : proportions of resistant fields (*r*), number of pathogen generations per growing season of the host (τ), multiplication factor of the pathogen per generation (λ), and

the proportion of spores leaving the host field in each generation of the pathogen (q). The model framework furthermore allows different proportions of the host in the landscape per department (reflecting the actual percentage of wheat per department in France) and a set degree of clustering of the host fields (c).

The description and the values of the model parameters are given in Table 1.

Table 1 parameter values of model at national scale (see Annex II for derivation of parameter values)

Name	Description	Value
r	Fraction of resistant fields	0.1 – 0.9
c	Measure for clustering of wheat fields	0 , 0.9
τ	Number of pathogen generations per growing season of the host	6
λ	Multiplication factor of the pathogen	35
q	Fraction of pathogen spores leave the field after reproduction	0.05
β	Initial fraction of single virulent spores in the pathogen population	10^{-4}
θ_e	Threshold fraction of virulent spores in the pathogen population	0.45
m	Mutation rate	10^{-6}
i	Infection efficiency (chance that a spore becomes one of the λ daughter lesions)	10^{-3}
K	Carrying capacity wheat field	$1.5\ 10^{11}$
s	Fraction of between season survival	10^{-3}
u	Length scale of pathogen dispersal (in km)	25
v	Shape parameter of dispersal model, affects frequency of long distance dispersal	5

3.3 Simulation set-up

3.3.1 Life history traits

We consider two possible starting points for aquiantance of virulence in the population. Either virulence is already present in a very small proportion of the pathogen population before a resistant variety is introduced or it is not present and has to emerge by mutation. In the case where virulence is already present, the proportion remains small because a pathogen with a specific virulence gene does not have a selective advantage whilst the matching resistance gene is not in use. The virulence in the population will increase from the moment that the matching virulence gene is introduced. In the other case, virulence first has to emerge by mutation.

Data analysis on *Puccinia striiformis* f.sp. *tritici* showed that generally disease was first detected in the departments in the North-West of France, also experts say that the first disease is found in fields near the North-West coast of France (personal communication with Claude de Vallavieille-Pope and Marc Leconte). Furthermore, not all spores will survive between two growing seasons. We assume that a fraction *s* of the spores that were produced and dispersed in the last pathogen generation of the growing season survive locally in the fields, depending on spatial location (§3.3.5). This will drastically reduce the total population size and potentially affect the occurance and persistence of new mutants (‘over summer’ bottleneck). Therefore, we also check whether relaxing this assumption would give similar outcome. For this extend we also run simulations where a fraction *s* of the lesions present at the end of the previous growing season could survive in all compatible host fields in France. To know the durability of resistance genes both for a bottleneck in between season survival and without any bottleneck makes generalisation to other pests possible.

3.3.2 Management strategies

To assess which is the most durable way to use resistance genes four options for variety choice are tested for a range of combinations of fraction of resistant fields and degree of clustering. There are four scenarios for variety choice:

1. "sequential use". In this scenario one single resistant variety is used until resistance is considered broken down at the end of a growing season when $\theta > \theta_e$. At the start of the next growing season a new single resistant variety is then deployed,

2. "pyramiding". In this scenario one variety has two resistance genes, while the other is susceptible,

3. "multiple varieties". In this scenario multiple varieties with single resistance genes are deployed simultaneously. This is tested for 2 and 4 resistant varieties, each having one resistance gene,

4. "concurrent use". In this scenario a variety with two resistance genes and two varieties with single resistance genes are used simultaneously.

3.3.3 Effect of deployment parameters

We furthermore test the effect of the *fraction of resistant fields* and the *degree of clustering* of on the selection of resistance breaking (virulent) genotypes of the pathogen and thus the useful life of the resistance genes. We test the effect of clustering (at the scale of departments) on the durability by comparing between random distribution of wheat fields with very strong clustering.

Crop rotation can, by removing the host from a field, reduce disease pressure in the following growing season especially for pathogens that can only disperse for short distances. Here we

study wether it can also have a positive effect on useful life of resistance when pathogens can move over long distances.

We studied the *effect of spatial patterns* on the useful life of resistance against *P. striiformis* at a very large spatial, based on the fact that *P. striiformis* can disperse over very long distances, up to several hundreds of kilometres. We choose for an easy to implement spatial configuration, where the deployment of a specific resistant variety was allocated per department.

3.3.4 Landscape

We use France as a landscape for the spatial scenario testing because France had the most detailed dataset on pathotype distribution at a national level. The data consists of isolates of *Puccinia striiformis* f.sp. *tritici*, from 1984 to 2012 in France that were phenotyped for virulence (on average 71 samples per year) (de Vallavieille-Pope et al., 2012). From 1985 onwards this data contains the name of the location (nearest village) and the name of the department in which the sample was collected. Furthermore, information on percentage wheat used per department was available from 1989 to 2013 (Agreste, 2013) (percentage wheat per department in 2006 is depicted in Figure 1b). Furthermore, detailed information on land use in France was available for GIS: Corine Land Cover raster data 2006 (European Environment Agency, 2012) (Figure 1a).

To generate a landscape with wheat fields interspersed with non-host area, a part of the arable fields in a department, in area equal to the area of wheat in that specific department, was randomly designated as wheat field.

3.3.5 Simulation set-up

Each scenario covered a time period of 30 growing seasons. To reduce differences in outcome between scenarios due to random differences in spatial set-up of the host fields between scenarios, 30 replicate landscapes were generated for the two degrees of clustering of the host fields (random and very clustered). For the scenario with crop rotation only 3 landscapes were generated and used in sequence ten times. In these 3 landscapes, fields marked as arable land in Corine were allocated with wheat in only once. We tested 3 replicates of 3 landscapes (9 landscapes in total).

The initial pathogen population started in six departments located at the north-west coast of France: Nord, Somme, Calvados, Yvelines, Eure-et-Loir and Cote d'Armor. In these departments, yellow rust can already be found very early in the season, therefore we assume that a small fraction s of the spores can overwinter in these departments. We furthermore assume that no spores are able to survive the period between growing seasons in the other departments. The initial population starts from 300 randomly chosen wheat fields.

In our model, we keep track of the total number of avirulent, A_{tot}, and virulent spores in France, V_{tot}, and use these to monitor the change in fraction of virulent pathotype $\theta_{tot} = V_{tot}/(V_{tot} + A_{tot})$ over time. For each strategy we determine the useful life, defined as the number of growing seasons during which the fraction of resistance breaking genotypes θ_{tot} in the pathogen population stays below the threshold θ_e.

For the simulations with multiple single resistant varieties and the simulations with a mixed strategy where both single resistant and double resistant varieties are deployed simultaneously, we keep track of multiple virulent pathogens. Both for the "concurrent use" and the strategy of "simultaneous use" of two single resistant varieties we keep track of the total number of spores in France and per department of both single virulent pathotypes V_1 and

V_2 and the double virulent pathotype V_{12}. For all these scenarios we also keep track of the total number of avirulent spores in France and per department.

For the the simulations with simultaneous use of four single resistant varieties, we consider all 16 possible avirulent and virulent genotypes; the universally avirulent genotype V_0, the four single virulent genotypes (that are virulent on one specific variety and consequently avirulent on the three other varieties), the six genotypes with two virulences, the four genotypes with three virulences and the universally virulent genotype V_{1234}.

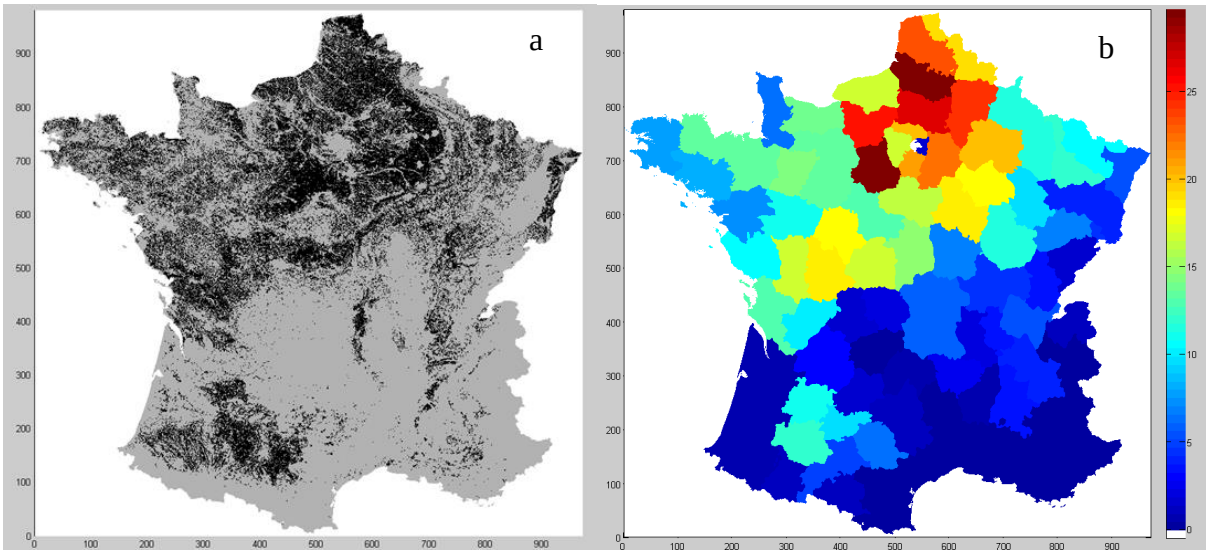


Figure 1 (a) Arable land (black) in France (grey) as converted from Corine Land Cover raster data 2006, grid cell size 0.25 km x 0.25 km, and (b) percentage of area grown with wheat per department in 2006. Scale 980 (N-S) x 971.5 (W-E) km.

3.4 Results

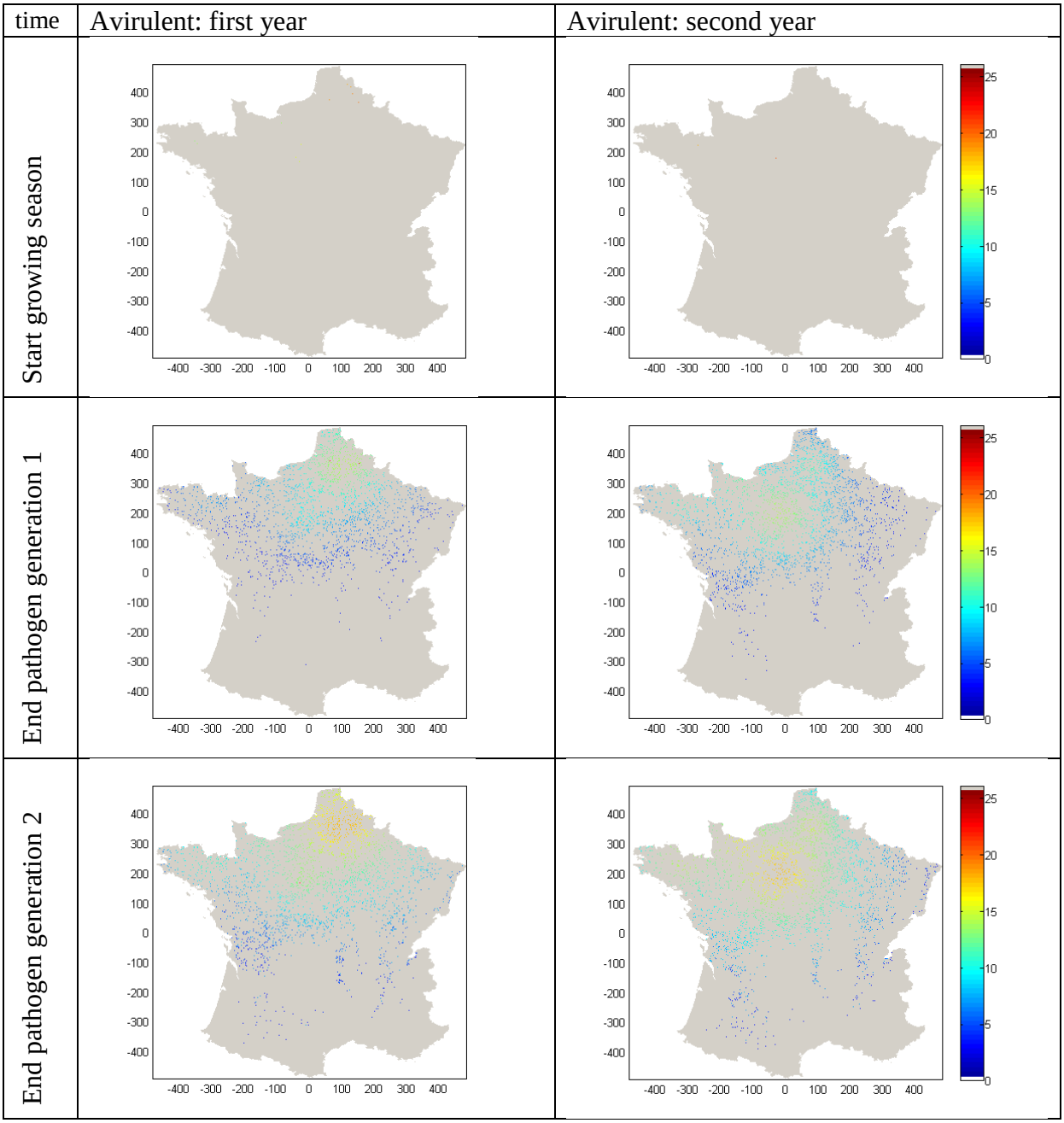
3.4.1 Population dynamics

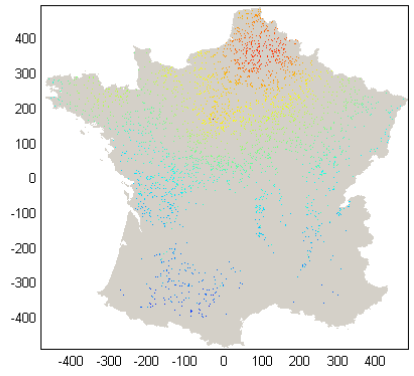
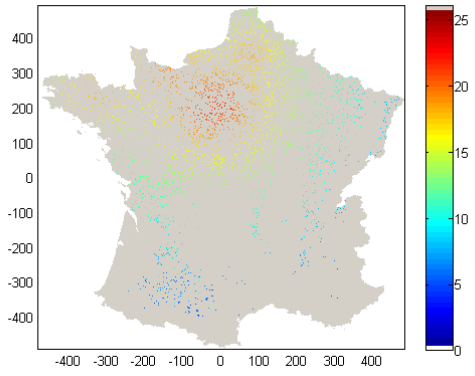
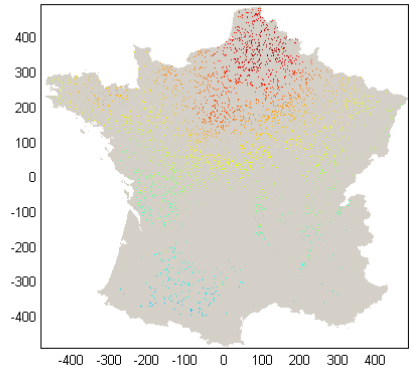
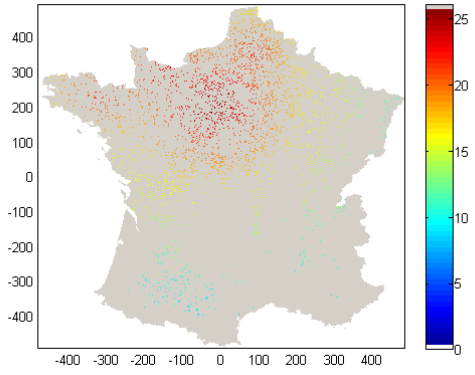
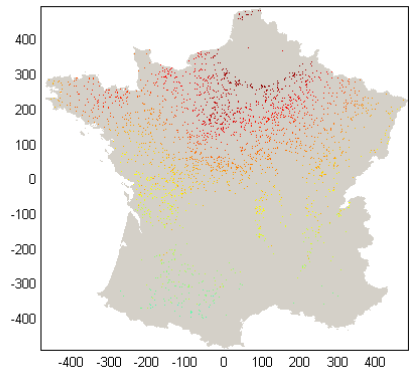
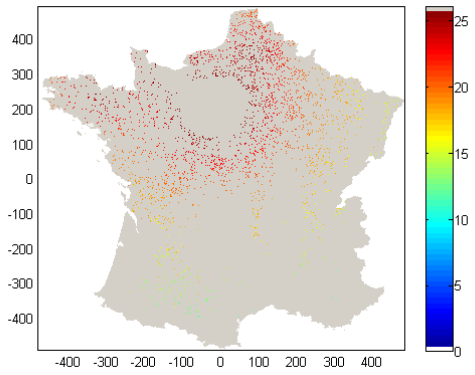
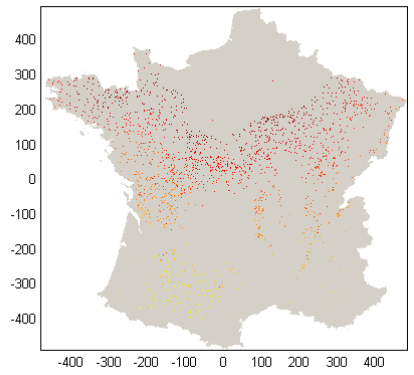
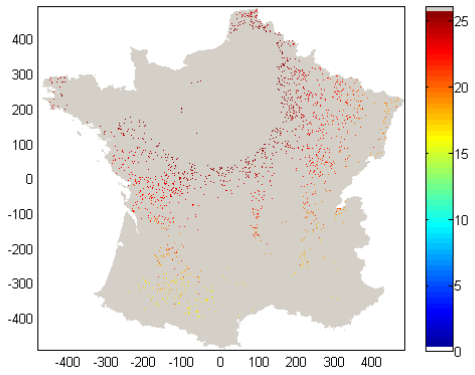
Between growing seasons the pathogen population can only survive in selected fields in the north-west of France. The position of these wheat fields differ from year to year. After one pathogen generation spores already reached the center of France and even a few fields in the South of France (Figure 2). However, at this stage the density is so low (dark blue color corresponds to between 10^{-5} and 10^{-3} lesion/m^2) that they are below the detection threshold. In the spatial maps colors ranging from green to red are at or above the detection threshold, and blue colors are below the threshold for detection. The population continues to spread and increases in population size. Until in generation five the carrying capacity is reached in many fields in the north-west of France. This process is very similar for each year, but the exact location may differ. This also affects the size of the avirulent population in the next generation.

With sequential use (Figure 3), the virulent pathogen population is very small at the beginning of the first growing season. Only a few of the avirulent spores mutated into virulent spores. (With pyramiding (results not shown) no virulent genotypes were present at the start of the first growing season). The pattern of seasonal spread of the virulent pathogen follows the increase of the avirulent population. As the virulent population is so small at the beginning of the growing season, the population spread and increase are mostly recently mutated genotypes (Figure 4). The virulent genotype reaches the level of detection late in the season (the 5^{th} and 6^{th} pathogen generation) in the north-west of France. The second year, the virulent population is larger and the level of detection is reached earlier in the season. The virulent genotypes reach the south of France, however still in numbers too low for detection.

For simultaneous use of four single-gene resistant varieties, the pathogen genotypes with only one virulence gene show a very similar pattern of spread as with sequential use (Figure 5), however the total virulent population is smaller than for sequential use. Furthermore, can be seen that the spatial patterns of increase and spread can differ between the different virulent genotypes due to random effects of where a mutation appears and is able to settle. For instance, genotype V1 appears in Calvados in the third pathogen generation, while the other virulent genotypes are not present yet. This affects the population size at the end of the first growing season and even the population size in the next growing season (Figure 5).

Figure 2. Example of seasonal dynamics of an avirulent genotype in France, in a landscape with a susceptible host and a single-gene resistant host (sequential use), in the first two growing seasons of the simulation. Colorbar depicts log(number of avirulent lesions per field), on this scale 15 is ~ 13 avirulent lesions m^{-2}. Depicted for fraction of resistant host, r_{tot}=0.6. The other parameter values can be found in Table 1.



End pathogen generation 3		
End pathogen generation 4		
End pathogen generation 5		
End pathogen generation 6		

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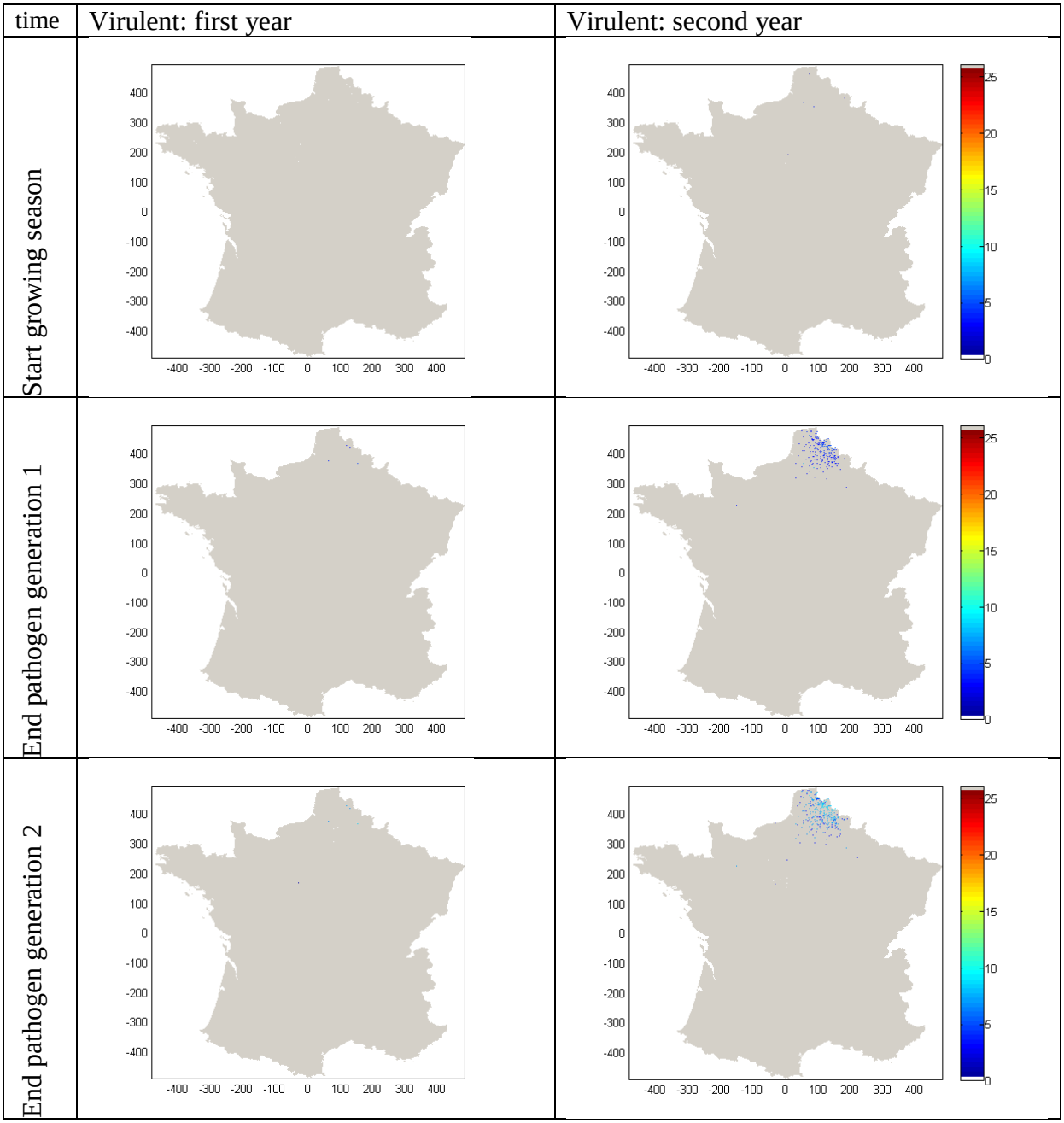


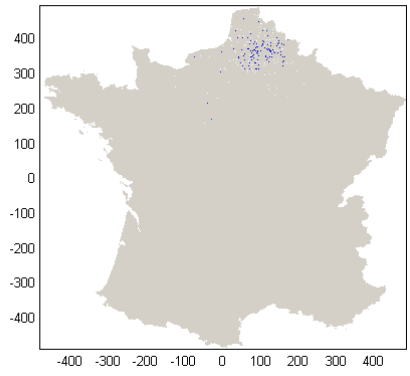
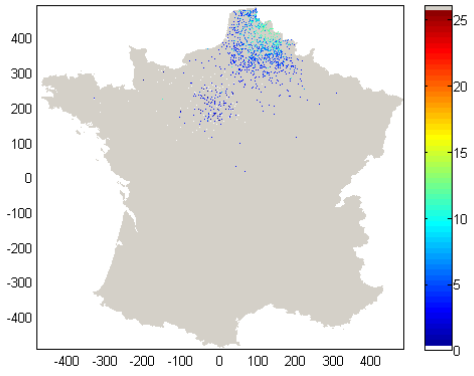
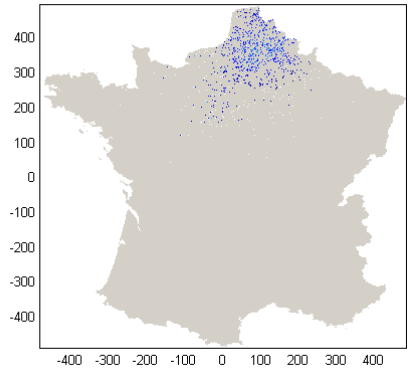
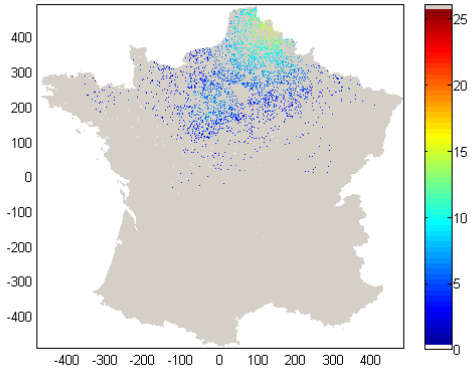
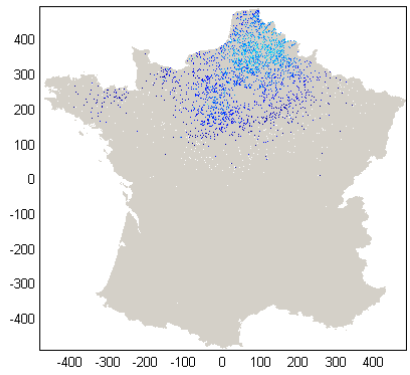
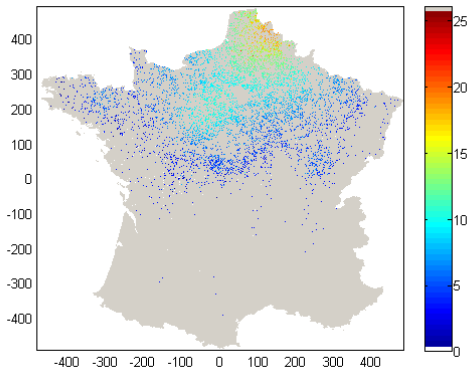
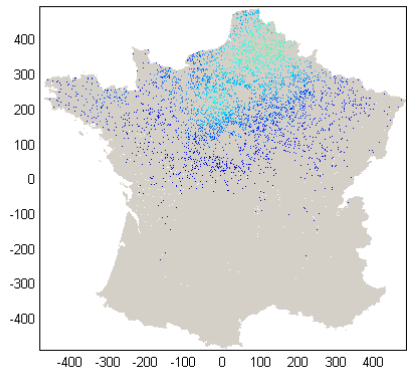
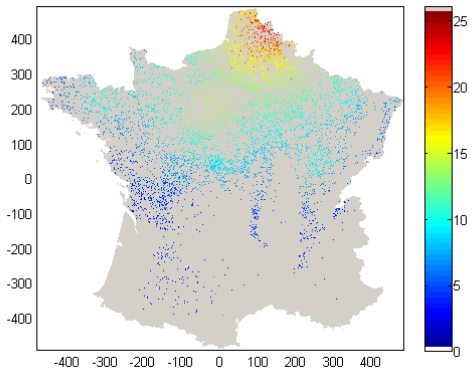
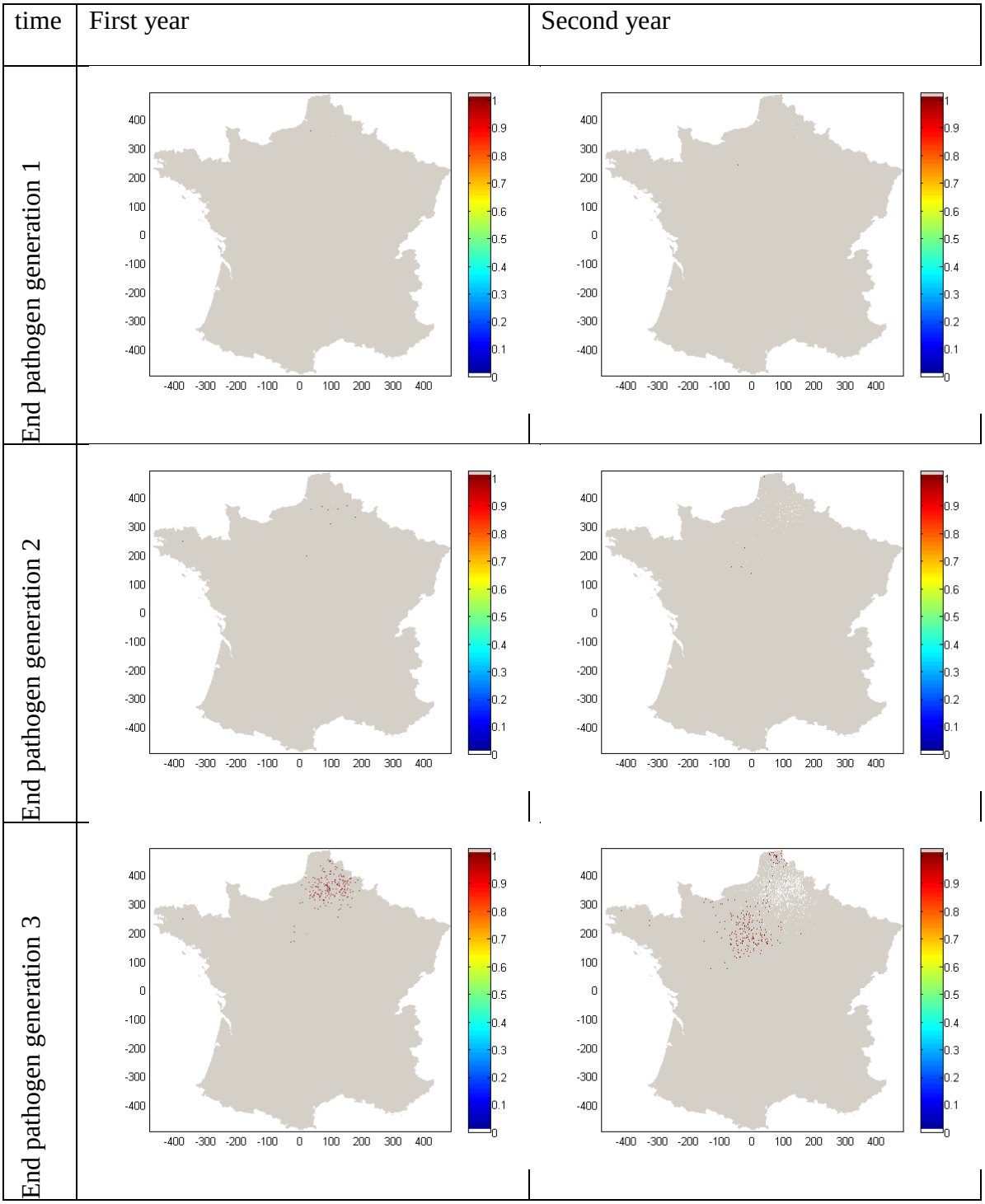
End pathogen generation 3		
End pathogen generation 4		
End pathogen generation 5		
End pathogen generation 6		

Figure 4. Example of seasonal dynamics emergence virulent genotype in France, in a landscape with a susceptible host and a single-gene resistant host (sequential use), in the first two growing seasons of the simulation. Colorbar depicts fraction of new virulent lesions of total virulent lesions in field. Red marks a high fraction of new mutations to virulence, blue (and white within France) marks a high fraction of virulence already present. Depicted for fraction of host r_{tot}=0.6.



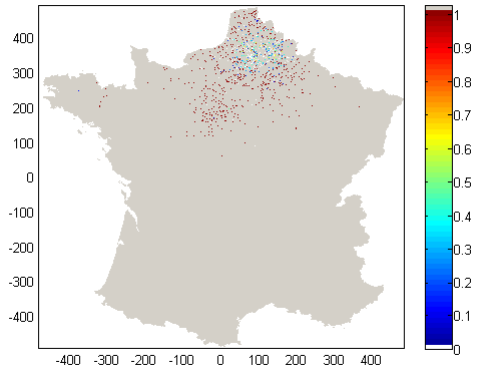
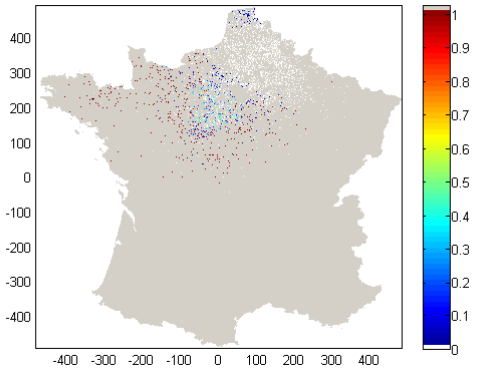
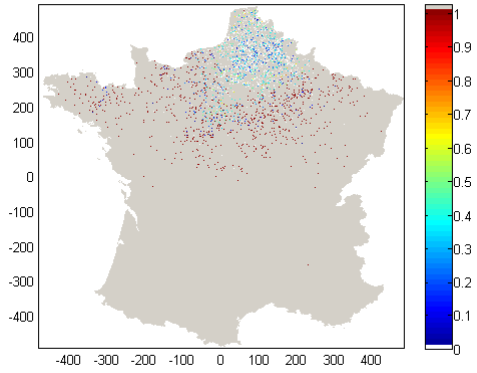
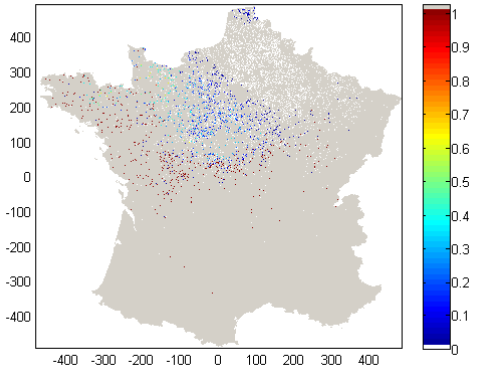
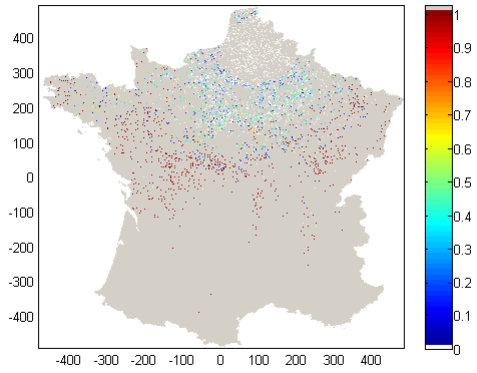
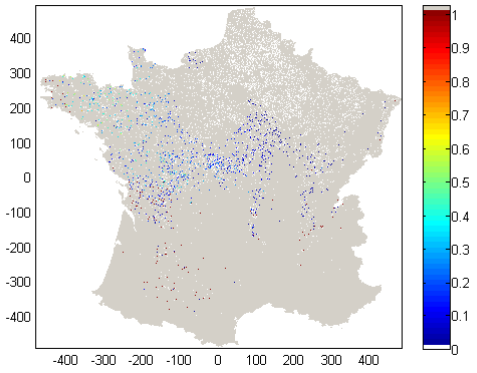
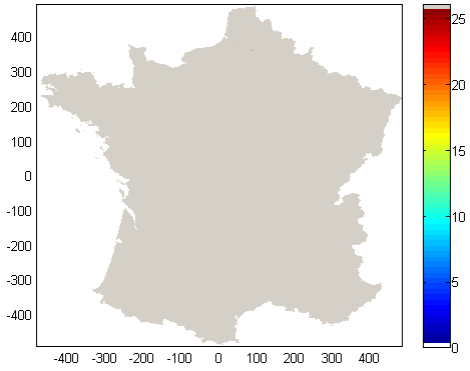
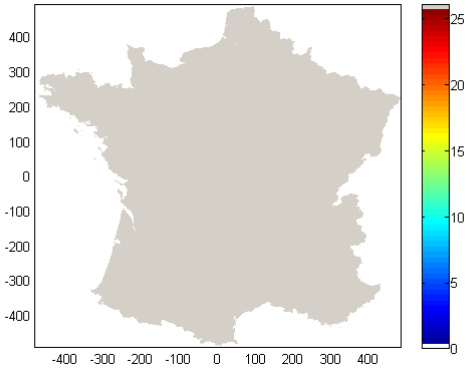
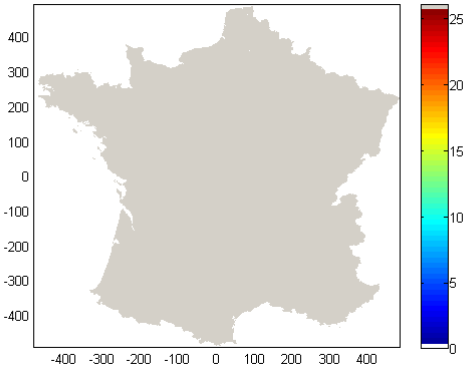
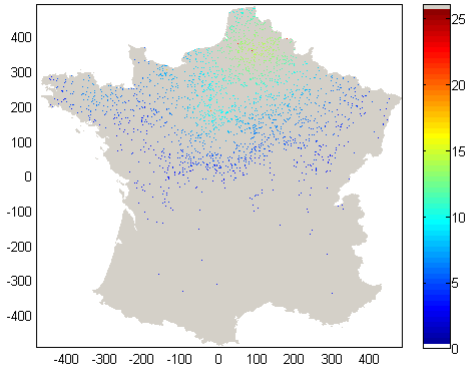
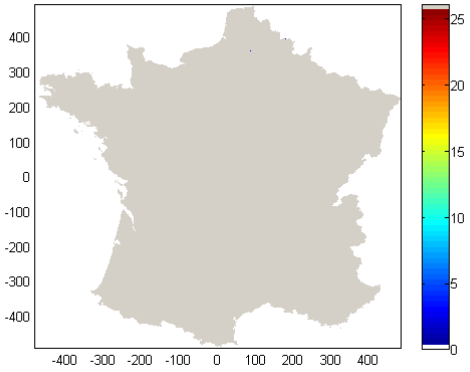
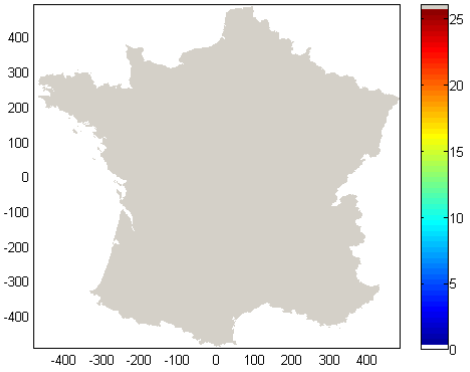
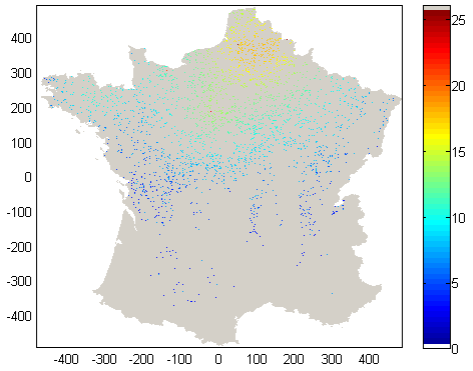
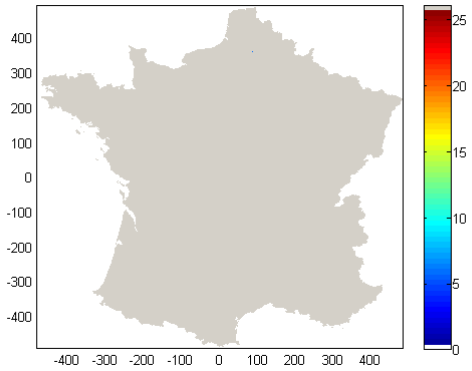
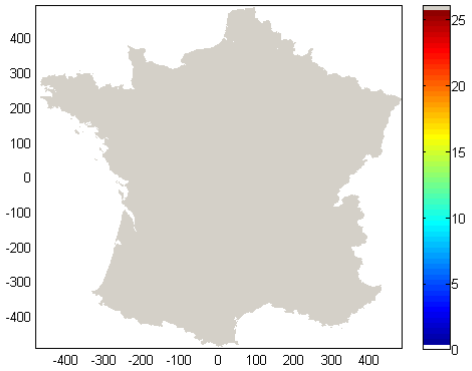
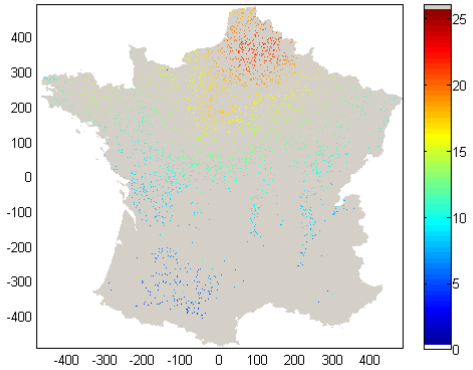
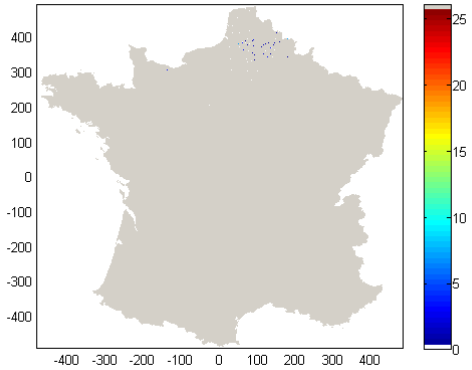
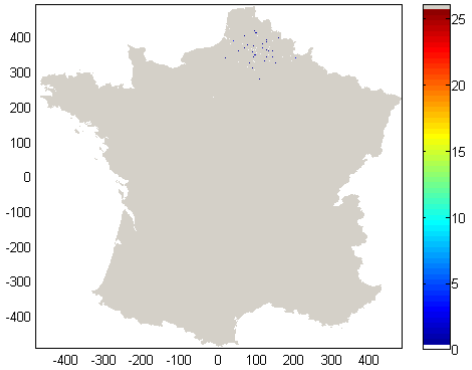
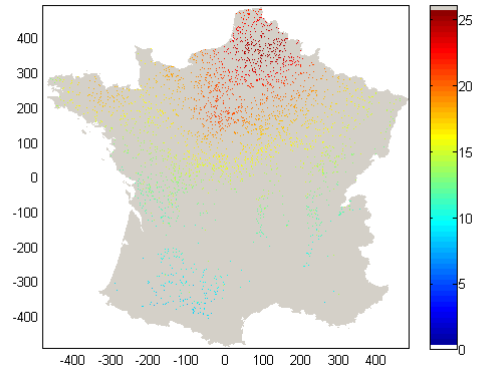
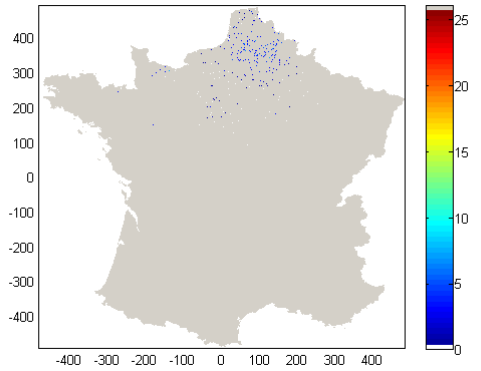
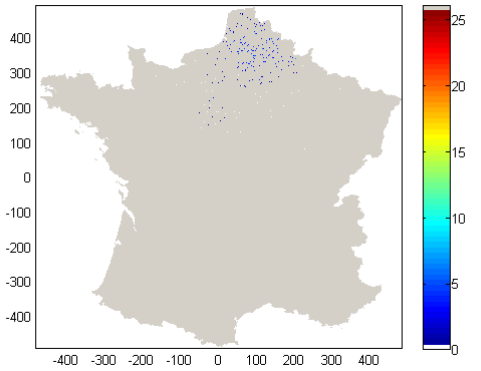
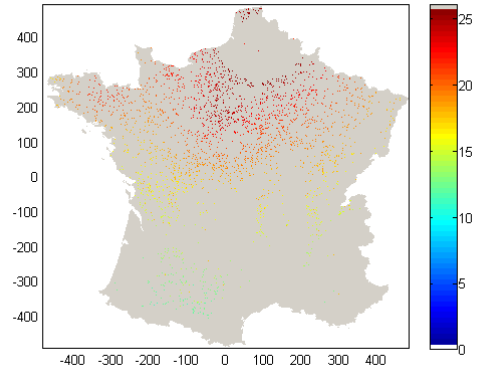
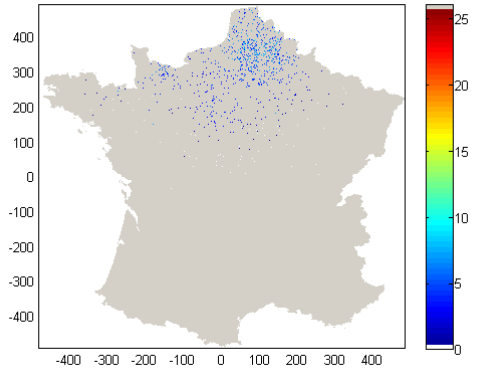
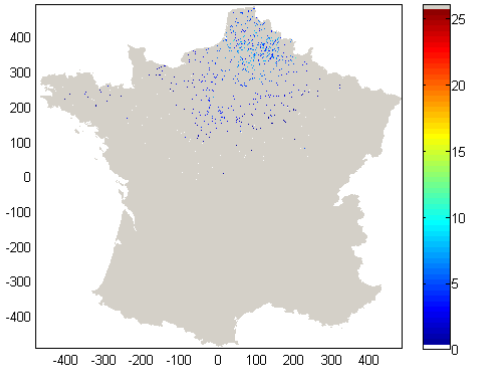
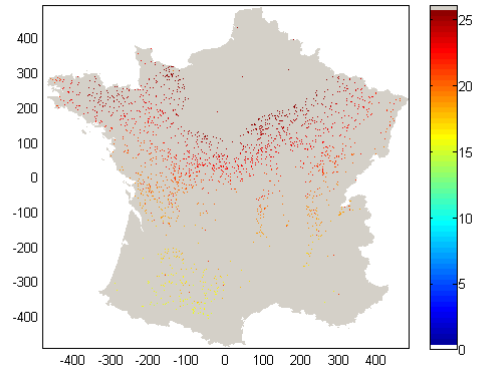
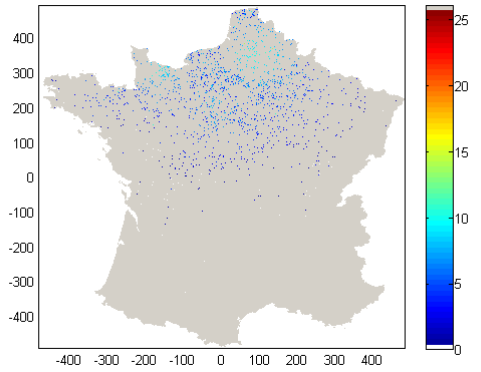
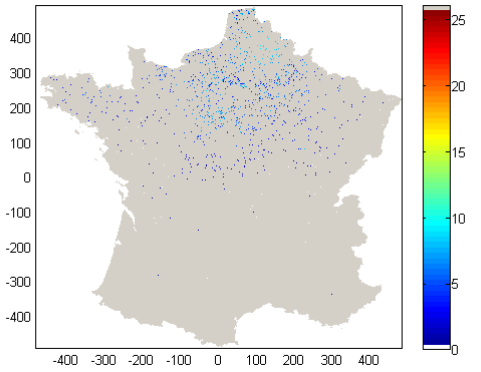
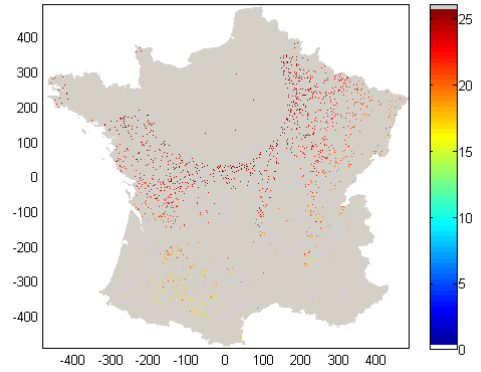
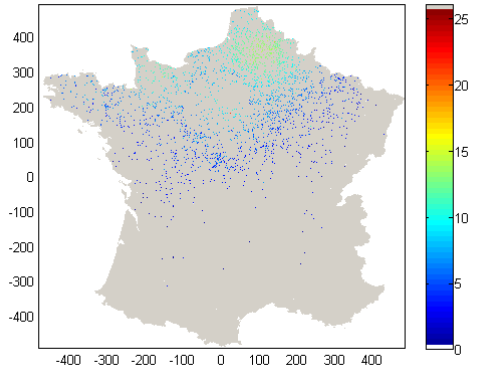
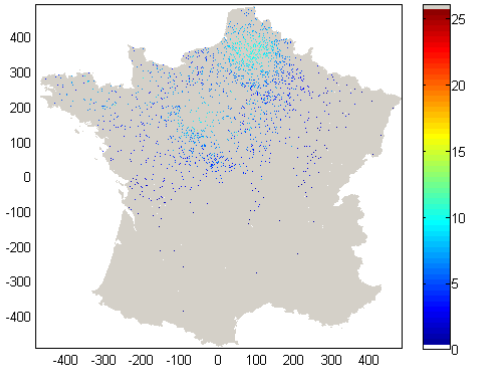
End pathogen generation 4		
End pathogen generation 5		
End pathogen generation 6		

Figure 5. Example of seasonal dynamics of the avirulent and two virulent genotypes in France. Colorbar depicts log($A(x, y, g, t)$), respectively log($V_1(x, y, g, t)$) and log($V_3(x, y, g, t)$). Depicted for simultaneous use of four single-gene resistant varieties, with total fraction of host r_{tot}=0.6.

time	Avirulent: first year	Virulent on R1: first year	Virulent on R3: first year
Start growing season			
End pathogen generation 1			

End pathogen generation 2			
End pathogen generation 3			

End pathogen generation 4			
End pathogen generation 5			

End pathogen generation 6			
	Avirulent: second year	Virulent on R1: second year	Virulent on R3: second year
End pathogen generation 6, 2nd			

3.4.2 Useful life

When virulence is already present in a very small fraction of the pathogen population, the useful life of a resistance gene was usually low and differences between deployment strategies are very small (blue bars in Figure 6). This picture completely changes when virulence has to emerge by a single mutation for sequential use and by stepwise mutation for varieties with a pyramid of two resistance genes (green bars in Figure 6). The pyramid of two resistance genes in one variety, was in 30 growing seasons never broken down. Not once in all three replicates of all tested fractions of resistant fields. Furthermore, as compared to virulence that was already present the useful life was longer and now two single resistant varieties had a longer useful life if used in sequence as compared to when they were grown simultaneously. Simultaneous use reduced the useful life on average with 4 years. The degree of clustering had no effect on the useful life (result not shown).

When virulent genotypes of the pathogen population have to emerge by stepwise mutation, concurrent use of varieties with single resistance and a variety with pyramid of (the same) two resistance genes, has a strong negative effect on the useful life of the double resistant variety (Figure 6). A pyramided variety on its own was never broken down in 30 growing seasons. When a double resistant variety is deployed together with single resistant varieties with the same virulence genes, a single virulent genotype has a selective advantage over the avirulent population and thus has a chance to increase in numbers. This also increases the chance that a pathogen genotype with two virulences emerges. The single resistant varieties serve as stepping stones for the double virulent genotype. This effect is strongest when the fraction of single resistant varieties is high (see the green bars at the right hand side of Figure 6).

Crop rotation prolongs the useful life of resistance genes, especially when virulence has to emerge by mutation (Figure 7). Crop rotation reduced the total population size and therefore the chance that a virulent genotype emerges and settles is lower.

If there is no bottleneck in between season survival (e.g. when a fraction *s* of the lesions could survive in all compatible host fields in France) the useful life was drastically reduced, for sequential use this reduction was between 2 to 4 year (selection scenario) and 3 to 7 years, when virulence had to emerge by mutation. In all cases, the reduction was largest for lower fraction of resistant fields. It also affected the useful life for pyramiding when virulence had to emerge by mutation. The better survival, and thus larger population size, of both the virulent and avirulent drastically reduces the effectiviness of a double-gene resistant variety. The useful life was now ranged between 3 to 30 years of effectiviness, with large variation.

When four single resistant varieties are grown simultaneously, and virulence has to emerge by stepwise mutation, the useful life is very variable (Figure 8). We studied the effect of three management strategies for when the resistance of one of the initially four simultaneously grown single resistant varieties is broken down: 1. remove and replace by a new resistant variety (blue dots in Fig. 8), 2. prolong the use of variety of which resistance is broken down (red dots in Fig. 8), 3. remove and reallocate the remaining resistant varieties over the total fraction of resistant fields (green dots in Fig. 8). The useful life of four resistance genes is highest when the use of a resistance gene that is broken down is prolonged. This variety is susceptible for part of the population, but still effective to the rest of the pathogen genotypes. For this management strategy the useful life is on average higher than for sequential use and in several simulations the useful life was longer than 30 years. The useful life of four resistance genes is lowest when a resistance gene is removed and replaced the moment it is broken down. The useful life for this management strategy is on average lower than for sequential use of four single-gene resistant varieties.

A large scale spatial pattern, where the used variety was allocated at the level of departments, for the four simultaneously grown single-gene resistant varieties reduced the useful life was on average 6 to 8 years as compared to sequential use (results not shown).

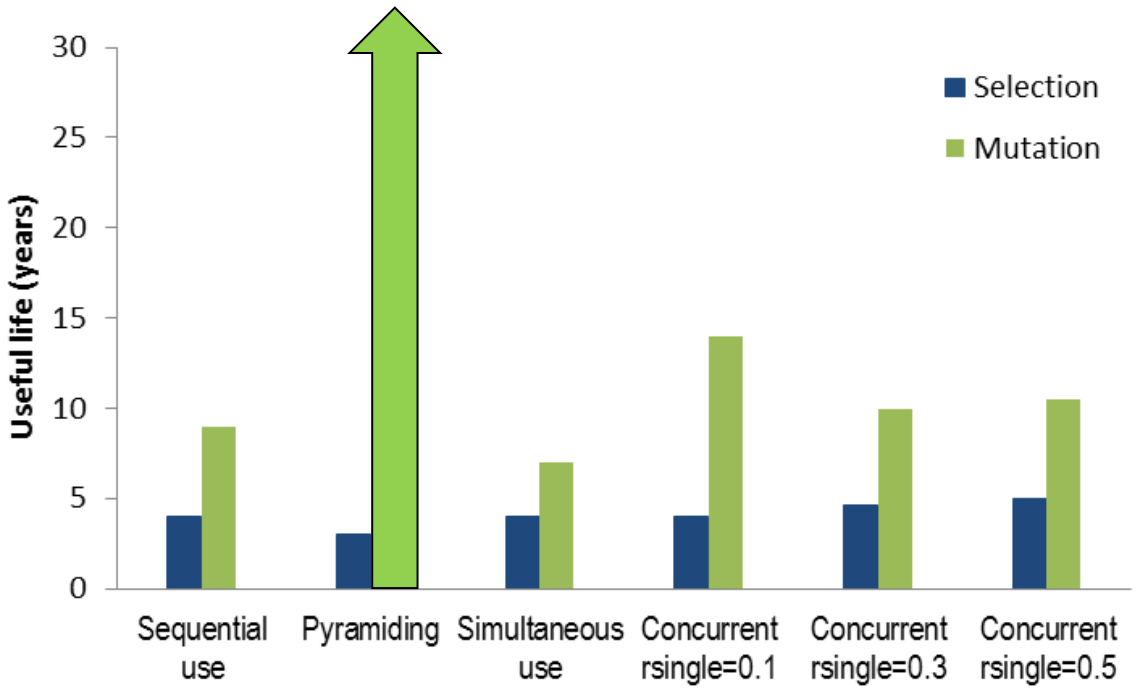


Figure 6. Useful life in years for sequential use of two single-gene resistant varieties, pyramiding of two genes in one variety and concurrent use of two single-gene resistant varieties together with a pyramided variety, where r_{single} denotes the total fraction of the two single resistant varieties. The useful life for the selection scenario is depicted by the blue bars, and the useful life for the mutation scenario is depicted by the blue bars. Results depicted for total fraction of resistant host, r_{tot}=0.6. The other parameter values can be found in Table 1.

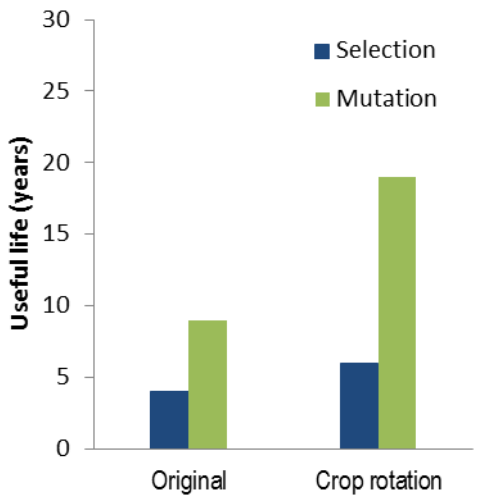


Figure 7. Useful life in years for sequential use of two single-gene resistant varieties for random placement of the host fields between growing seasons and for 3-year crop rotation cycle. The useful life for the selection scenario is depicted by the blue bars, and the useful life for the mutation scenario is depicted by the blue bars. Results depicted for fraction of resistant host, r=0.6.The other parameter values can be found in Table 1.

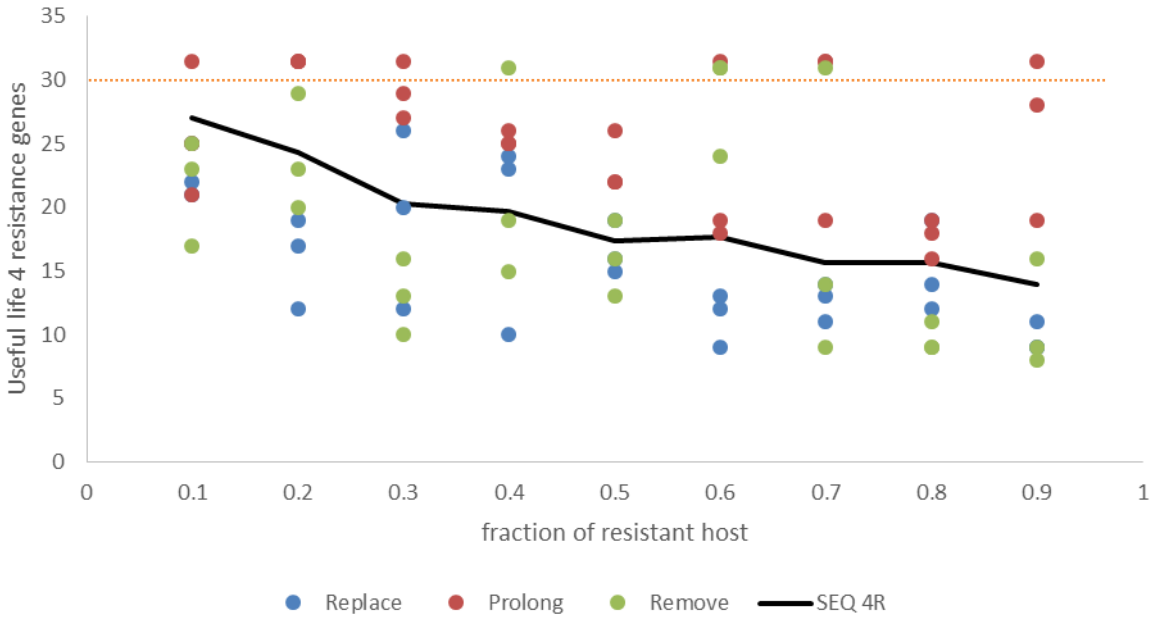


Figure 8. Effect of management strategy and fraction of resistant host on useful life in years for simultaneous use of four single-gene resistant varieties. With management strategies; remove and replace variety when resistance is broken down (blue dots), prolong use of variety with broken down resistance (red dots) and remove broken down variety and reallocate effective varieties (green dots), and, for reference, the average useful life (over three replicates) for sequential use of four single-gene resistant varieties (black line). Dots above the orange dotted indicate that for that replicate the resistance gene(s) of one or more of the four single-gene resistant varieties did not break down with 30 years.

4. General conclusion and discussion

The deployment of resistant cultivars is a widely used strategy for pest and disease management. The limited durability of qualitative resistance remains a major problem in systems where pathogens have a high evolutionary potential. Breeding a new high-yielding variety with new resistance genes takes time and the genetic pool for new resistance genes to replace the broken ones is limited, therefore it is important deploy new resistance genes so that the useful life is prolonged.

To study which management strategies can prolong the useful life of resistance genes, we developed a spatial explicit generic model to simulate population dynamics, selection and spread of air-borne diseases that is easily scalable to smaller or larger scale. We parameterized for *Puccinia striiformis* f. sp. *tritici* the causal agent of yellow rust in wheat. For this spatial explicit model we developed blueprints for spatial strategies of resistance gene deployment to find a management strategy that deploys plant resistance genes in the most durable way. These blueprints consist of variety choice (e.g. use of single resistant varieties, stacking of resistance genes, using multiple resistant varieties simultaneously), and characteristics of spatial deployment (e.g. fraction of resistant fields and degree of clustering of wheat fields).

When virulence is already present in a very small fraction of the population and only the selection process plays a role, then the useful life of two resistance genes is generally low for all management strategies.

However, *when virulence has to evolve by mutation* the useful life is higher for all management strategies. The useful life was highest for pyramiding (a double-gene resistant variety did not break down within 30 years), followed by sequential use. Simultaneous use reduced the useful life of two resistance genes on average with 4 years as compared to sequential use. Concurrent use of varieties with single resistance and a variety with pyramid

of (the same) two resistance genes, has a strong negative effect on the useful life of the double resistant variety. The single resistant varieties serve as stepping stones for the emergence of double virulent genotype. This effect is strongest when the fraction of single resistant varieties is high.

Crop rotation reduces the total population size at the start of a new growing season and therefore has a postive effect on the useful life of resistance genes when virulence has to appear by mutation.

Other measures to prolong useful life

Variety choice and spatial deployment of varieties are two cultural practises that can be used in an integrated pest management strategy to prevent the occurrence of disease. Due to the fact that resistance in plants cannot made durable these two management options always have to be combined with other measures like monitoring for disease and if disease is higher than the economic threshold, responsible pesticide use. Furthermore, useful life and effectiveness of qualitative resistance could be prolonged if these would be combined with quantitative resistance, which slows down selection once the qualitative resistance gene is broken down.

In conclusion

Our results show that without fitness penalties for pathogen virulence, plant resistance cannot be made permanent, but durable life can be modified by the deployment strategy. Simulation results from the spatial explicit model in a realistic setting (based on the existing pattern of arable land in France and the percentage wheat grown per department in France) show that when a certain virulence gene is already present in a very small fraction the pathogen population the use of a resistance gene is generally low. When virulence has to arise by mutation, pyramiding of two new resistance genes is the most durable management strategy.

The useful life for sequential use is much lower, and simultaneous use reduces the useful life even more. Using single-gene resistant varieties together with pyramided varieties breaks down the effectiviness of the pyramided variety and reduces the useful life. Crop rotation has a positive effect on the useful life of resistance genes.

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Annex I: Choice of parameter values for the spatial explicit model at a national level

In this appendix we derive parameter values for the population model for *Puccinia striiformis* f. sp. *tritici* in France, the causal agent of yellow rust (stripe rust) in wheat, *Triticum aestivum*, based on literature and calculations.

Population dynamics of *Puccinia striiformis*

P. striiformis in France is generally present from early March when wheat starts to grow to mid-June when the temperatures become too warm. *P. striiformis* has a latent period of 14 days (Milus et al., 2009). Therefore on average it can complete $\tau = 6$ generations in one growing season.

In the literature we found values of apparent infection rates r = 0.2-0.3 (Zeng and Luo, 2008) and taking a generation time of 14 days (i.e. equal to the latent period) would give a value for the multiplication factor of *P. striiformis*, λ, in the range of 16 to 66. Based on a rough calculation where we assume that disease starts off in spring with 5 leaves per hectare with 1% of the leaf area covered with yellow rust and ends with 50% infestation on all the leaves. Taking into account that the leaf area index (LAI) meanwhile increases from 0.1 to 4 and that the increase in disease is reached in $\tau = 6$ pathogen generations. If we assume that there are 400 culms/hectare, we can calculate the increase in disease by, (0.5 % infestation * 4 LAI)/(5 culms * 0.01% infestation * 0.1 LAI / (400*10000 culms per hectare)) = $1.6*10^9$. The multiplication factor per pathogen generation is then $(1.6*10^9)^{(1/6)}$ = 34.2. We set the

multiplication factor of the pathogen at $\lambda = 35$. This is within the range of 16 to 66 based on the apparent infection rates found in the literature.

Most studies on dispersal of *P. striiformis* has been done at a field scale (Soubeyrand et al., 2007). Mainly because on larger scales there is a limited spore load and therefore disease caused by these spores are often below practical detection thresholds. Soubeyrand et al. (2007) found maximum dispersal distances, of 225 m approximately equal to the maximum length from the source that was measured in the experiment. We therefore assume that even though a very large fraction of pathogen spores remain in the field still a small part of the spores is able to leave the field and thus take $q = 0.05$.

Virulence frequencies

We assume that the initial fraction of single virulent spores in the pathogen population β is set at 10^{-4}, because we expect that when the matching resistance is not yet in use this genotype of pathogens will have no selective advantage in the population and will occur in only a fraction of the population equal to the mutation rate, which is between 10^{-6} for loci not subject to selection and 10^{-3} for loci under selection (Hovmøller et al., 2008). We take the initial fraction of double virulent genotypes to be β^2 and the initial fraction of triple virulent genotypes β^3 up to β^5 for pathogens that are virulent on 5 resistance genes.

We take the threshold fraction of virulent spores in the pathogen population at which we consider the resistance variety to be broken down to be θ_e=0.45 based on the fact that the fraction of virulent pathogens can develop from this threshold value to 0.99 in one growing season.

Dispersal of *Puccinia striiformis*

To estimate the spread of *P. striiformis* we tested a set of parameter combinations of the length scale of pathogen dispersal *u*, and the shape parameter of the 2Dt model ν. We tested a range of parameter combinations starting from a length scale *u*=10 km to 30 km and a very fat tail (ν=2), to a thin tail ν=100 (approaching normal distribution). The dispersal kernel was fitted on the data of 5 genotypes of *P. striiformis* (233E137V17, 237E141V17, 233E169V17, 237E173V17 and 239E175V17) that were selected because they were present in multiple years, and were observed multiples times per year. It is important to have enough data points to estimate spread. For each pathotype and each year, the first observation was marked to be generation 1, each observation within the first two weeks was also marked as generation 1. The observations between two weeks and four weeks from the first observation were marked as generation 2, and the remaining observations where also marked with a generation number depending on the timing since the first observation. For each genotype and year combination we used the first observation in a department as the timing that the pathogen reached the department. For the estimation, departments 22, 80, 28, 59, 78 and 14 were the starting departments as most first observations were in these departments. We used the sum of squared differences to find the parameter combination that minimized this difference. We used several parameter combinations of *u* and ν that gave similar good results on the national scale. We run 5 replicates to see which combination had the best result over several simulations. We choose the combination *u*=25 and ν=5 as the average sum of squared differences was the least for this combination.

length scale, *u*	shape parameter, ν	SOS				
25	**5**	832	830	828	828	831
20	**4**	833	829	830	830	828
15	**3**	836	836	836	836	859