ENDURE

European Network for Durable Exploitation of crop protection strategies

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Recommendations on minimum requirements for biological data acquisition to assist the choice of adequate strategies for durable resistance breeding and management

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Dissemination Level	
PU Public	**PU**
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Glossary

ENDURE	European Network for Durable Exploitation of crop protection strategies

Definitions

Differential fitness: differential survivorship and reproductive success among genotypes in a given studied population.

Fitness costs of virulence: loss in survivorship and/or reproductive success of a pathogen strain that is associated with the presence of a particular virulence.

Major resistance gene (also called R-gene): confers complete resistance usually specific to a pathogen strain carrying the corresponding avirulence; can be overcome by a virulent pathogen strain, according to the gene-for-gene relationship.

QTL (quantitative) resistance: Quantitative Trait Locus; each QTL confers a partial (incomplete) resistance effect to a pathogen genotype.

Multigenic resistance: genetic resistance of a genotype controlled by multiple resistance factors (either major resistance gene(s) and/or QTL(s)).

Non-specific resistance: resistance that is effective against a broad spectrum of pathogen virulences; sometimes called “horizontal resistance”.

Summary

Write a short summary of your Deliverable. This summary must be 2 pages maximum but very informative and must include the following elements:

Objectives of your deliverable

Mathematical modelling is an effective tool that can be used to evaluate resistance deployment strategies to identify or design the most effective strategies for durable management of plant diseases through intelligent deployment of host resistance in time and in space. Successful application of mathematical models to these ends requires a minimum level of input, for example on basic characteristics of the respective pathosystems, their structure, state and rate variables, dynamics and driving forces. The type and level of required input information varies with the modelling approach and its ability to describe demo-genetic dynamics of pathosystems. The objective of our deliverable is to provide recommendations on the minimum requirements for biological data suitable for mathematical modelling to assist in developing adequate strategies for durable disease resistance breeding and management.

Rationale: describe the approach/methodology you chose to reach the objectives

In RA4.2 we used three different modelling approaches at different levels of time and space to rationalize and optimize the exploitation of disease resistant varieties carrying multigenic resistance in agroecosystems where high infection pressure induces fast pathogen adaptation to resistance. As a result of the specific representation of time and space, each model has different data needs. However, all three approaches encompass some general principles on describing host-pathogen dynamics that make them widely applicable across pathosystems and agroecological conditions. Their requirements for biological data can thus be summarized to yield a generic protocol for a minimum standard data set for the durable management of disease resistant varieties.

Degree of validation and operability of findings: Specify the degree of validation and applicability of the findings described in this deliverable (still development stage, not practical to adopt, effective scientifically sound, only practiced at experimental farms, applicable in the field, practical to adopt and cost effective, etc.)

Our data protocol is applicable for designing and assessing strategies of durable management of diseases through deployment of host resistance at various temporal and spatial scales. It is necessary for and will facilitate linking theoretical and practical studies on the sustainable use of disease resistance in arable and orchard crops.

Teams involved: Specify the list of ENDURE partners and other contributors that have worked on this Deliverable (Just the name of the organism, not the name of the persons).

RA4.2 teams: INRA, WUR, AU.

Geographical areas covered: Specify the list of the geographical areas covered by your deliverable (can be a list of countries, pedo-climatic regions, all Europe, etc.)

The suggested data protocol has universal application to any pathosystem, independently of its geographical location.

1. State of the art

The use of mathematical models describing the dynamics of host-pathogen systems for practical purposes, as management of resistant varieties, requires adequate biological information and data to derive credible recommendations.

Being mechanistic, the reaction-diffusion models (see section 3.1) describe quite precisely the spatial dynamics of plant epidemics and can be applied to a wide range of pathosystems (Okubo & Levin 2000). The advantage of this type of models is that parameters have physical units and can be estimated in reasonable time due to available characteristics of epidemic dynamics, i.e. severity dynamics, and existing powerful numerical methods. The application of a host-pathogen model to the management of quantitative resistance in diversified agroecosystems increases the number of parameters, since it requires the splitting of host and pathogen populations into sub-populations representing different varieties and pathogen pathotypes respectively. In section 3.1, we illustrate our approach of the host-pathogen model use by the example of wheat-yellow rust pathosystem.

Strategic spatial deployment of crops and crop varieties could make agricultural landscapes less vulnerable to plant disease epidemics. A mechanistic multi-scale model was used to investigate the effect of the (short or longer range) airborne dispersal capability of the pathogens included in RA4.2 on the contribution of field or landscape level measures to the overall resistance of the landscape to pathogen invasion (see section 3.2). The model framework comprises a landscape generator, a field-scale model of the host and pathogen life cycles including management, and an atmospheric dispersion model. It was originally developed for the potato late blight pathosystem and used to study interrelationships between invasion of the pathogen, spatial heterogeneity of the host, genotypic heterogeneity of the host at different levels of spatial grain, and weather (Skelsey et al., Phytopathology, accepted). In this study, spatial heterogeneity in host populations exerted a large effect on disease incidence. Within a single growing region, the more effective strategies limited deployment of a highly susceptible host and/or decreased the overall amount of the host (potato). Due to the capacity of *P. infestans* for long distance transport of viable inoculum, regional designs that focused on creating large separation distances between production areas (through manipulation of field size and clustering of potato fields) were non-limiting to disease spread, and resulted in severe epidemics within areas of dense potato cultivation. Strategies that induced finer-grained spatial and genotypic heterogeneities in host populations were consistently limiting to epidemic spread. Genotype mixing (within fields) was a consistently effective option for generating individual growing regions that were more resilient to disease invasion. The magnitude of host diversity effects was highly dependent on meteorological conditions.

A relatively simple (“parsimonious”, see section 3.3.) population genetic model has successfully been applied to describe changes in frequencies of (a)virulence genes and pathotypes of the air-borne pathogen barley powdery mildew (*Blumeria graminis f. sp. hordei*) over time as driven by the proportion of agricultural areas planted to host genotypes carrying mildew resistance genes exerting selection pressure on the pathogen population (e.g. Hovmøller et al. 1993, Bousset et al. 2002). The parsimony of this model and its apparent capability to describe essential features of the evolution of pathogen populations suggest its use as a simple and generic tool for exploring and optimizing strategies for resistance gene deployment over time. The model has not yet been applied to pathosystems other than barley powdery mildew although this is principally possible. Also, it lacks input options to accommodate partial (specific and non-specific) resistance on the host side and fitness costs of virulence on the pathogen side. The work described in 3.3. incorporated the above mentioned additional features and aimed at applying the approach to other pathosystems such as wheat yellow rust.

2. Harmonization of material and methods among the Network

Please describe the reflection on the adjustment of protocols and harmonization of materials and methods that have occurred in different studies of your sub-activity contributing to this Deliverable. Could these adjustments and harmonization be adopted by the whole Network and how?

A meeting among modellers and experimental researchers (22-23 May 2008, Rennes, France) was held aiming at harmonizing the work of these groups. In particular, the type of biological data, parameters and details on how to measure them were conveyed. This deliverable outlines the data needs for the described modelling approaches and provides suggestions on a generic data protocol facilitating the use of models in research aiming at breeding for sustainable disease resistance and management in agricultural and orchard crops.

3. RA4.2 Modelling Activity

Here we present three modelling approaches used in RA4.2 for deriving effective strategies of multigenic resistance deployment in time and space. For each model, data requirements are detailed in "Host Input" and "Pathogen Input" items.

3.1. Reaction-diffusion model of host-pathogen dynamics (INRA)

3.1.1. The model

We built a new spatially explicit model for evolutionary and epidemiological dynamics of a host–pathogen system in a two-dimensional landscape (Sapoukhina et al. 2009). The model was developed in the context of the reaction–diffusion models with integration of sexual and asexual reproduction for a pathogen population and multilocus gene-for-gene interactions. The model allowed us to understand how the synergy between genetic and spatial composition of the host population affects pathogen spread through postimmigration recombination. We examined evolutionary and invasive responses of the pathogen on the designed spatial and genetic compositions of the host population. We concluded that rational spatial deployment of resistance genes is crucial to control the pathogen population with differential fitness.

Although the model includes an all-or-nothing qualitative response, it can be easily adopted and used for the management of quantitative forms of resistance. Wheat-yellow rust pathosystem was chosen to illustrate the model extension and its application for designing well-suited strategies for the spatial deployment of quantitative resistance at the field scale.

3.1.2. Host Input

- We assume that all varieties composing diversified host population have identical growth rate, carrying capacity and initial density. Data on Leaf Area Index (LAI) temporal dynamics allowing us to assess the model parameters representing varieties growth and their initial density. If this information is available for the each considered variety, the assumption of 'identical rates' can be relaxed.
- Scenarios of spatial arrangements of resistant varieties in space including: (i) the field size, (ii) the number of different varieties, (iii) their geometric arrangement at the chosen spatial scale.

3.1.3. Pathogen Input

- We assume that all pathotypes of the pathogen population have an identical rate of spread. The rate of spread (m^2/t) of the pathogen population can be estimated if the mean square displacement of organisms per time unit after their release is known. If

this information is available for the each pathogen pathotype, the assumption of 'identical rates' can be relaxed.

- Pathogen dynamics on the susceptible variety represented by severity dynamics helps us to estimate initial density, the attack rate, the efficiency rate and the mortality rate of an avirulent pathogen pathotype.
- Differential fitness within pathogen population (assessed by a differential reproduction rate) allows us to split pathogen population into pathotypes with different efficiency rates. The efficiency rate is a quantitative notion of the pathogen response on the genetic background of a plant variety. A value of the pathogen efficiency rate characterizes implicitly the type of plant resistance, that can be quantitative or qualitative, and its capacity to reduce pathogen density. For instance, '0' efficiency rate means no interaction with a variety carrying a major resistance gene. Initial pathotypes density, their attack and mortality rates are assumed to equate to the rates of the avirulent pathotype.
- If the risk of the pathogen adaptation to resistance is high, the scenarios of potential pathogen adaptation can precise the derived recommendations on the the spatial deployment of quantitative resistance in diversified systems at the field scale.

3.2. Large-scale epidemic dispersal model (WUR)

3.2.1. The model

The model framework comprised a landscape generator, a field-scale model including host and pathogen life cycles and fungicide management, and an atmospheric dispersion model. Landscapes consisted of a growing region (6.4 x 6.4 km) embedded within a larger area of non-host space.

Host and pathogen life cycles, host-pathogen interactions, and fungicide applications are simulated on gridded (raster) landscapes. Landscapes are composed of host and non-host fields arranged according to a set of user defined spatial design parameters including the fraction host in the landscape, the susceptible fraction of the host, field size and the level of clustering of fields. A recently validated (Skelsey et al. 2009) adaptation of the model originally developed by Skelsey et al. (2005) is used to provide grid cell dynamics. Individual grid cells in the landscape are linked through models describing spore dispersal and survival (Skelsey et al. 2008). Within this modelling framework, the composition, configuration and connectivity of host populations are manipulated in order to reveal the influence of these measures on epidemic progress both within and between regions. Multiple growing seasons and multiple landscapes satisfying the same set of user defined spatial design parameters were simulated to capture random effects of weather and exact spatial configuration. The results of these manipulations are used to derive spatial strategies for the deployment of resistance genes.

For the purpose of the current study it was not feasible to develop process based field level biological models for all pathosystems included in RA4.2. Instead, it was decided to focus on the effect of the considerably different dispersal capabilities of these pathogens on the contribution of individual landscaping measures to the overall resilience of the landscape to pathogen invasion. Thus, the dispersal model was changed to adopt a wide range of dispersal characteristics covering the entire range found for fungal spores from very poor to exceptionally well dispersing spores. The original, potato – *P. infestans*, biological model describing pathogen and host dynamics was maintained representing a worst case scenario in terms of spore production capacity.

3.2.2. Host Input

Also the original model describing host dynamics is maintained and is not replaced with a pathosystem specific model. The sub-model for host dynamics is described in full in Skelsey et al. (2009b). Leaf area development is simulated through thermal time

accumulation. Leaf area index, LAI, is initialized at 0.05, and increase in LAI is modeled as a logistic function of growing degree days. LAI is increased until the temperature sum reaches a maximum cultivar specific value at which point net leaf growth becomes net leaf death. Shedding of leaves is also calculated as a logistic function of growing degree days. LAI values are not spatially indexed, i.e., the same leaf area dynamics are used for each host cell in the landscape.

3.2.3. Pathogen Input

The potato late blight model is comprised of five process based sub-models; a model of the disease cycle in planta, models for spore release from sporangiophores, spore escape from the potato canopy and atmospheric spore dispersal and survival, a model for host growth, and a model for fungicide management. The model for the disease cycle is described in Skelsey et al. (2005, 2009a), the host growth and fungicide management models is described in Skelsey et al. (2009b) and the model describing atmospheric dispersal is described in Skelsey et al. (2008).

For the current study, the model describing pathogen dynamics at field level was maintained assuming all pathogens sporulate as abundantly and under the same circumstances as *P. infestans*. The more the biology of the pathogen under consideration deviates from *P. infestans*, the more this assumption is at odds with reality. For the current purpose it is however assumed to be acceptable as it very likely represents a worst case scenario in terms of the production of propagules.

The models describing atmospheric spore dispersal and survival were however adapted to cover a wide range of dispersal capabilities:

- Spore dispersal: The partial reflection Gaussian plume model of Overcamp (1976) is used to compute spore transportation and deposition as it is a fully analytical atmospheric dispersion model. Since this is a physical model for dispersal of botanical spores, the pathogen specific parameter settling velocity was changed to represent the full range of possibilities for fungal spores: A minimum settling velocity of 0.003 cm/s representing *Coccidioides immitis*, an intermediate settling velocity of 0.85 cm/s representing *P. infestans* and a maximum settling velocity of 2.78 cm/s representing *Helminthosporium sativum* was used.
- Spore survival: The experimental results of Mizubuti et al. (2000) are used to determine the fraction of deposited spores that remained infective during atmospheric transport. Survival of spores during transportation is made dependent on the dose of global radiation received during transportation. For the purpose of this study, the UV sensitivity of spores during aerial transport was modified to cover a range of 5x, 1x and 1/5x the sensitivity of *P. infestans* to UV.

All possible combinations of settling velocity and UV sensitivity were used in the simulations and applied to 10 landscapes and 10 weather data sets (growing seasons) each.

3.3. Parsimonious model of pathogen population evolution (AU)

3.3.1. The model

The parsimonious model is a modified version of the model described by Østergård & Hovmøller (1991) that is based on elementary population genetic principles outlined by Hartl (1980). It depicts a system of three loci of the haploid stage of a pathogen, each with two alleles (either avirulent or virulent), interacting with three corresponding loci for major gene resistance in the host, likewise each with two alleles (resistant or susceptible). It computes the relative frequency of pathogen propagules (air-borne spores) of each of the eight possible pathogen genotypes over consecutive seasons. This is driven by the probability that spores of a particular pathogen genotype are establishing infections on a particular host genotype, depending on their relative fitness on individual host genotypes and the relative area planted to host genotypes with different resistance genes over time. The model was

extended to accommodate specific and non-specific partial resistance effects (QTLs) as well as the effects of varying fitness costs of virulence. It was assumed that the pathogen reproduces asexually, selection is the only evolutionary force, spore dispersal is proportional to the respective relative host areas and spore production is identical across pathogen genotypes and host varieties.

3.3.2. Host Input

- Fraction of an agroecological area planted with individual host genotypes carrying particular resistance sources (R-genes and/or QTLs) and types (partial or complete, avirulence-specific or non-specific resistance) over consecutive cropping seasons.
- Resistance sources and types present in the individual host genotypes.
- Quantitative expression of the respective resistance sources or types with regard to their effect on the fitness of individual pathogen genotypes (0 = no effect; …, 1 = 100% effective). Note: this feature allows to emulate the quantitative effect of any source and type of resistance on any pathogen strain, i.e. whether and to what degree resistance effects express differentially across individual pathotypes.

3.3.3. Pathogen Input

- Relative frequency of individual pathotypes, i.e. of pathogen genotypes with particular virulences and avirulences that correspond to specific resistance sources in the host cultivars, at the beginning of the new growing season and/or at the end of the previous growing season.
- Relative fitness costs associated with the presence of particular virulences in individual pathotypes.

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Conclusion

The presented models allow us to suggest minimum requirements for biological data acquisition to assist in choosing adequate strategies for durable resistance management. Table 1 summarizes a data protocol accounting for essential information needed to design sustainable strategies for deploying host plant resistance.

Table 1. Protocol for a minimum standard data set for the durable management of disease resistant varieties.

	Data	Descriptors
1	Host population growth	• LAI (leaf area index) temporal dynamics.
2	Tested strategies of resistance management	• Spatial scale. • Relative proportion of the agroecological region planted to individual crop cultivars possessing particular resistance types and sources over time. • Arrangement of varieties in space at the chosen scale.
3	Pathogen: spread	• Settling velocity and UV sensitivity of spores or the mean square displacement of spores per time unit.
4	Pathogen: efficiency	• Qualitative and quantitative information on disease resistance factors and properties of the crop cultivars used in a particular agroecological region, i.e. presence of individual major resistance genes and sources for partial resistance (e.g. QTLs) and their quantitative effects on the fitness of corresponding pathogen genotypes (partial versus complete). Eventually, such information would have to be obtained from trials in which individual cultivars are inoculated with a set of single spore isolates representing the relevant range of virulence patterns. However, the presence of major genes for specific types of resistance in a cultivar and/or the corresponding molecular markers are often known for important pathosystems such as wheat yellow rust. • Quantitative data on the fitness costs for single and multiple virulences in individual pathotypes. This type of information could eventually be obtained from appropriately modified experimental setups mentioned above and in 5.
5	Pathogen: initial conditions	• Data on frequencies of individual pathogen genotypes (where the avirulence and virulence properties of these correspond to the resistance types and sources in the grown host cultivars) at the end of the previous season respectively at the beginning of the new season. Since functional molecular markers are not (yet) available for this purpose, the respective data could be obtained via classical virulence surveys followed by pathotype analyses using differential cultivars.

The treatment of this biological information by mathematical models helps us to outline the primary paths for the durable management of resistant varieties.

The reaction-diffusion model of host-pathogen dynamics (section 3.1) allows us to select varieties for the mixture composition and to predict the efficiency of the diversification strategy. Accounting for differential fitness of the pathogen genotypes allows us to understand the effects of the heterogeneous fitness landscape of the pathogen population on

its dynamics. With parameterized model for the dynamics of wheat-rust system we showed under which conditions quantitative plant resistance could be used to design effective varietal mixtures. The model demonstrates that the use of susceptible varieties in mixtures with highly or moderately resistant varieties decreases mixture efficacy, favoring coexistence of multivirulent pathotypes. Varieties with the moderate level of resistance can be effectively exploited in three-component mixtures including highly resistant varieties. The model results show the key-role of differential pathogen fitness for the designing sustainable diversification strategies of agro-ecosystems.

Results from the large-scale epidemic dispersal model (section 3.2) suggest that the effects of different landscaping measures over the wide range of UV sensitivity and settling velocity were fairly stable. Also the effect of mixing (between fields versus within fields) is stable for all levels of UV sensitivity and settling velocity. These results were obtained by modifying a set of models representing the potato late blight pathosystem. Host and pathogen models were not adapted to the various pathosystems represented in RA4.2 except for the settling velocity and the UV sensitivity of aerially dispersed propagules. This approach did not require any experimentation since the necessary parameters can be found in literature but it turns the current approach into a " helicopter screening" with results that are generally valid but that may deviate in specific cases. For specific cases the biological models representing pathogen and host dynamics should be replaced or adapted to represent the pathosystem of interest. The dispersal model can be easily adapted by using pathogen specific values for the settling velocity and UV sensitivity.

Results of the parsimonious model (section 3.3) strongly suggest that maintaining a high proportion of crop cultivars possessing partial resistance, either effective "horizontally" (= suppressing all virulent pathotypes to some degree) or specifically (= allowing some level of reproduction of pathotypes carrying corresponding avirulence), provides a high degree of sustainability in resistance management, because it helps to keep the mean fitness of the pathogen population and the frequency of pathotypes with complex virulences at a low level while keeping the frequency of pathogen genotypes with multiple avirulences at a high level over time. The magnitude of this effect is hard to beat by any resistance deployment strategy solely relying on specific (major gene) resistance sources. However, the pathogen genotype frequency at the beginning of a resistance deployment strategy and the fitness costs that pathotypes "have to pay" for possessing particular virulences have very significant effects on resistance durability and stability.