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A Deterministic Model to Evaluate and Improve the Strategy of Insect Resistance Management (IRM) to Genetically Modified Plants Synthesizing a Cry Toxin

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The recommended IRM strategy is to use High Dose and Refuge Strategy to slow down the development of resistance to *Bacillus thuringiensis* modified plants in the target insect. We developed a model to determine the optimal values of the parameters characterizing this strategy of how to best slow down the development of resistance. With the aid of our simulations, we determined that the resistance development accelerates in relation to the increase of the resistance allele dominance, the larval speed and the mortality of the susceptible insect on the plants synthesizing Cry toxin. Each parameter was varied independently. However, the development of resistance is inversely proportional to the size of the refuge proportion. These conclusions can contribute to improve the IRM strategy but it is necessary to keep in mind the feasibility of using this approach on the field.

Introduction

Bacillus thuringiensis (Bt) plants are genetically modified plants synthesizing Cry toxins and their main targets are members of the Lepidoptera. These modified plants have been on the market since 1996 and they are grown globally on about 20 millions of hectares (1). One risk linked to this intensive use is the development of insects resistant to *Bt* modified plants. To limit this resistance development, a solution is to apply strategies of Insect Resistance Management (IRM) (2). Today, the strategy recommended by EPA is the High Dose/ Refuge strategy (HDR) (2).

Materials and methods

We have developed a mathematical and theoretical model to determine the optimal values of the parameters characterizing the HDR strategy for the best slowing down of the development of resistance. It is a deterministic model based on Mallet's population genetics model and is programmed in R language (3). We assumed that the fitness cost is nil for homozygous resistant insects and that the fitness is maximal in the refuge for all the genotypes. In this model, we have introduced two kinds of parameters: operational parameters characterizing the strategy (size of the refuge zone proportion and mortality of the susceptible insect on the *Bt* plants) and biological parameters (resistance allele dominance, initial frequency of resistance allele, proportion of larvae moving from the *Bt* zone to the refuge and from the refuge to the *Bt* zone).

The schematisation of the system with the principal steps composing the mathematical model is illustrated Fig. 1.

Results and discussion

This model allows to follow the evolution of the resistance allele frequency in relation to the generations. When we varied each parameter one by one and independently, we noticed that the development of resistance accelerated in relation to the increase of the allele resistance dominance, the proportion of moving

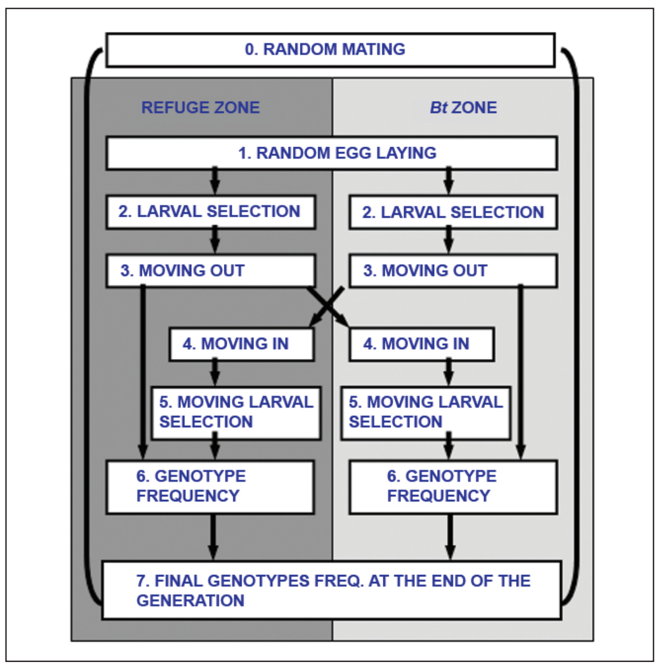

FIG. 1. Main steps of the model.

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larvae and of the mortality of the susceptible insect on the *Bt* plants. However, the development of resistance decreases when the proportion of the refuge zone increases. The conditions to slow down or minimize the development of resistance are a high proportion of refuge zone, a recessive resistance allele, a low insect mortality on the plants synthesizing Cry toxin and a low proportion of moving larvae.

Some results from our model correspond to those in the published literature, but one conclusion differs from the initial assumptions of the HDR strategy. Indeed, according to the HDR theory, *Bt* plants have to produce high toxin titre to increase the heterozygote mortality and to decrease the resistance allele frequency in the insect population (2). However, according to our model's results, *Bt* plants have to produce low toxin titre to increase the heterozygotes survival and to increase the susceptible allele frequency in the population. This increase will allow better dilution of the resistance allele in the next generations and thus, will delay the development of resistance. Vacher et al. (4) has also proposed this conclusion.

In practice, we can only modify the operational parameters to improve the IRM strategy. We recommend studying the possibility of decreasing the toxin titre in Bt plants and to increase the proportion of the refuge zone but these recommendations can increase the amount of pest damage to the crops. However, we have to keep in mind the equilibrium between crop productivity and resistance management. To study this equilibrium, we have to adapt this model and follow the population density evolution. Indeed, this would be useful to evaluate the resistance management impact on crop damage. We also want to increase the number of biological parameters introduced in the model. These biological parameters would be experimentally measured in a pyralidae species, *Plodia interpunctella* (Lepidoptera: Pyralidae). These modifications would improve the fitness evaluation of the two genotypes on the two zones and would also make the model more realistic. Finally, we have noticed that some parameters are not independent. We want to assess the impact of the correlation between the dominance of the resistance allele and the toxin titre in Bt plants on the resistance evolution.

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