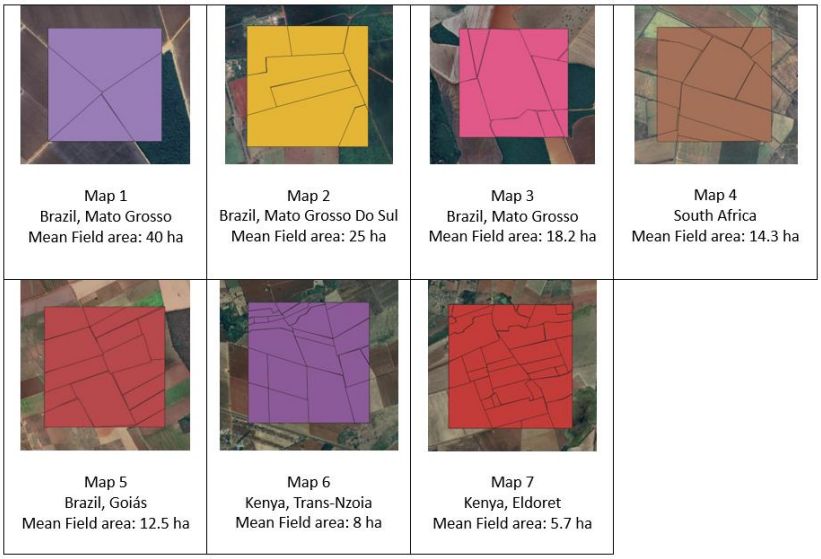
UNIVERSITY OF GOTHENBURG

DEPARTMENT OF BIOLOGICAL AND ENVIRONMENTAL SCIENCES

DO DIVERSE AGRICULTURAL LANDSCAPES LOWER THE RISK OF BIOPESTICIDE RESISTANCE EVOLUTION?



Hugo Boström

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Supervisor: Luc Bussiére

Examiner: Staffan Andersson

Figure 2 from thesis

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Abstract

Pesticide resistance decreases food security and leads to increased pesticide use and associated environmental damage and higher costs to farmers from increased applications. Alternative pesticide resistance management systems are needed to sustain future food security while protecting environments. Using a spatial matrix of different biopesticides instead of synthetic pesticides could possibly impose enough fluctuating selection to prevent directional resistance evolution, as long as there are trade-offs between traits that improve survival in the presence of different biopesticides. However, the scale at which divergent selection is needed to prevent evolution is unknown, and field experiments to examine the importance of gene flow are too time-consuming and logistically difficult. My project uses computer agent-based simulations to examine the effect of using two, three or four biopesticides in different landscapes to look at how diversity in agricultural land use affects resistance evolution. These simulations allow evolution in populations of digital pests with complex genomes. I further extract information from real world maps having a range of field sizes to incorporate the characteristics of realistic landscapes. My simulations showed substantial resistance evolution when only two or three biopesticides were used, but that using a larger number of biopesticides arrested resistance evolution. Surprisingly, the size of fields had no effect on resistance evolution regardless of biopesticide number: even in landscapes with large monocultures, there was enough gene flow in the computer population to prevent local resistance evolution and create sustainable pest control. I discuss my findings in the context of fundamental evolutionary principles, the demographics and dispersal abilities of pests, and the applied implications of my work for sustainable agriculture.

Sammanfattning

Resistens mot bekämpningsmedel minskar trygg livsmedelsförsörjning och leder till ökad användning av bekämpningsmedel vilket är förknippat med miljöskador och högre kostnader för jordbrukare till följd av ökad användning. Alternativa system för hantering av bekämpningsmedelsresistens behövs för att upprätthålla framtida livsmedelssäkerhet samtidigt som miljöerna skyddas. Att använda en geografisk matris av olika biologiska bekämpningsmedel i stället för syntetiska bekämpningsmedel kan eventuellt leda till ett tillräckligt fluktuerande selektionstryck för att förhindra riktad resistensutveckling, så länge det finns trade-offs mellan egenskaper som förbättrar överlevnaden i närvaro av olika biologiska bekämpningsmedel. Det är dock okänt i vilken skala divergent selektion behövs för att förhindra evolution, och fältexperiment för att undersöka betydelsen av genflöde är för tidskrävande och logistiskt svåra. I mitt projekt används agentbaserade simuleringar för att undersöka effekten av att använda två, tre eller fyra biologiska bekämpningsmedel i olika landskap för att undersöka hur mångfald i jordbruksmarkanvändning påverkar resistensutvecklingen. Dessa simuleringar möjliggör evolution i populationer av digitala skadedjur med komplexa genom. Jag extraherar dessutom information från verkliga kartor med olika fältstorlekar för att spegla egenskaperna hos verkliga landskap. Mina simuleringar visade en betydande resistensutveckling när endast två eller tre biologiska bekämpningsmedel användes, men att resistensutvecklingen avstannade när ett större antal biologiska bekämpningsmedel användes. Förvånansvärt nog hade storleken på fälten ingen effekt på resistensutvecklingen oavsett antalet biologiska bekämpningsmedel: även i landskap med stora monokulturer fanns det tillräckligt med genflöde i datorpopulationen för att förhindra lokal resistensutveckling och skapa hållbar skadedjursbekämpning. Jag diskuterar mina resultat i samband med grundläggande evolutionära principer, skadedjurens demografi och spridningsförmåga och de tillämpade konsekvenserna av mitt arbete för hållbart jordbruk.

Introduction

Food Security

The human population is continuing to increase (*World Population Prospects - Population Division - United Nations*, 2024) putting a high demand on food security (Godfray et al., 2010). Protecting crops from pests plays a key role in global food security, with pests consuming a fifth of crops produced (Oerke & Dehne, 2004). Chemical pesticides are commonly used for pest control, and global food security has benefited from intense use of pesticides (Wang et al., 2022). However, these large quantities of synthetic pesticides (Zhang, 2018) are harming our environment (Rani et al., 2021; Sharma et al., 2020), increasing the demand for alternative solutions.

Biopesticides

Biopesticides are botanical compounds such as bacteria, viruses and fungi as well as semi chemicals such as pheromones that are produced to suppress populations of pests (Glare et al., 2012). They offer a more targeted activity compared to most synthetic pesticides (T. R. Glare et al., 2016). Biopesticides decompose faster than traditional pesticides, which decreases the pest population's exposure to the pesticide This decreases the risk of pests evolving capacity to withstand the harmful effects of pesticides called pesticide resistance (Thakore, 2006). Risk of pesticide resistance is lowered by decreasing population-level exposure, reducing selection and thereby decreasing directional evolution. The global use of biopesticides increases by about ten percent a year (Mangan et al., 2023). An increased use of biopesticides will increase selection pressure on pests to develop resistance, especially if the same pesticide is used continuously creating a massive selection pressure on pest populations to develop resistance. A long-term solution for managing resistance is needed to manage food security (Bass et al., 2015; Mangan et al., 2023).

Biopesticide management

One interesting solution for management with chemical pesticides involves alternating selection between negatively correlated traits (Chapman & Penman, 1979). Genetic trade-offs occur when one adaptive trait evolve for adaptation while destressing another unselected trait to suffer from reduced performance. This means that pests that increase their chance to survive one pesticide decrease their chance to survive a different pesticide, if relevant traits are negatively correlated.

Mangan et al., (2023) take altering selection for pesticide management further using a spatial matrix of different biopesticides. A spatial matrix of different biopesticides is an agricultural landscape were different biopesticides are used on different fields creating different habitats on fields. This means that we get patches of different habitats with different pressures of selection. If more biopesticides are in use at the same time it means that more patches of habitats are created. This lowers the selection pressure on each trait by spreading the total selection over more traits. If there also are trade-offs between traits this means that a pest living in a field lower their chances to survive in a neighboring field. If pests mate between two fields over generations this will lead to a lower fitness against both biopesticides since a high enough geneflow will lower the rate of resistance evolution. If the trade-off were strong enough that evolving one trait reduced performance in the other trait with the same rate this could prevent resistance with an 100% geneflow between fields. However, Trade-offs aren't strong enough. Therefore, more disturbances are needed to prevent evolution of resistance. The first additional disturbance is to deploy more biopesticides that are acting on negatively correlated traits. This causes more trade-offs to occur prohibiting resistance evolution even more. The second is to start a rotation of biopesticides over time, creating a new landscape of biopesticide patches. This is important because it means that even with lower geneflow there is a local environmental change that make the fields pest population less fit to its environment.

This managing system is also utilizing the complex parasite-host interactions to avoid fixation of alleles which should provide a strong selection pressure on hosts to develop successful parasite defenses. Plant hosts show a high variability for parasite resistance traits (Cabalzar et al., 2019) due to variable selection preventing the fixation of resistance alleles, called Red Queen dynamics (Ametrano et al., 2022; Edelaar, 2018). Resistance is also less likely to evolve if negatively correlated traits are selected for (Bras et al.,

2022). Using biopesticides that are attacking traits that are negatively correlated would be an optimal solution if biopesticides could coevolve with the pests, unfortunately biopesticides are grown from stock in a factory preventing coevolution.

However, another source of environmental variation could prevent or delay resistance by changing the conditions before resistance can spread throughout the population. By engineering environments in which different negatively covarying traits are favored in different parts of the landscape, time spent in one part can help negate or reverse evolution in the population that occurred in a different part. A fluctuating pest landscape can be a landscape that varies in biopesticides in different areas that are too small for resistance to develop due to the high geneflow between patches. If the fields are smaller this should mean a lower risk of resistance since more of the matings will occur with partners from a different patch. If we also rotate biopesticides on fields this should mean that selection pressure is more altering, thus slowing down evolution, especially if there are trade-offs between the traits affected of the biopesticides. If these assumptions prove correct, it should be possible to alter selection pressure in an efficient way, thereby preventing resistance evolution.

Industrial Agriculture

Globally, a contrast between large monocultural farms and small holder farms occurs with a wide diversity of land-use patterns depending on crop and geographical area (Samberg et al., 2016). Larger fields with one crop are favored by companies due to a lowered cost of labor where large machinery can increase efficiency (Heinrichs et al., 2021). Brazil in 1990 is an example of a boom of production in maize and soybean where they stood for more than 80 percent of Brazil's total crop production area creating a low crop diversity (Cattelan & Dall'Agnol, 2018). Similar homogenization has happened all over the world in cycles where crops get popular and grown in massive scale (Castella et al., 2023). This often leads to an increase of pests due to the monocultures ability to nurture pest by giving them endless food sources without habitats for predators or competitors. This results in an intense usage of pesticides to manage pests to prevent loses in food production (Bortolotto et al., 2015). A crop rotation system where crops are rotated between fields is showing an increase in production (Canalli et al., 2020) opening possibilities for a new biopesticide resistance management system (Mangan et al., 2023) with spatial rotation of crops and biopesticides.

Objective of this study

How landscape heterogeneity affect biopesticide resistance is hard to study empirically due to the extensive time and space needed to demonstrate evolution. In addition, the many genes that are assumed to affect biopesticide resistance make analytic models unfeasible (Hoy, 1998). Fortunately, new software (Duthie et al., 2023) allows agent-based simulation models of evolution in "digital organisms" with complex simulated genomes. Using this software, I hope to increase knowledge about how agricultural landscapes affect biopesticide resistance evolution in a biopesticide manage landscape where biopesticides are rotated over time and across fields.

Expectations are that I will find that more biopesticides rotating in a landscape will lower resistance evolution due to selection alternating across more traits and more trade-offs occurring. I also expect to find an association between field size and resistance evolution where a larger average field size will increase resistance evolution in pests. A larger field size should mean fewer matings between fields, decreasing geneflow between biopesticide habitats, and as a consequence, an increasing rate of resistance evolution.

Methods

Map extractions

In order to study the effects of landscape properties on resistance evolution in digital pests, I extracted information from real images of agricultural landscapes. I wanted a sample of landscapes that represented the range of global land-use patterns, from very smallholders to vast industrial monocultures, as shown in fig 1. To do this I choose maps sizes that provided acceptable resolution while also containing interesting field sizes. After some testing a 200 hectares map came to be the standard for all maps since it could include even the largest of fields. This were concluded from Samberg et al., (2016) paper where field sizes

are set in the categories and category's "Very Large" and "Large" could fit in a map without losing resolution. In figure 1 we can see Samberg's different categories and where they are found across three different continents. 7 maps were then extracted from the blue areas in figure 1 that are representing the two categories. 7 maps were used to get a range of field sizes without increasing the simulation time to much. In figure 2 maps with location and average field sizes are presented where average field sizes range between 40 ha and 5.7 ha. This was range that was deemed sufficient to show association between field size and resistance evolution.

Polygon maps were made using google satellite as base layer and shapefile layers with a base polygon. These base polygons were then used as boundaries for each map and within them a new polygon was drawn over each field to represent them (see *Fig.2*). All polygons representing a field hade a number representing them so that when each shapefile was then exported to R Studios they could be represented by that number. Using R (R Core Team 2024) I transformed maps to a 128 by 128 matrix with different numbers in each cell representing the different fields.

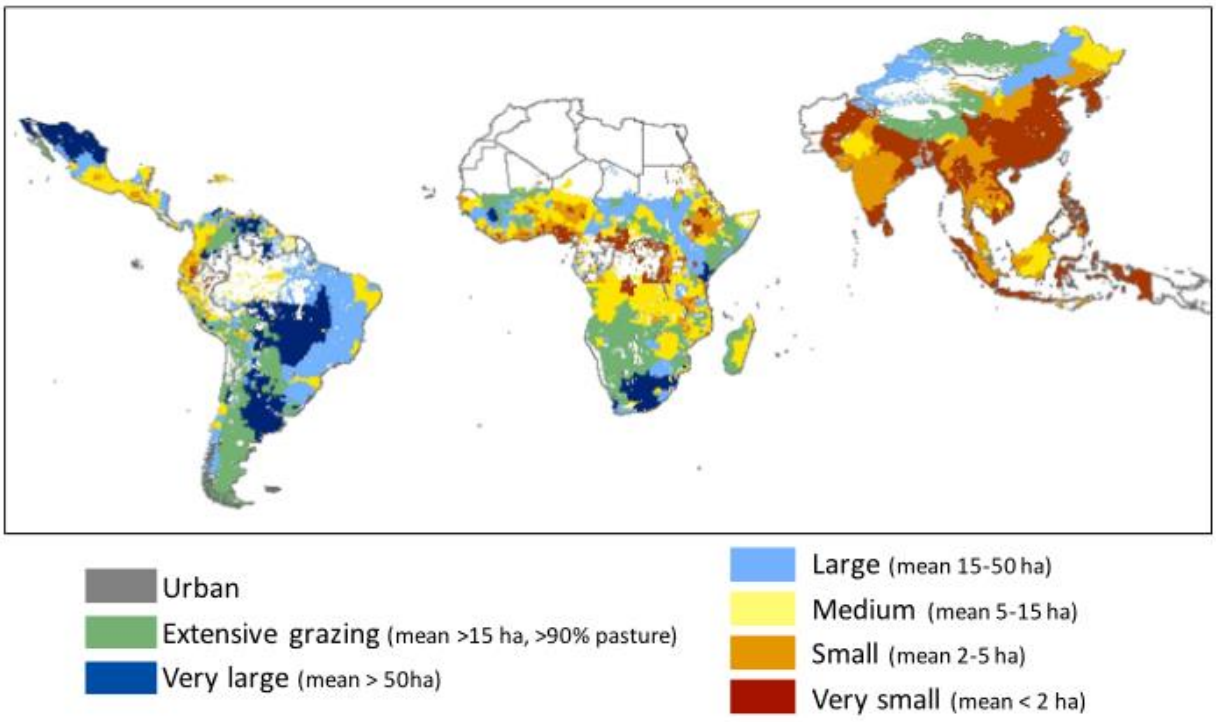

Figure 1. Map of variation in mean agricultural area incorporating croplands. (Samberg et al., 2016)

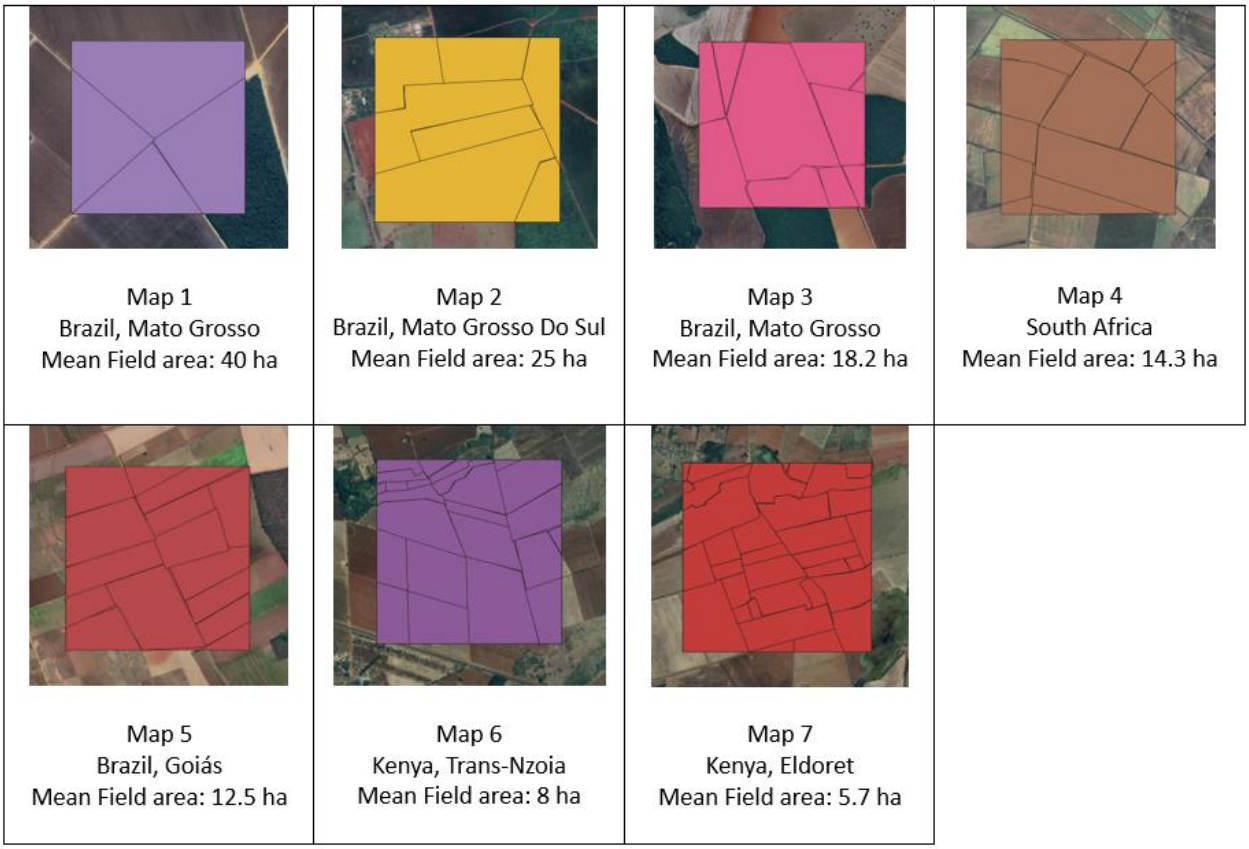

Fig.2 Shape-file maps with location and mean field size that later was turned into matrixes and used in simulations.

Simulating method

Simulation was done using the code language R (R Core Team, 2024) using the resevol package (Duthie et al., 2023). Pre-simulated genomes (provided by Blair Matarlo), containing 100 loci each represented by numbers were used. Pre simulated genomes were used to minimize simulation time and since these had already been tested, we could more easily choose an appropriate number of loci with regards to time and efficiency of the simulation.

Three different genomes were used separately for simulations with two, three and four biopesticides so that the genomes had the same number of traits as biopesticides. Each trait was affected by one biopesticide and had a negative trade-off of -0.375 with other traits meaning that improvement for one trait predicts a negative performance (with a correlation coefficient of -0.375) in the other traits. This degree of trade-off had been suggested from previous work (Matarlo et al., unpublished), since at this level of trade-off, intermediate rates of resistance evolution were observed. We hoped that using this strength of trade-off would expose effects of farm size, however small.

All fields hold one biopesticide at any time step with initial biopesticides for each field randomized and rotated randomly every sixteen timesteps, starting from the fiftieth timestep to let populations to establish. Pest age at the start of the simulation was set to be randomized to imitate an existing population.

Pests were made to imitate a flying pest that could live for four timesteps. Between the age of zero and two timesteps pests were they able to move up to 22 meters, and when sexually mature at the age of four timesteps they could reproduce sexually if they could find a partner within 220 meters. To get an overview of simulation events see figure 3 and for specifics of my simulations see programing code under

appendixes.

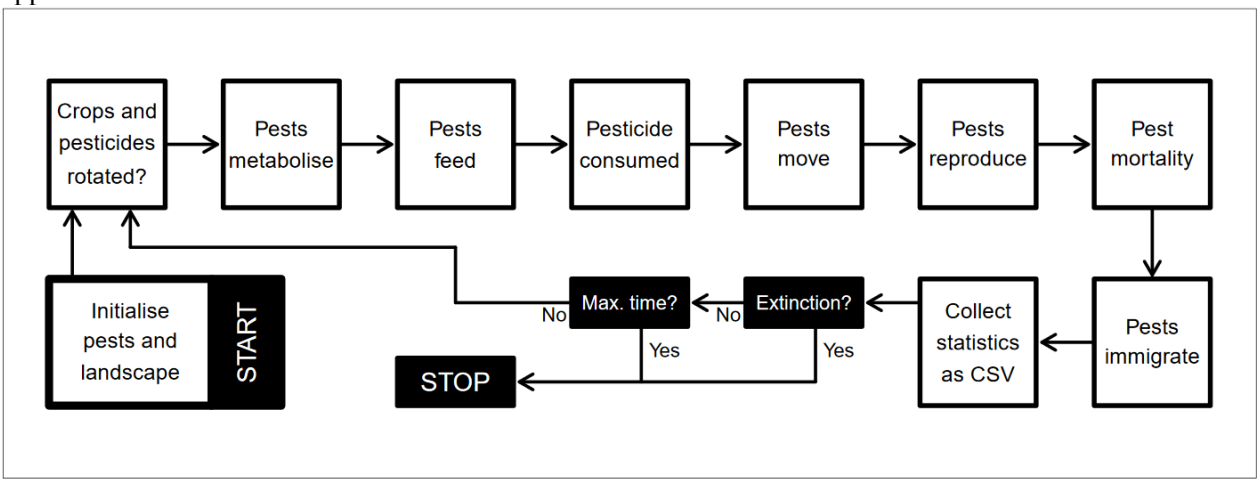

***Fig.3 Simulated events in resevol R package where metabolism, feeding, biopesticide consumption, movement, and reproduction can be set as functions of pest age, in an order to imitate a specific pest's life history* (Duthie et al., 2023).**

To maximize simulation efficiency pilot simulations where made to see at which time step susceptibility were stabilized. Because I found that simulations tended to equilibrate around 200-250 timesteps after initiation, I ran all subsequent simulations for 300 timesteps, representing 75 generations of pest. Each set of conditions (number of biopesticides and field size) was repeated 50 times to allow generalizations despite the stochastic behavior of each sim.

Results

Simulations two biopesticides

My simulations tracked phenotypic susceptibility for each biopesticide separately (in the figures below, each biopesticide is associated with a numbered trait). Therefore, for each map simulated we could follow how resistance developed by getting a mean trait value for every timestep. A lower susceptibility shows stronger resistance in pests, making them more successful at surviving in an environment with the biopesticide associated with that trait.

In *Fig.4* we see a typical example of how resistance developed after two biopesticides were applied at the 50th time step. Resistance for both traits evolved at almost the same pace and stabilized at about the same time and trait value.

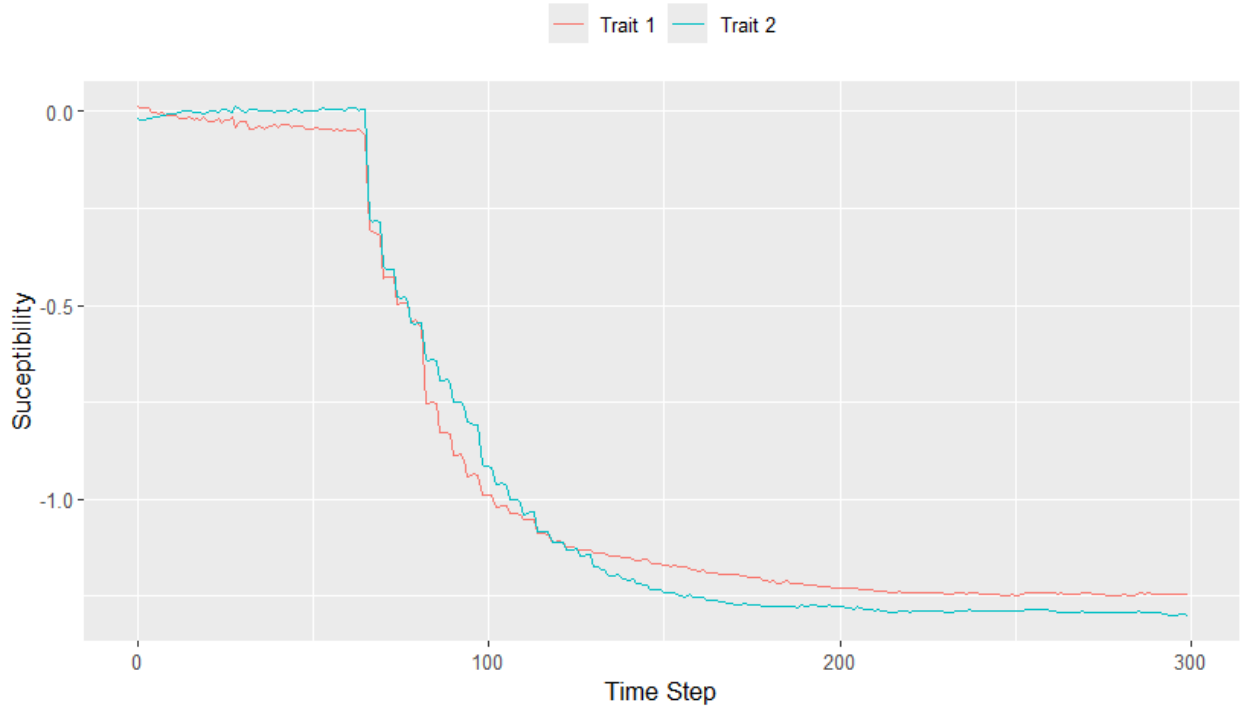

Fig.4 An example of how resistance forms in a simulation with two biopesticides. The Y-axis shows the susceptibility (mean trait value) of 50 replicated simulations on one map.

Simulations three biopesticides

Simulations with three biopesticides generally showed a slower development of resistance, and more varied evolution between traits, see Fig. 5. We also saw that there seemed to be more stochasticity than in simulations with two traits, perhaps reflecting a greater role for genetic drift or the random nature of biopesticide choice by farmers. Traits were still starting to stabilize near the end of the simulations but often with a larger difference between traits, as well as lower susceptibility closer to zero (reflecting less resistance evolution relative to the starting point) than in the simulations with two traits.

We could also see susceptibility could often be positive for one of the traits shortly after the start of biopesticide use (e.g., the blue line in Fig. 5 at roughly the 75th time step). This indicates the evolution of a higher susceptibility to one of the biopesticides for a short period of time (presumably because of negatively correlated responses to selection on other traits) before eventually becoming negative trait values.

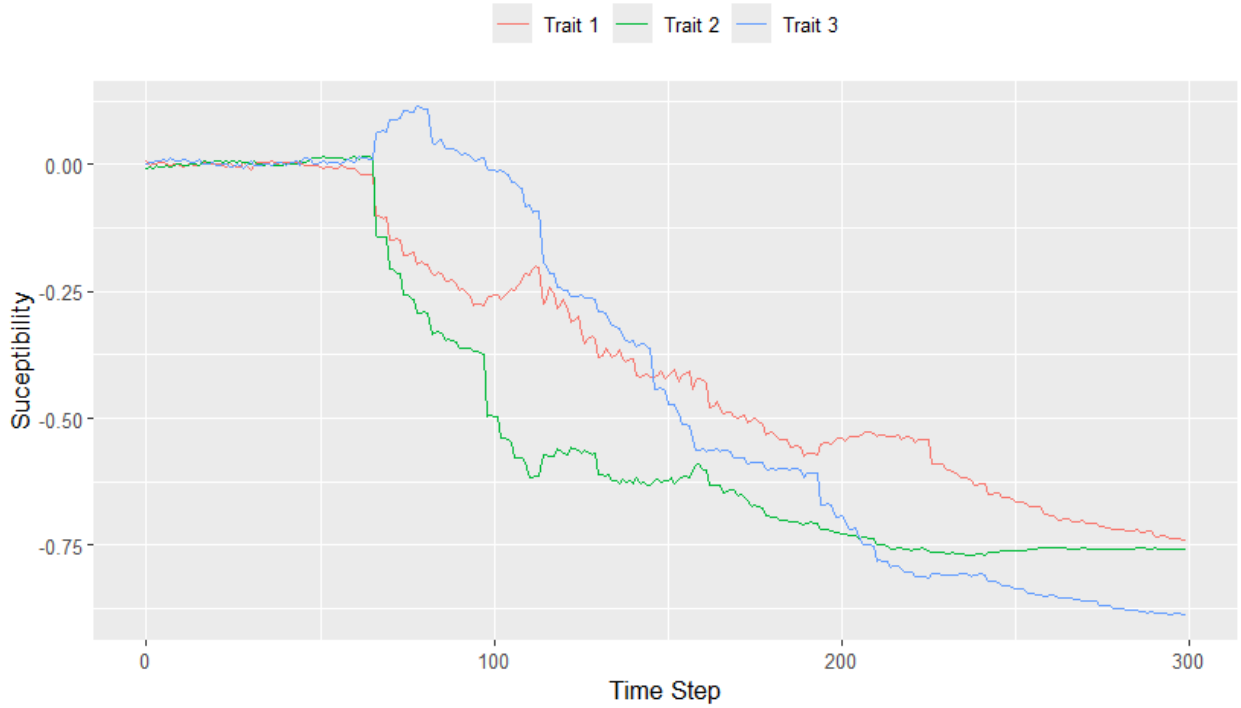

Fig.5 An example of how resistance forms in a simulation with three biopesticides. Y-axis show the susceptibility (mean trait value) of 50 repeated simulations on one map.

Simulations four biopesticide

In simulations with four biopesticides we found no indication of traits stabilizing and could see a much higher stochasticity (Fig.6), where one or two traits had positive susceptibility at the same time as others were negative. However, if we took all four traits at any given time and made a new mean from them it was always close to zero (Fig.7). This demonstrates that a spatial rotation of four biopesticides can sustain the susceptibility of at least one biopesticide at any given time. Although resistance evolution is still happening, the negative trade-offs mean that resistance against one biopesticide tends to produce populations that are more susceptible to another.

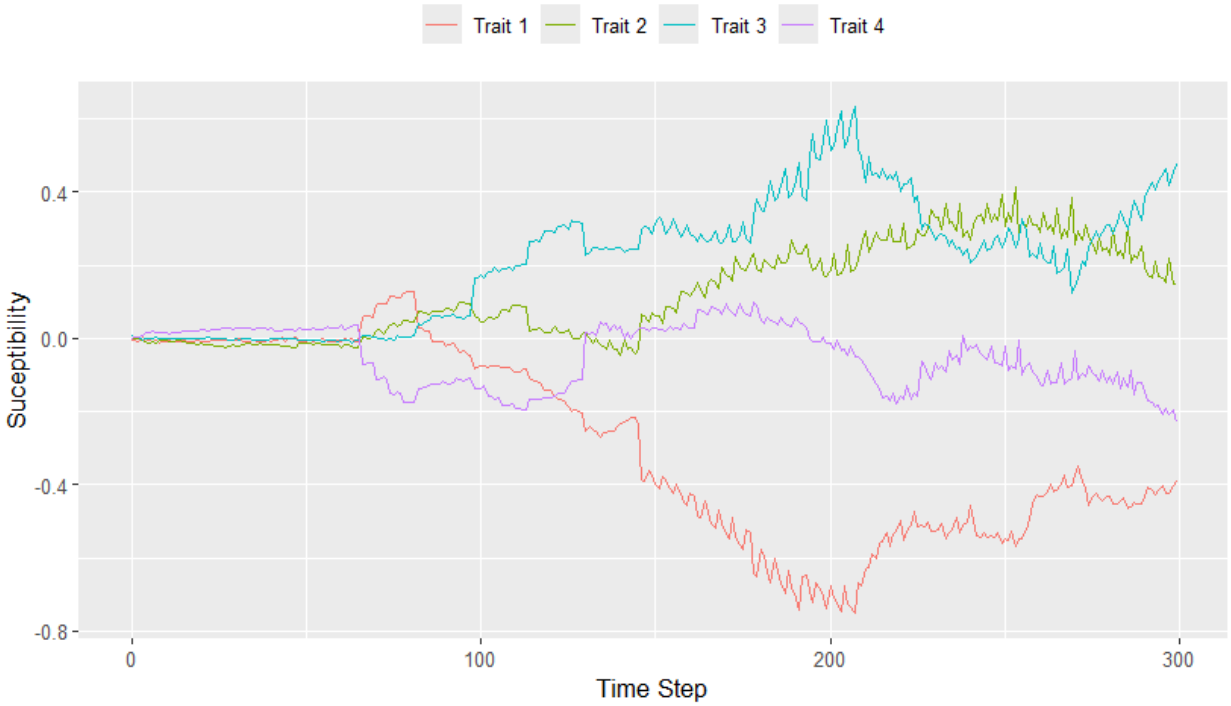

Fig.6 An example of how resistance forms in a simulation with four biopesticides. Y-axis shows the susceptibility (mean trait value) of 50 repeated simulations on one map.

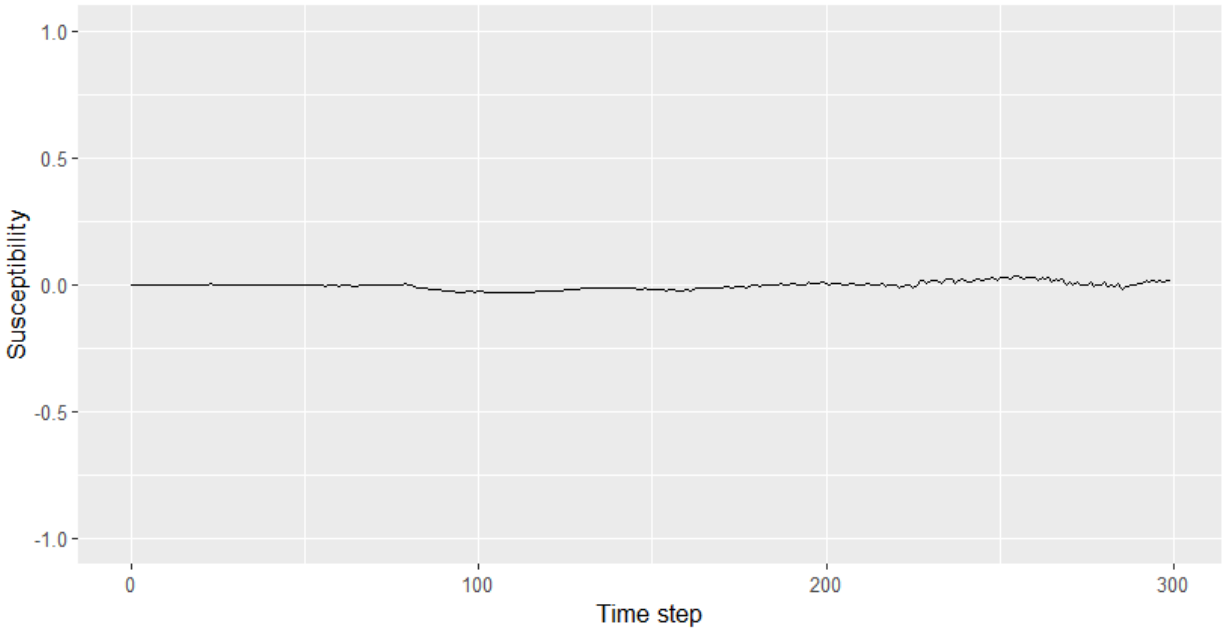

Fig.7 An example simulation illustrating the mean susceptibility value for all traits combined in a simulation with four biopesticides.

Simulations over different field sizes

In figure 8 we can see how for each number of biopesticides, the susceptibility is unaffected by field size. All treatments with four biopesticides are along the 0-line showing that regardless of average field size, all these treatments have been effective in constraining mean biopesticide resistance. For treatment with two and three biopesticides, resistance has formed in both cases (to a greater extent under a two biopesticide regime than for three), but again in both cases this situation is almost entirely insensitive to average field size throughout the entire range of field sizes studied.

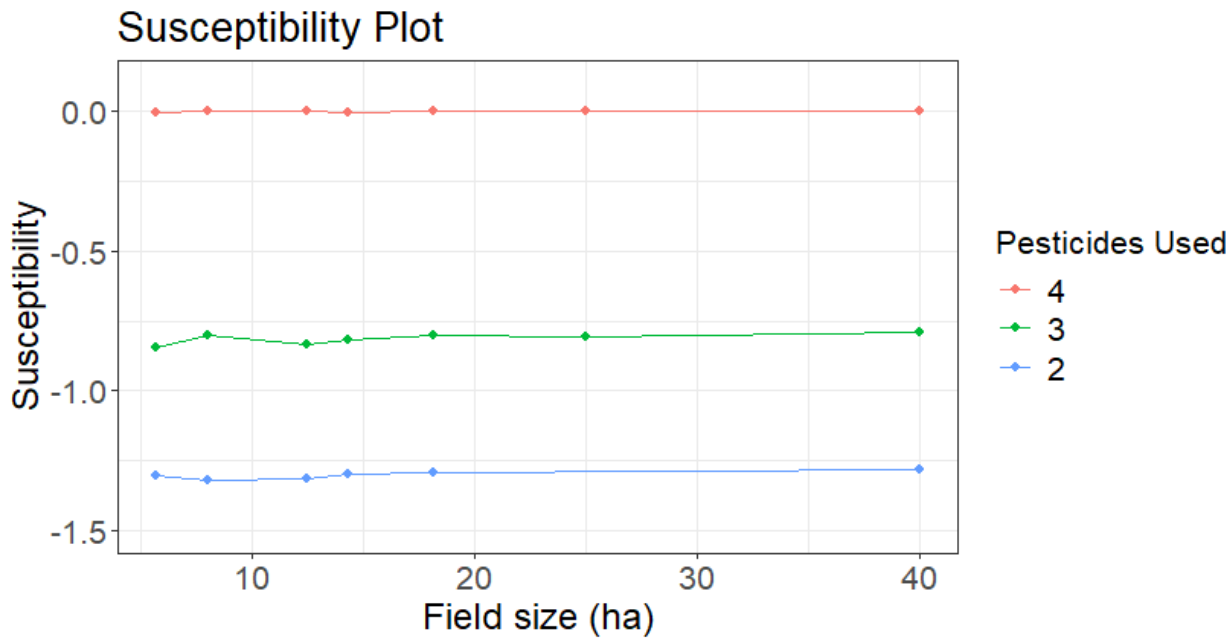

Fig.8 Plots the mean susceptibility at the last time step for every simulation. Mean susceptibility is the mean of all runs and across all traits. Every point in the graph is represented by one map and one number of biopesticides.

Discussion

Simulations indicate that resistance evolution depended on the number of biopesticides used, following previous suggestions (Mangan et al., 2023) and our own expectations. More biopesticides sustained susceptibility in pests resulting in no effective resistance accruing in treatments with four biopesticides. This very exciting result supports assertions that rotations of biopesticides can help engender sustainable pest control. This was because the trade-off between traits was strong enough so that changes in selection across the landscape can reverse resistance thanks to trade-offs between resistance traits.

Farm diversity constrains resistance

We could also see that trade-offs are insufficient in simulations with two or three biopesticides, as evolution of resistance occurred despite the rotation of biopesticides providing a fluctuating selection for negatively correlated traits. Once more this result underlines the enormous amount of selection pressure we put on pests by using biopesticides. This fact is further highlighted by examining the rate of evolution by looking at the time point and susceptibility level where resistance stabilizes. In figure 5 simulating with three biopesticides resistance starts to stabilize close to the 300th time step in values between -0.7 and -0.9 while figure 4 simulating two biopesticides resistance has stabilized at the 210 time step in values between -1.2 and -1.3. This shows that simulations with three biopesticides take longer to stabilize and are more susceptible

than the simulations with two biopesticides pointing once again at the conclusion that a rotation of biopesticides affects the rate of resistance development in the populations of pests.

We can also see the difference in the stochasticity of evolution as the number of biopesticides in rotation increases. Trade-offs are strong enough to make pests more susceptible to certain biopesticides than they were from the start, as can be seen in figure 5 for trait three between time step 60 and 100, and seen in figure 6 for all traits where traits two and three have a positive value for most of the simulation, as well as at the last time step. This is something that should be expected to happen if the traits in question are more affected by the trade-offs than by negative selection from a biopesticide.

My simulations used a somewhat arbitrary magnitude of trade-offs because previous work had shown that it produced intermediate levels of resistance evolution, which might therefore be sensitive to changes in field size. However, if trade-offs in natural systems are stronger (i.e., more negative), then this would constrain evolution more than in my simulations. In contrast, if trade-offs were weaker (i.e., closer to zero) then the potential for differences among fields to constrain evolution would be less. In fact, the magnitude of genetic correlations across biopesticides or farm patches are almost entirely unknown. In as-yet unpublished laboratory work, Mangan et al. (unpublished) document that trade-offs across fields could be in the order of -0.2, which would imply less constraint on resistance evolution because trade-offs are typically weaker than in my simulations.

No effect of field size on resistance evolution

I did not expect the absence of an effect of field size. Instead, I predicted that smaller fields would allow more gene flow in pest populations, as more pests would be mating with partners that had been selected in a different biopesticide patch. This gene flow should have made resistance evolution especially unlikely in the smallest fields. My simulations suggest that in the range of real field sizes represented by my maps (which were selected to represent a broad range of real agricultural systems around the world) field size has a smaller impact than expected. Field sizes have no effect on evolution of resistance if its effect on migration is not of importance. Migration is affected by the ability of the population to mate between the fields, something dependent on field size and the dispersal capacity of pests. If dispersal capacity of pests is enough for pests to mate between fields sufficiently even with larger field sizes, then there would be no difference in resistance evolution throughout all maps used.

The importance of field size for a given pest is likely to be highly dependent on the dispersal ability and life history of the pest in question. In my simulations pests were able to move as a flying insect that can move relatively far during its feeding stage of life and then fly to find a mate. Pest of similar movement (E.g. *Melanotus okinawensis* average dispersal 274 m, *Cylas formicarius* average dispersal 237-318 m and *Cydia pomonella* average dispesal 282 m) are common and of large importance to manage for food security (Mazzi & Dorn, 2012). There are Pests with wider dispersal abilities to that are known to cause problems for food security such as the moth *Helicoverpa armigera* (Tay et al., 2013) that disperse several kilometers (Fitt et al., 1995). A pest with these dispersal ranges is likely to have an amount of gene flow large enough as to not be affected by large field sizes and are still of importance to control.

Future directions for research

For taking the simulations to the next step I recommend that investigations both on flying pest with a lower ability to move during its feeding stage and non-flying insects should be simulated. From these simulations one would get a better indication of what field sizes might be relevant for biopesticide resistance for low-dispersing insects as well. Another interesting aspect to

investigate would be to look at a landscape that is not only including fields but also other environments where pests are not exposed to biopesticides. Such landscapes can provide biopesticide refugia, where other forms of selection may reduce resistance evolution, although no studies yet exist that quantify trade-offs in such scenarios.

Applied implications

Even if my results only apply to highly dispersive pest species they nevertheless provide welcome news for efforts to generate sustainable pest control. If field sizes are not as important for pest resistance as previously thought, this would be much easier to implement in a large scale. In the goal of food security this will mean that we can come a long way by just implementing a spatial rotation of biopesticides (or other land management practices that similarly affect pest resistance). This will likely be easier to convince both farmer and governments since the cost and work needed would be much lower, and would require no great change in how to manage farms. Large fields will still be worse in a biodiversity point of view (Fahrig et al., 2015; Šálek et al., 2018) but thanks to decreases in synthetic pesticide use, it would still be a win for biodiversity; if biopesticides were used at a large scale due to their targeted activity and faster degradation (T. R. Glare et al., 2016; Thakore, 2006) it would mean that fewer off-target organisms would be affected.

Words of thanks

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Appendixes

Simulation code

Hugo_Bostrom_bachelor_project_code.R