# Multinomial logistic regression

A multinomial logistic regression was run for two metrics:

1. The effective life – the number of years until the insect mortality following a spray fell below a threshold, here defined as 50% four days after spraying
2. T25 one gene – the number of years until the resistance frequency of one of the two resistance genes increased above 25%

In each case, the global analysis of the different strategies was performed by simulating the model presented in the paper for 10,000 unique realisations of an insect / insecticide interaction, in which each realisation had parameters drawn from random distributions. The insect / insecticide dynamics were then simulated over 200 consecutive years under each of the four management strategies described in the paper: a sequential application (SA) of the two insecticides, a label-dose mixture (LM), a label-dose rotation (LR), and a reduced-dose mixture (RM).

A multinomial logistic regression model (MLR) was used to determine which parameters in the model were the most critical to determining the optimal strategy for any insect / insecticide realisation. The categorical variable is which, of SA, LM, LR, or RM was the optimal strategy (either for effective life or T25), while the dependent variables were (potentially transformed, see below) independent variables and factors from the model (where variables were collinear, such as the intercept of the logit-dose relationship and the LC50, one of the variables was chosen). The initial parameters included in the MLR are shown in Table SI 2.1.

Several of the parameters were transformed to follow a uniform distributed: the insecticide decay rate was inverted, the LC50 of each insecticide was square-root transformed, and the emergence rate was log-transformed. Additionally, one derived variable was included: whether or not the pest included a stage insensitive to the insecticide. Several (but not all) interaction terms were included, being every interaction between paired variables (such as the dominance of resistance gene A and the dominance of resistance gene B, or the immigration rate and the external population size), as well as an interaction between SEXUAL, the immigration rate, and the efficacy of each insecticide, which had previously been found to be related when looking at a single dose (Helps, Paveley et al. 2017). All continuous parameters were standardised, so that the mean and variance of all parameters was the same.

The model was further refined by stepwise selection, using the step function in R. p-values were examined using Wald z-tests (testing the ratio of the coefficients to standard error against a two-tailed z-test). The final terms and coefficients in the MLR, together with the p-values, may be seen in Table SI 2.2.

The ‘multinom’ function inside the ‘nnet’ package (Venebales and Ripley 2002) in R (R Core Team 2018) was used for the analysis.

Table SI 2.1 The parameters and factors in the MLR. Factors are in capitals.

|  |  |
| --- | --- |
| **Variable / factor / interaction name** | **Variable description** |
| efficacy1, efficacy2 | The efficacy of a label-dose of insecticide 1 or 2 |
| dominanceA, dominanceB | The dominance of each target-site resistance gene |
| SEXUAL | Whether the insect reproduces sexually  |
| HAPLODIPLOID | Whether the insect has a haplodiploid life-history |
| immigration | The immigration and emigration rate from the external untreated population |
| extPopnSize | The relative size of the external population size |
| birthRate | The birth rate of the insect |
| fitnessCost1, fitnessCost2 | The fitness cost of target-site resistance gene 1 and 2 on the birth rate of the insect |
| HOLOMETABOLOUS | Whether the insect is holometabolous (has a full life-history) |
| cropProportionProtected | The proportion of the treated crop that is not hit by the insecticides |
| movementRate | The movement rate of insects between the treated and untreated crop areas |
| carryingCapacity | The carrying capacity of the insect density |
| emergenceRate | Rate of emergence from the overwintering stage |
| lifespanE, lifespanL, lifespanP, lifespanA | The lifespan of the eggs, larvae, pupae and adults respectively |
| mortalityE, mortalityL, mortalityP, mortalityA | The natural mortality of each insect stage |
| INSENSITIVESTAGE | Whether there is a stage that is insensitive to the insecticide or not |
| resistanceFrequencyA, resistanceFrequencyB | The initial resistance frequency of resistance genes A and B |
| decay1, decay2 | The decay rate of insecticides 1 and 2 |
| LC50\_1, LC50\_2 | The LC50 of insecticide 1 and 2 on a sensitive pathogen strain |

The following tables present the coefficients and p-values for those variables that were incorporated in the final model for each output metric. Each coefficient can be interpreted as: a unit increase in this variable increases the log odds of LM, LR or RM relative to SA. The coefficient being positive does not say that each strategy is better than LM, but rather that that strategy becomes more likely relative to SA, from the starting point of the intercept.

## Effective life: full model

The effective life under each strategy was summarised as the time (in years) until the mortality of the insect pest fell below 50% four days after application of the insecticide. For each realisation the optimal strategy was the strategy that resulted in the longest time until the mortality fell below the threshold.

Table SI 2.2. Coefficients and p-values of all the terms in the final multinomial regression model. Interactions are denoted by a colon (:).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **LM (coef)** | **LR (coef)** | **RM (coef)** | **LM (p-value)** | **LR (p-value)** | **RM (p-value)** |
| SEXUAL | 8.03 | 2.18 | 6.16 | 0.00 | 0.00 | 0.00 |
| (Intercept) | -2.76 | -1.37 | -0.92 | 0.00 | 0.00 | 0.00 |
| efficacy2:SEXUAL | -1.03 | -0.20 | -0.43 | 0.00 | 0.51 | 0.07 |
| efficacy1:SEXUAL | 0.21 | 0.67 | 0.42 | 0.46 | 0.04 | 0.09 |
| fitnessCost1 | 0.52 | 0.59 | 0.52 | 0.00 | 0.00 | 0.00 |
| efficacy1:SEXUAL:immigration | 0.26 | 0.58 | 0.53 | 0.30 | 0.05 | 0.01 |
| SEXUAL:immigration | 0.56 | 0.57 | 0.78 | 0.04 | 0.08 | 0.00 |
| efficacy2:SEXUAL:immigration | -0.35 | -0.48 | -0.25 | 0.15 | 0.09 | 0.22 |
| holometabolous1 | -0.38 | -0.48 | -1.22 | 0.03 | 0.01 | 0.00 |
| efficacy1:efficacy2: SEXUAL:immigration | -0.40 | -0.43 | -0.59 | 0.07 | 0.09 | 0.00 |
| SEXUAL:HAPLODIPLOID | -0.43 | -0.24 | -0.22 | 0.01 | 0.29 | 0.19 |
| INSENSITIVESTAGE | -0.40 | 0.36 | 0.85 | 0.01 | 0.02 | 0.00 |
| fitnessCost2 | 0.35 | 0.39 | 0.37 | 0.00 | 0.00 | 0.00 |
| decay1:decay2 | 0.34 | 0.30 | 0.10 | 0.00 | 0.00 | 0.04 |
| immigration | 0.33 | 0.09 | 0.01 | 0.02 | 0.18 | 0.86 |
| birthRate | -0.31 | -0.04 | -0.16 | 0.00 | 0.57 | 0.00 |
| efficacy1 | -0.20 | -0.31 | -0.45 | 0.19 | 0.00 | 0.00 |
| efficacy2 | 0.28 | -0.14 | -0.40 | 0.05 | 0.03 | 0.00 |
| extPopnSize | 0.11 | 0.27 | 0.03 | 0.07 | 0.00 | 0.58 |
| cropProportionProtected | -0.22 | -0.11 | -0.21 | 0.00 | 0.07 | 0.00 |
| fitnessCost1:fitnessCost2 | -0.05 | -0.21 | -0.13 | 0.43 | 0.00 | 0.01 |
| decay2 | -0.16 | -0.21 | -0.03 | 0.01 | 0.00 | 0.51 |
| dominance2 | -0.20 | -0.01 | 0.01 | 0.00 | 0.88 | 0.83 |
| lifespanL | 0.18 | -0.05 | -0.01 | 0.00 | 0.47 | 0.92 |
| decay1 | -0.18 | -0.16 | -0.05 | 0.00 | 0.01 | 0.36 |
| efficacy1:efficacy2 | 0.17 | 0.01 | 0.04 | 0.22 | 0.86 | 0.53 |
| dominance1 | -0.14 | 0.16 | 0.10 | 0.02 | 0.01 | 0.05 |
| efficacy1:immigration | 0.14 | -0.03 | -0.10 | 0.33 | 0.62 | 0.09 |
| efficacy2:immigration | 0.07 | 0.14 | 0.00 | 0.62 | 0.04 | 1.00 |
| mortalityA | 0.08 | -0.11 | 0.10 | 0.20 | 0.17 | 0.05 |
| efficacy1:efficacy2:SEXUAL | -0.08 | -0.02 | -0.06 | 0.74 | 0.94 | 0.77 |
| efficacy1:efficacy2:immigration | -0.06 | 0.04 | 0.09 | 0.65 | 0.53 | 0.12 |

## Effective life: three strategies in a sexually-reproducing insect pest

Table SI 2.3 shows a multinomial fit looking at the relative likelihood of LR and RM being optimal relative to LM in a sexually-reproducing insect pest. The sequential application strategy (SA) is not included in the analysis.

Table SI 2.3. Coefficients and p-values of a multinomial regression model looking into the best strategy to maximise the effective control of an insect pest. The data is the subset of simulations for which the insects reproduce sexually.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | LR (coef) | RM (coef) | LR (p-value) | RM (p-value) |
| immigration | -55.18 | -15.49 | 0.00 | 0.00 |
| efficacy1:efficacy2 | 1.67 | -30.33 | 0.00 | 0.00 |
| efficacy1 | 4.56 | 26.29 | 0.00 | 0.00 |
| efficacy2 | 4.31 | 25.61 | 0.00 | 0.00 |
| (Intercept) | -23.94 | -23.21 | 0.00 | 0.00 |
| fitnessCost1 | 10.82 | 1.08 | 0.00 | 0.00 |
| LC50\_A | 3.05 | -0.47 | 0.00 | 0.00 |
| dominance1:dominance2 | -1.89 | 0.98 | 0.00 | 0.00 |
| INSENSITIVESTAGE | 1.28 | 1.38 | 0.00 | 0.00 |
| dominance2 | 1.06 | 0.16 | 0.00 | 0.11 |
| HOLOMETABOLOUS | 0.65 | -0.99 | 0.00 | 0.00 |
| dominance1 | 0.74 | 0.29 | 0.00 | 0.01 |
| decayRate1 | 0.47 | 0.25 | 0.00 | 0.00 |
| HAPLODIPLOID | 0.41 | 0.46 | 0.00 | 0.00 |
| decayRate2 | 0.38 | 0.25 | 0.00 | 0.00 |
| resistanceFrequencyA | 0.33 | -0.01 | 0.01 | 0.66 |
| extPopnSize | 0.08 | -0.04 | 0.20 | 0.01 |
| decayRate1:decayRate2 | -0.06 | -0.04 | 0.00 | 0.00 |
| lifespanA | 0.06 | 0.00 | 0.00 | 0.38 |
| birthRate | 0.04 | 0.03 | 0.12 | 0.00 |
| lifespanL | 0.02 | -0.01 | 0.25 | 0.08 |
| lifespanL:lifespanA | 0.00 | 0.00 | 0.01 | 0.44 |

## T25 One Gene

The T25 for one gene was summarised as the time (in years) until one of the two resistance genes exceeded 25% frequency in the insect population.

Table SI 2.4. Coefficients and p-values of all the terms in the final multinomial regression when regressed against the time until one of the two resistance genes exceeds 25% frequency in the population.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | LM (coef) | LR (coef) | RM (coef) | LM (p-value) | LR (p-value) | RM (p-value) |
| SEXUAL | 3.31 | -0.57 | 0.15 | 0.00 | 0.00 | 0.31 |
| (Intercept) | 0.83 | 3.19 | 3.07 | 0.00 | 0.00 | 0.00 |
| INSENSITIVESTAGE | -2.45 | -1.11 | -1.34 | 0.00 | 0.00 | 0.00 |
| efficacy2 | -1.38 | -1.32 | -1.47 | 0.00 | 0.00 | 0.00 |
| efficacy1 | 1.42 | 1.28 | 1.00 | 0.00 | 0.00 | 0.00 |
| HOLOMETABOLOUS | 1.35 | 0.23 | 0.58 | 0.00 | 0.09 | 0.00 |
| decayRate1 | -0.81 | -1.11 | -0.91 | 0.00 | 0.00 | 0.00 |
| decayRate2 | 0.93 | 1.09 | 0.95 | 0.00 | 0.00 | 0.00 |
| efficacy1:efficacy2 | -0.24 | -0.45 | 0.04 | 0.00 | 0.00 | 0.58 |
| resistanceFrequencyA | 0.44 | 0.38 | 0.40 | 0.00 | 0.00 | 0.00 |
| resistanceFrequencyB | -0.36 | -0.40 | -0.36 | 0.00 | 0.00 | 0.00 |
| fitnessCost2 | 0.33 | 0.38 | 0.37 | 0.00 | 0.00 | 0.00 |
| dominance1 | 0.30 | 0.31 | 0.38 | 0.00 | 0.00 | 0.00 |
| lifespanL | 0.35 | 0.17 | 0.21 | 0.00 | 0.01 | 0.00 |
| efficacy1:SEXUAL | -0.35 | 0.18 | 0.00 | 0.04 | 0.13 | 0.99 |
| birthRate | -0.33 | -0.24 | -0.12 | 0.00 | 0.00 | 0.03 |
| efficacy2:SEXUAL | -0.17 | -0.32 | -0.05 | 0.32 | 0.01 | 0.70 |
| fitnessCost1 | -0.32 | -0.32 | -0.32 | 0.00 | 0.00 | 0.00 |
| dominance2 | -0.31 | -0.31 | -0.23 | 0.00 | 0.00 | 0.00 |
| decayRate1:decayRate2 | 0.22 | -0.06 | -0.29 | 0.00 | 0.33 | 0.00 |
| immigration | 0.22 | -0.01 | -0.03 | 0.16 | 0.91 | 0.75 |
| efficacy2:SEXUAL:immigration | 0.05 | -0.19 | -0.02 | 0.75 | 0.11 | 0.88 |
| extPopnSize | 0.14 | 0.16 | 0.05 | 0.01 | 0.00 | 0.30 |
| lifespanA | 0.10 | 0.13 | 0.15 | 0.06 | 0.02 | 0.00 |
| LC50\_A | 0.14 | 0.09 | 0.13 | 0.00 | 0.05 | 0.00 |
| sexual1:immigration | -0.13 | -0.07 | 0.05 | 0.44 | 0.54 | 0.67 |
| efficacy2:immigration | -0.04 | 0.12 | 0.03 | 0.79 | 0.16 | 0.71 |
| dominance1:dominance2 | -0.12 | -0.02 | -0.08 | 0.02 | 0.69 | 0.12 |
| mortalityL | -0.10 | 0.04 | -0.02 | 0.12 | 0.50 | 0.78 |
| efficacy1:immigration | -0.02 | 0.09 | 0.03 | 0.78 | 0.12 | 0.60 |
| SEXUAL:HAPLODIPLOID | 0.03 | 0.04 | 0.08 | 0.64 | 0.57 | 0.19 |
| carryingCapacity | 0.07 | 0.03 | -0.04 | 0.16 | 0.55 | 0.43 |