Article

A discretized dynamic model to describe the development of insecticide resistance

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Abstract

In this article, a discretized dynamic model was proposed to describe the development of insecticide resistance. Variables as dosage, timing and frequency of insecticide applications, mutation rate, insecticide-resistant individual's fitness, etc., were included in the model. The model was validated using sensitivity analysis. The model was finally used to evaluate the effect of mixed use of bioinsecticide and chemical insecticide to reduce insecticide resistance. The model can be used to predict the dynamic development of insecticide resistance and to evaluate the effect of various factors on insecticide resistance.

Keywords dynamic model; insecticide application; resistance development; insect's fitness; mutation rate.

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1 Introduction

Insecticide resistance management is an important component of integrated pest management (Zhang, 2018b). It is the selective adaptation of insect pests to insecticides. It is inheritable with various genes concerned (Ni and Pu, 2006; Zhang and Zhang, 2019, 2020). There are two major theories of insecticide resistance, i.e., election and induce variation (Tang, 2002; Zhang and Zhang, 2008). The election theory holds that insecticide-resistance genes exist in some individuals of insect population before insecticide applicaion. Insecticide resistance of these individuals cannot be expressed in the usual natural selection. The resistance will be expressed under insecticide pressure, and resistant insects survive, reproduce, and inherit this resistance to the next generation. Because resistance genes had already existed in some individuals, the resistance is thus a pre-adaptation. Insecticides play a selection role in the resistance development. The induce variation theory argues that some individuals in the insect population do not have insecticide-resistance genes. Due to insecticide application, some individuals in the population mutate, and result in resistance genes. It is a post-adaptation for insecticide resistance and the insecticide played a major role in mutagenesis of genes.

There are remarkable differences in morphological, physiological and biological characteristics between resistant and susceptible insects (Zhang and Zhang, 2018). The fitness of resistant insect genotype under insecticide selection is generally higher than that of the susceptible genotype, and the fitness of the resistant genotype is usually inferior when the insecticide pressure is reduced. When the insecticide is reduced, the fitness of the resistance genotype is degraded by the decline in the frequency of the resistance gene (Georghiou, 1983; Rough and Mckenzie, 1987). The development of insecticide resistance is dependent upon insect heredity, insecticide and insect fitness, etc (Tang, 2002; Liu et al., 2008; Zhang and Zhang, 2018).

In this study, we try to propose a discretized dynamic model to describe the development of insecticide resistance, which is expected to provide a fundamental tool for simulation of development of insecticide resistance.

2 Model

For a certain insect species, multiple insecticide application processes may occur, and each application process causes a different degree of theoretical mutation rate of insect individuals (i.e., the proportion of gene-mutatant individuals in whole population, 0≤theoretical mutation rate≤1). However, some of the mutant individuals caused by each insecticide application process will be the same as the existing mutant individuals. That is, the mutant individuals before and after the insecticide application process will overlap. The higher the proportion of existing mutant individuals, the greater the subsequent overlap. In the calculation of the mutation rate, the overlapping part should be removed.

Suppose the relationship between the mutation rate y and the dosage of insecticide application x is

$$y=f(x)$$

The dosage at time t_i is $x(t_i)$, i.e., $y(t_i)=f(x(t_i))$. The mutation rate y has a positive correlation with the dosage x. Generally, the relationship can be linearly approximated as

$$y=f(x)\approx a+bx$$

Suppose that for any insecticide application process, each individual has the same probability of being insecticide-applied and mutation respectively. The basic mutation rate of individuals is c, $c\geq 0$. The basic mutation rate c is only related to insect species and environmental conditions. At the same time, it is assumed that the mutation rate caused by each application process will not change before the next application process.

Assuming that the first application process occurs at time t_1, and the theoretical mutation rate caused by this application is $y(t_1)=f(x(t_1))$. Based on the principle of probability independence and the multiplicative theorem (Liu et al., 2020), the overlapping rate of mutant individuals caused by the first application process is

$$cy(t_1)$$

Therefore, the rate of newly increased mutant individuals after the first application process is

$$\Delta y(t_1)=y(t_1)-cy(t_1)=(1-c)y(t_1)$$

The total mutation rate after the first application process is $z(t_1)=c+\Delta y(t_1)$.

The second application process occurs at time t_2, and the theoretical mutation rate caused by this

application process is $y(t_2)=f(x(t_2))$. The overlapping rate of mutatant individuals caused by the two application processes is

$$z(t_1)y(t_2)$$

Therefore, the rate of newly increased mutatant individuals after the second application process is

$$\Delta y(t_2)=y(t_2)-z(t_1)y(t_2)=(1-z(t_1))y(t_2)$$

The total mutation rate after the second application process is $z(t_2)=z(t_1)+\Delta y(t_2)$.

In the same way, the third application process occurs at time t_3, and the theoretical mutation rate caused by this application process is $y(t_3)=f(x(t_3))$. Therefore, the overlapping rate of mutatant individuals caused by the third application process is

$$z(t_2)y(t_3)$$

And the rate of newly increased mutatant individuals after the third application process is

$$\Delta y(t_3)=y(t_3)-z(t_2)y(t_3)=(1-z(t_2))y(t_3)$$

The total mutation rate after the third application process is $z(t_3)=z(t_2)+\Delta y(t_3)$.

By analogy, we have the mutation rate model as follows

$$\Delta y(t_1)=(1-c)y(t_1),$$
$$z(t_1)=c+\Delta y(t_1),\ i=1;$$
$$\Delta y(t_i)=(1-z(t_{i-1}))y(t_i),$$
$$z(t_i)=z(t_{i-1})+\Delta y(t_i),\ i=2,3,\ldots$$

where $\Delta y(t_i)$ is the rate of newly increased mutatant individuals after the ith application process, t_i is the time of the ith application process, and $y(t_i)$ is the theoretical mutation rate of the ith application process.

Actually, according to the dynamic model of the changes of resistant population (x) and sensitive population (y) (Zhang, 2018a; Zhang and Zhang, 2018)

$$dx/dt=r_1(d, t)x+g_1(d, t)y-\alpha(d, t)xy$$
$$dy/dt=r_2(d, t)y-g_2(d, t)y-\beta(d, t)xy$$
$$d=u(t)$$

where t is time, $d=u(t)$ is the application dosage at time t. According to the general principles and the results of this model, after the insecticide application, due to the disappearance of pesticide pressure, the low fitness of insecticide-resistant individuals, and intraspecific competition, the proportion of resistant individuals naturally decreases. For the total mutation rate, suppose the decline relationship is

$$z(t)=h(z(t),t)$$

Without loss of generality, it can be set

$$z(t)=z(t_i)\exp(-r(t-t_i))+c,\ t_i\le t<t_{i+1}$$

where t is the time and c is the basic mutation rate. Introducing it into the previous formula to obtain the mutation rate model

$$\Delta y(t_1)=(1-c)y(t_1),$$
$$z(t_1)=c+\Delta y(t_1),i=1;$$
$$\Delta y(t_i)=(1-c-z(t_{i-1})\exp(-r(t-t_{i-1})))y(t_i),$$
$$z(t_i)=c+z(t_{i-1})\exp(-r(t-t_{i-1}))+\Delta y(t_i),t_i\le t<t_{i+1},\ i=2,\ 3,\ \ldots$$

where $\Delta y(t_i)$ is the rate of newly increased mutatant individuals after the ith application process, $z(t_i)$ is the total mutation rate after the ith application process, t_i is the time of the ith application process, and $y(t_i)$ is the theoretical mutation rate of the ith application process.

Expressing the above formula as the dosage-driven one, $y(t_i)=f(x(t_i))$, then the mutation rate model above can be written as

$$\Delta y(t_1)=(1-c)f(x(t_1)),$$
$$z(t_1)=c+\Delta y(t_1),\ i=1;$$
$$\Delta y(t_i)=(1-c-z(t_{i-1})\exp(-r(t-t_{i-1})))f(x(t_i)),$$
$$z(t_i)=c+z(t_{i-1})\exp(-r(t-t_{i-1}))+\Delta y(t_i),\ t_i\le t<t_{i+1},\ i=2,\ 3,\ \ldots$$

where $x(t_i)$ is the application dose at time t_i.

For a certain insect individual, the more times the pesticide is applied, the more mutation sites of the individual will be, and the stronger the insecticide resistance of the individual will be. Suppose the relationship between the pest population resistance (such as LC_{50}) $R(t_i)$ and the rate of newly increased mutant individuals $\Delta y(t_i)$ (i=1, 2, 3, …, i) after the ith application process is

$$R(t_i)=g(\Delta y(t_1),\ \Delta y(t_2),\ \ldots,\ \Delta y(t_i))$$

The linear approximation after expansion is

$$R(t_i)=a+b_1\Delta y(t_1)+b_2\Delta y(t_2)+\ \ldots+b_i\Delta y(t_i)$$

Actually, the relationship is more complicated. At any time, the proportion of individuals with different mutation sites is also different, depending on time, survival, and reproduction rate, etc. Therefore, it can be approximated that the population resistance depends on the total mutation rate. Thus, we have

$$R(t_i)=p+q/(1-z(t_i))$$

3 Sensitivity Analysis

3.1 Effect of insecticide-resistant individuals' fitness

If the fitness of insecticide-resistant individuals does not decrease (r=0), the long-term use of insecticides will

result in a continuous increase in insect's resistance (Fig. 1). If the fitness of insecticide-resistant individuals decreases when the insecticide is not applied ($r \neq 0$), the lower the fitness of the insecticide-resistant individuals under multiple insecticide applications, the slower the increase in insecticide resistance and the possibility of decline (Fig. 1).

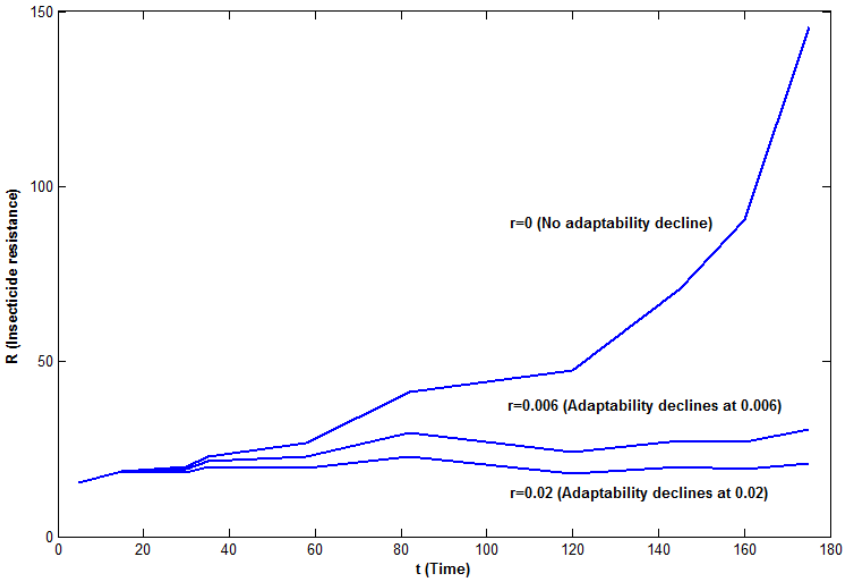

Fig. 1 Effect of insecticide-resistant individuals' fitness (i.e., adaptability) (a=0.02;b=0.005;c=0.01;p=10;q=5; t_i=[5 15 30 35 58 82 120 145 160 175]; $x(t_i)$=[10 70 20 35 40 85 18 62 25 54]).

3.2 Effect of mutagenicity

Mutagenicity (b) mainly depends on the types of pesticides and insect species. The greater the mutagenicity, the faster the insecticide resistance will rise (Fig. 2).

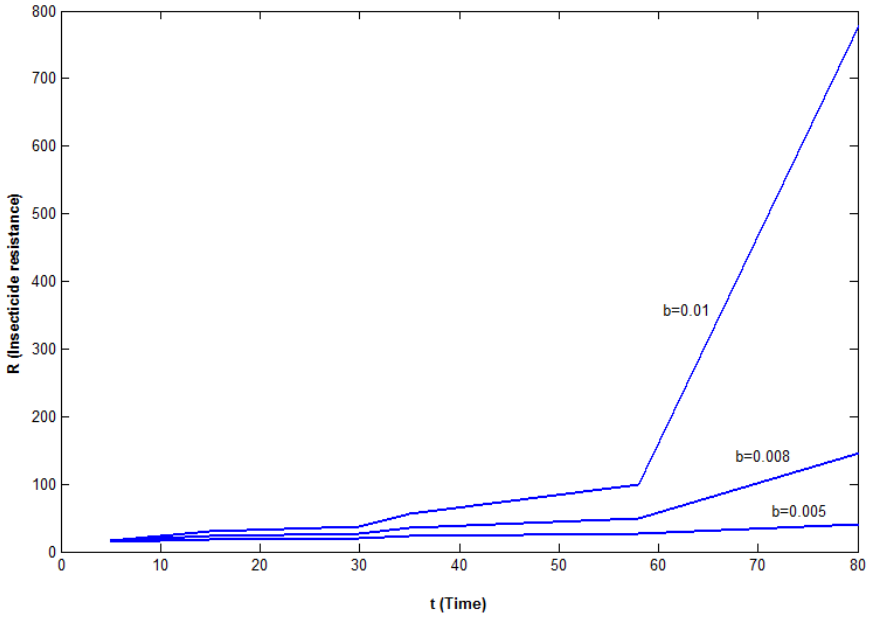

Fig. 2 Effect of mutagenicity (b) (a=0.02; c=0.01; p=10;q=5; r=0; t_i=[5 15 30 35 58 82 120 145 160 175]; $x(t_i)$=[10 70 20 35 40 85 18 62 25 54]).

3.3 Effect of application dosage of insecticide

The higher the application dosage, the faster the insecticide resistance will rise (Fig. 3).

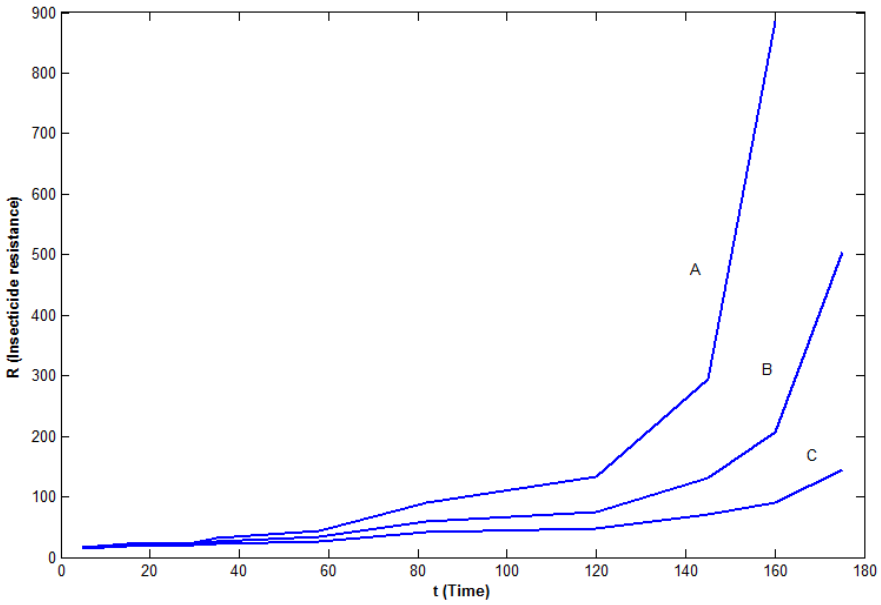

Fig. 3 Effect of application dosage of insecticide (a=0.02; b=0.005; c=0.01; p=10;q=5; r=0; t_i=[5 15 30 35 58 82 120 145 160 175]; A: $x(t_i)$=[30 90 40 55 60 105 38 82 45 74]; B: $x(t_i)$=[20 80 30 45 50 95 28 72 35 64]; C: $x(t_i)$=[10 70 20 35 40 85 18 62 25 54]).

3.4 Effect of application frequency

The higher the frequency of insecticide applications, the faster the insecticide resistance will increase (Fig. 4).

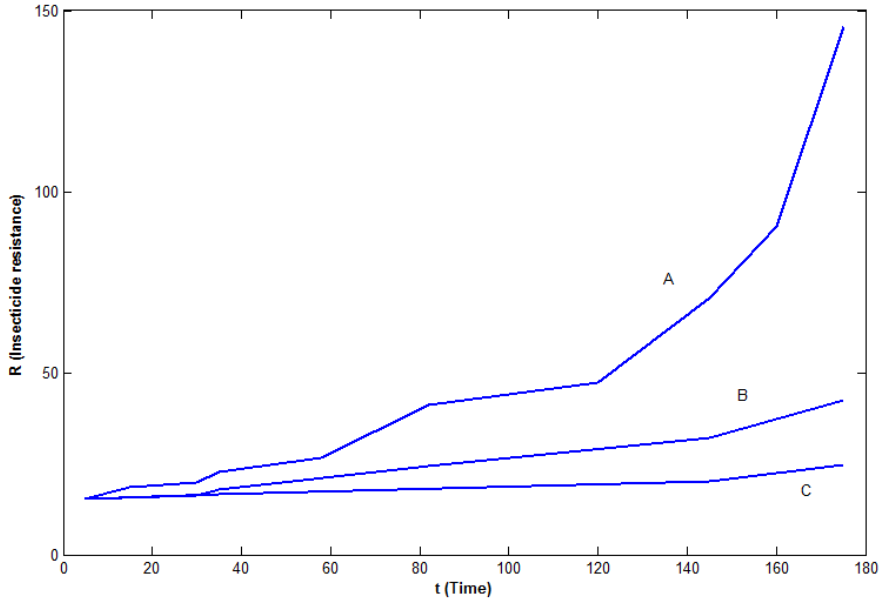

Fig. 4 Effect of application frequency (a=0.02; b=0.005; c=0.01; p=10; q=5; r=0; A: t_i=[5 15 30 35 58 82 120 145 160 175],$x(t_i)$=[10 70 20 35 40 85 18 62 25 54]; B: t_i=[5 30 35 82 145 175], $x(t_i)$=[10 20 35 85 62 54];
C: t_i=[5 35 145 175], $x(t_i)$=[10 35 62 54]).

4 Application of Model: Effect of Mixing Bioinsecticide and Chemical Insecticides on Reducing Insecticide Resistance

Suppose the single-use control effect of a certain dose (x_d) of the chemical insecticide is F. A certain bioinsecticide is mixed with the chemical insecticide to achieve the control effect F of the above-mentioned dose of the chemical insecticide. The dose of the chemical insecticide in the mixed insecticide is x_h, $x_h<x_d$. Under the same frequency of applications and fitness of insecticide-resistant individuals, the insecticide (chemical insecticide) resistance of mixed insecticides will increase slowly. The specific effect is shown in Fig. 5. Therefore, the model can theoretically estimate the specific effects of mixed use of bioinsecticides and the chemical insecticide to reduce insecticide resistance, such as the percentage of insecticide resistance reduction, the time of insecticide resistance reduction, etc. For example, suppose that A and B in Fig. 5 are the two cases of single use of the chemical insecticide and the mixed use of bioinsecticide and the chemical insecticide. After the ninth application, the resistance of the mixed use of two insecticides and the single use of the chemical insecticide are 145.557 and 885.3227, respectively. The reduction percentage of insecticide resistance is 83.6%. If the insecticide resistance reaches 145, the time required for the mixed use of bioinsecticide and the chemical insecticide is 175, and the time required for the chemical insecticide alone is 125, which is delayed by 40%.

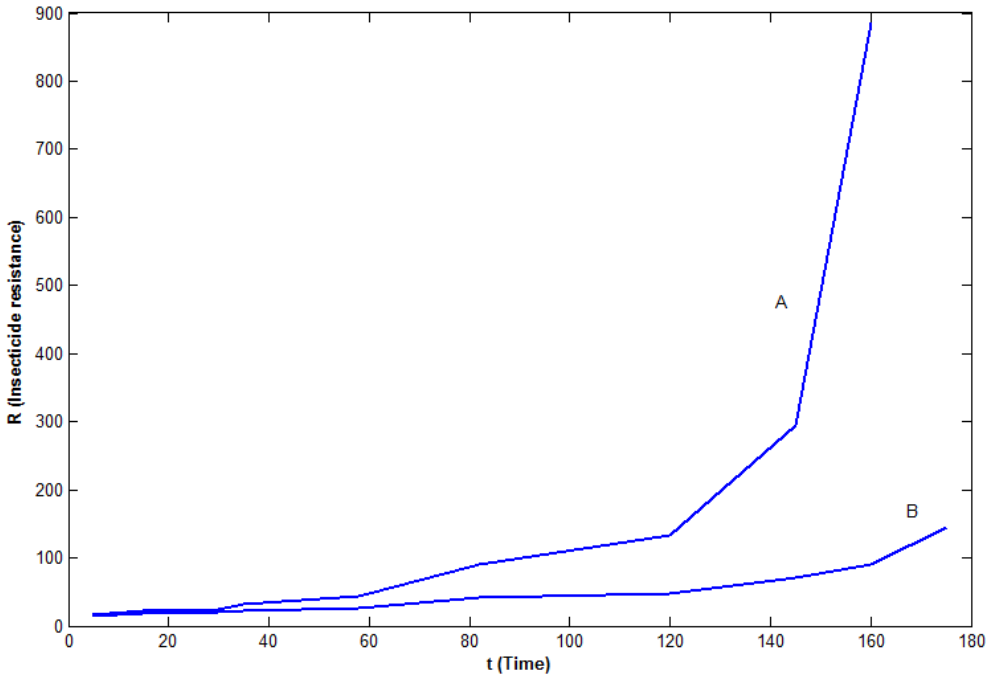

Fig. 5 Effect of mixed insecticide use on reducing insecticide resistance (a=0.02; b=0.005; c=0.01; p=10;q=5; r=0; t_i=[5 15 30 35 58 82 120 145 160 175]; A: $x(t_i)$=[30 90 40 55 60 105 38 82 45 74]; B: $x(t_i)$=[10 70 20 35 40 85 18 62 25 54]). A and B are the two cases of single use of the chemical insecticide and the mixed use of bioinsecticide and the chemical insecticide.

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