Article

A dynamic model to simulate the development of insecticide resistance

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Abstract
In this article, we described a dynamic model to simulate the development of insecticide resistance. The variables as insecticide use dosage, timing and frequency of insecticide uses, genetic mutagenicity of insect individuals, insecticide-resistant individuals' fitness, etc., were included in the model. Sensitivity analysis of the model indicated that the lower the fitness of the insecticide-resistant individuals is, the slower the increase of insecticide resistance will be. Simulation of the model showed that the greater the insect individuals' mutagenicity is, the more quickly the insecticide resistance will rise. The greater the insecticide use dosage is, the more quickly the insecticide resistance will increase. The higher the frequency of insecticide uses is, the greater the insecticide resistance will increase. The results showed that the insecticide dosage is more important than usage frequency in determining the development of insecticide resistance, which highlights the importance of joint use of reducing insecticide dosage and adopting IPM technologies. The model can be used to not only the dynamic simuation of development of insecticide resistance but also the assessment of IPM technologies in reducing insecticide resistance. For example, with a set of specific parametrical values, the simulation of the model demonstated that insecticide resistance will reduce 83.74% when the insecticide dosage is reduced from 180 to 20 by jointly using IPM technologies. Full codes of Matlab, R and BASIC programs for the model were given.

Keywords insecticide resistance; dynamic development; mathematical model; Matlab; R; genetic mutation; insect fitness; Integrated Pest Management.

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1 Introduction

Reducing crop loss from insect pests is a crucial measure to ensure food supply (Zhang et al., 2007, 2011; Peshin et al., 2009; Peshin and Zhang, 2014; Zhang, 2018b). According to the report, about 9000 species of insects and mites jeopardize crops around the world (Zhang et al., 2011). Crop loss from pests may decline by

35% to 42% if pesticides are used (Pimentel, 1997, 2009a, b). So far, crop pests are mainly controlled by using pesticides. It has been reported that about 1/3 of the food products are produced by using pesticides (Liu et al., 2002; Zhang et al., 2011). Without pesticide uses, the loss of cereals from pests would reach 32% (Cai, 2008).

On the other hand, the overuse and pollution of pesticide has been increasing (Carson, 1962; Pimentel, 2009b; Liu et al., 2008; Zhang and Liu, 2017). In 2013, The Greenpeace reported that 70% of pesticide use in China was not absorbed by plants (Fan, 2017). Global pesticide uses have resulted in loss of biodiversity (Kumar et al., 2013; Zhang et al., 2011). For example, more than 20000 species of bees live on the Earth, and they pollinate more than 90% of 107 major crops around the world. Nevertheless, populations of bee have significantly declined. About 75% of the honey around the world has been found to contain pesticides (Harvard School of Public Health, 2015; Sheridan et al., 2017). In addition, insects have been declining in the past decades, and pesticide uses were identified as a major contribution. For example, researchers have investigated species and abundance of insects in Western Europe since 1980s', and found that the insect population in a nature reserve has declined by about 78%. 143 species of hoverflies in 1989 and 104 species in 2014 were found respectively (Jin, 2017). Pesticide uses may have caused human and animal diseases, and injured human fecundity and intelligence quotient (Chen et al., 2004; Zhang et al., 2011). In addition, the increasing pesticide resistance is another outcome of long-term pesticide uses.

Aiming to lower the negative impacts of pesticides, Integrative Pest Management (IPM) is widely adopted as a powerful and successful solution for the sustainable prevention and control of crop pests (Peshin et al., 2009; Peshin and Zhang, 2014). IPM covers various technologies, including biopesticide uses (Sanjaya et al., 2013; Darvishzadeh et al., 2014; Jafarbeigi et al., 2014; Sharifian and Darvishzadeh, 2015; Gupta et al., 2017; Moghimi et al., 2018; Fig. 1), agri-biodiversity conservation (Zhang, 2011a-b, 2018a-b; Zhang et al., 2014; Iamba and Teksep, 2021; Fig. 2), releases of natural enemies (Abdolmaleki et al., 2021), induced plant resistance (Mahmoud, 2013), uses of genetic modified crops (Azimi et al., 2016; Zhang and Pang, 2009), etc.

Management of insecticide resistance holds an important position in IPM (Zhang, 2018b). Insecticide resistance is the natural adaptation of insect pests to insecticides. It is inheritable with various genes concerned (Tang, 2002; Ni and Pu, 2006; Zhang and Zhang, 2019, 2020). If the insecticide uses are reduced, the fitness of the resistant genotype will degrade due to the decline in the frequency of resistance genes (Georghiou, 1983; Rough and Mckenzie, 1987; Zhang, 2018a-b). The dynamic development of insecticide resistance depends on insect heredity, insecticide use and insect fitness, etc (Tang, 2002; Liu et al., 2008; Zhang and Zhang, 2018).

In this chapter, we describe a mathematical model to simulate the dynamic development of insecticide resistance, based on the prototype of the past study (Zhang and Liu, 2021), which is expected to provide a fundamental tool for the assessment of IPM technologies in reducing insecticide resistance.

Fig. 1 A demonstration farmland for the integrated use of seed pest prevention, insecticide use, bioinsecticide (genetically modified *Bacillus thuringiensis*, Bt-G033A) use, and insect stiky trap to control insect pests on Choy sum (*Brassica rapa* var. *parachinensis*), Huiyang, Guangdong, China. Huiyang is one of the most important vegetable suppliers of Hong Kong (Picture by Prof WenJun Zhang, Apr 7, 2019)

Fig. 2 Upper: Prof Zhang (left) and his lab members (right) are investigating arthropods in rice fields, Guangxi Province, China (Picture by Prof WenJun Zhang, September 23, 2016). Arthropod biodiversity in farmlands is highly valued, which helps to maintain natural equilibrium of insects and reduce insecticide uses. Lower: Researchers in Prof Zhang's lab are sucking arthropod samples for biodiversity catalogue using the modified sprayer in a rice field of Pearl River Delta, Guangdong Province, China (Picture by Prof WenJun Zhang, September 10, 2008).

2 Model and Program Codes

2.1 Model

Multiple uses of an insecticide may occur in the control of a certain insect species. Each use will lead to a certain theoretical mutation rate of insect individuals (i.e., the proportion of gene-mutant individuals *vs* whole population, and 0 ≤ theoretical mutation rate ≤ 1). Nevertheless, some of the mutant individuals resulted from each insecticide use are just the existing mutant individuals, i.e., the mutant individuals before and after the insecticide use will overlap. The higher the proportion of existing mutant individuals is, the greater the subsequent overlap will be. The overlapping part should be removed in the calculation of the mutation rate (Zhang and Liu, 2021).

Assume that the relationship between the mutation rate (y) and the dosage of insecticide use (x) is

$$y=f(x) \quad (1)$$

where $0 \le y \le 1$, and the insecticide use dosage at time t_i is $x(t_i)$, i.e., $y(t_i)=f(x(t_i))$. The mutation rate (y) shows a positive correlation with the insecticide dosage (x). Without the loss of generality, the relationship can be linearly approximated as

$$y=f(x)\approx a+bx \quad (2)$$

where b: insect individuals' mutagenicity, which is dependent upon insect species, insecticide type, etc. The greater b value means the greater mutagenicity.

Suppose that for any insecticide use, each insect individual has the same probability of being insecticide-applied and has the same probability of mutation respectively. The basic mutation rate of individuals is assumed as c, $0 \le c \le 1$. The basic mutation rate (c) is only related to the insect species and environmental conditions. Meanwhile, it is supposed that the mutation rate resulted from each insecticide use will not change before the next insecticide use.

Assume that the first insecticide use occurs at time t_1, and the theoretical mutation rate resulted from the use 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 resulted from the first insecticide use is

$$cy(t_1)$$

Hence the rate of newly increased mutant individuals after the first insecticide use is

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

While the total mutation rate after the first insecticide use is $z(t_1)=c+\Delta y(t_1)$.

The second insecticide use occurs at time t_2, and the theoretical mutation rate resulted from the insecticide use is $y(t_2)=f(x(t_2))$. The overlapping rate of mutant individuals resulted from the two insecticide uses is thus

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

Thus the rate of newly increased mutant individuals after the second insecticide use is

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

And the total mutation rate after the second insecticide use is $z(t_2)=z(t_1)+\Delta y(t_2)$.

Similarly, the third insecticide use occurs at time t_3, and the theoretical mutation rate resulted from the insecticide use is $y(t_3)=f(x(t_3))$. The overlapping rate of mutant individuals resulted from the third insecticide use is thus

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

The rate of newly increased mutant individuals after the third insecticide use is

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

And the total mutation rate after the third insecticide use is $z(t_3)=z(t_2)+\Delta y(t_3)$.

Finally, we have the mutation rate model as follows

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

where $\Delta y(t_i)$: the rate of newly increased mutant individuals after the ith insecticide use, t_i: the time of the ith insecticide use, and $y(t_i)$: the theoretical mutation rate of the ith insecticide use.

According to the dynamic model of the changes of resistant population and sensitive population (Zhang, 2018a; Zhang and Zhang, 2018), after an insecticide use, due to the disappearance of pesticide pressure, the low fitness of insecticide-resistant individuals, and intraspecific competition, the proportion of resistant individuals will decrease naturally. For the total mutation rate, assume that the declining relationship is

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

Without the loss of generality, it can be expressed as

$$z(t)=z(t_i)\exp(-r(t-t_i))+c,\ t_i\le t<t_{i+1}\qquad(4)$$

where r: insecticide-resistant individuals' fitness, which is dependent upon insect species, insecticide type, etc. The greater r value means the smaller fitness; t: the time; c: the basic mutation rate. Introducing (4) into the equation (3), we obtain the following mutation rate model

$$\begin{aligned}&\Delta y(t_1)=(1-c)y(t_1),\\&z(t_1)=c+\Delta y(t_1), i=1;\\&\Delta y(t_i)=(1-c-z(t_{i-1})\exp(-r(t-t_{i-1})))y(t_i),\\&z(t_i)=c+z(t_{i-1})\exp(-r(t-t_{i-1}))+\Delta y(t_i), t_i\le t<t_{i+1},\ i=2,\ 3,\ \ldots\end{aligned}\qquad(5)$$

where $\Delta y(t_i)$: the rate of newly increased mutant individuals after the ith insecticide use, $z(t_i)$: the total mutation rate after the ith insecticide use, t_i: the time of the ith insecticide use, and $y(t_i)$ the theoretical mutation rate of the ith insecticide use.

Representing the above equation (5) as the dosage-driven one, $y(t_i)=f(x(t_i))$, then the mutation rate model can be written as

$$\Delta y(t_1)=(1-c)f(x(t_1)),$$
$$z(t_1)=c+\Delta y(t_1),\ i=1;$$
$$\Delta y(t_i)=(1-c-z(t_{i-1})\exp(-r(t-t_{i-1})))f(x(t_i)),$$
$$z(t_i)=c+z(t_{i-1})\exp(-r(t-t_{i-1}))+\Delta y(t_i),\ t_i\le t<t_{i+1},\ i=2, 3, \ldots \qquad (6)$$

where $x(t_i)$: the insecticide dosage 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 that the relationship between the pest population resistance (e.g., LC_{50}), $R(t_i)$, and the rate of newly increased mutant individuals, $\Delta y(t_i)$ (i=1, 2, 3, …), after the ith insecticide use is

$$R(t_i)=g(\Delta y(t_1), \Delta y(t_2), \ldots, \Delta y(t_i)) \qquad (7)$$

And without the loss of generality, its linear approximation 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, which depends on time, survival, and reproduction rate, etc. Thus, it can be approximately considered that the population resistance depends on the total mutation rate. We thus have

$$R(t_i)=p+q/(1-z(t_i)) \qquad (8)$$

2.2 Program codes

Matlab codes for the model above are as follows (insRes.m):

```
clear
% The relationship between the mutation rate y and the dosage of insecticide use x is: y=f(x)≈a+bx
% The total mutation rate, z(t), after the ith insecticide use changes with time t:
% z(t)=z(ti)exp(-r(t-ti))+c, ti≤t<ti+1
% Insect mutation rate model is
% Δy(t1)=(1-c)f(x(t1)),
% z(t1)=c+Δy(t1),i=1;
% Δy(ti)=(1-c-z(ti-1)exp(-r(t-ti-1))) f(x(ti)),
% z(ti)=c+z(ti-1)exp(-r(t-ti-1))+Δy(ti),ti≤t<ti+1, i=2, 3, …
% where Δy(ti): the rate of newly increased mutant individuals after the ith insecticide use, z(ti): the total mutation rate
% after the ith insecticide use, ti: the time of the ith insecticide use, and y(ti) the theoretical mutation rate of the ith
% insecticide use.
% The relationship between the pest population resistance (e.g., LC50), R(ti), and the total mutation rate
```

```
% after the ith insecticide use z(ti), is
% R(ti)=p+q/(1-z(ti))
a=input('a (e.g., 0.001) =');
b=input('b (e.g., 0.0008) =');
c=input('c (e.g., 0.001) =');
r=input('r (e.g., 0.0001) =');
p=input('p (e.g., 5) =');
q=input('q (e.g., 20) =');
tsimu=input('Simulation time (e.g., the maximum time (an integral) in the data file) =');
str=input('Input the file name of insecticide uses data (e.g., data.xls, etc. The file has two rows. The 1st row are values for t and the 2nd row are corresponding values for x(t)) : ','s');
% The Excel format should be Microsoft Office Excel 97-2003
tx=xlsread(str);
tt=tx(1,:);
xx=tx(2,:);
nn=size(tt,2);
f=a+b*xx;
n=1;
deltay(1)=(1-c)*f(1);
z(1)=c+deltay(1);
if (z(1)>1) z(1)=1; end
if (z(1)<0) z(1)=0; end
n=2;
for t=1:tsimu
if ((t>tt(1)) & (t==tt(n)))
deltay(n)=(1-c-z(n-1)*exp(-r*(t-tt(n-1))))*f(n);
z(n)=c+z(n-1)*exp(-r*(t-tt(n-1)))+deltay(n);
if (z(n)>1) z(n)=1; end
if (z(n)<0) z(n)=0; end
n=n+1;
end
if (n>nn) break; end
end
R=p+q./(1-z);
tAndR=[tt;R]
plot(tt,R, 'k-', 'LineWidth',2);
xlabel('t (time)');
ylabel('R (Insecticide resistance)');
box off
```

BASIC codes for the model above are as follows (insRes.bas):

```
REM The relationship between the mutation rate y and the dosage of insecticide use x is: y=f(x)≈a+bx
REM The total mutation rate, z(t), after the ith insecticide use changes with time t:
REM z(t)=z(ti)exp(-r(t-ti))+c, ti≤t<ti+1
```

```
REM Insect mutation rate model is:
REM Δy(t1)=(1-c)f(x(t1)),
REM z(t1)=c+Δy(t1),i=1;
REM Δy(ti)=(1-c-z(ti-1)exp(-r(t-ti-1))) f(x(ti)),
REM z(ti)=c+z(ti-1)exp(-r(t-ti-1))+Δy(ti),ti≤t<ti+1, i=2, 3, …
REM where Δy(ti): the rate of newly increased mutant individuals after the ith insecticide use, z(ti): the total mutation rate
REM after the ith insecticide use, ti: the time of the ith insecticide use, and y(ti) the theoretical mutation rate of the ith
REM insecticide use.
REM The relationship between the pest population resistance (e.g., LC50), R(ti), and the total mutation rate
REM after the ith insecticide use z(ti), is:
REM R(ti)=p+q/(1-z(ti))
input "a = (e.g., 0.001)"; a
input "b = (e.g., 0.0008)"; b
input "c = (e.g., 0.001)"; c
input "r = (e.g., 0.0001)"; r
input "p = (e.g., 5)"; p
input "q = (e.g., 20)"; q
print
input "Total number of insecticide uses = (e.g., 10)"; nn
print
input "Simulation time = (e.g., the maximum time (an integral) in the data file)"; tsimu
print
input "Directory and filename of insecticide uses data : "; a$
open "I", 1, a$
open "O", 2, "RESULTS.txt"
REM Insecticide use data in the data file are, e.g., as follows (The file has two rows. The 1st row are
REM values for t and the 2nd row are corresponding values for x(t)):
REM 5 15 30 35 58 82 120 145 160 175
REM 10 70 20 35 40 85 18 62 25 54
REM The BASIC program, the data file, and the running platform QBASIC.exe should be in the same
REM directory. QBASIC.exe can be downloaded at: http://www.iaees.org/publications/software/qbasic.exe
REM The results are stored in the file, RESULTS.txt
dim tt(nn),xx(nn),deltay(nn),z(nn)
for i=1 to nn
input #1, tt(i)
next i
for i=1 to nn
input #1, xx(i)
f(i)=a+b*xx(i)
next i
n=1
deltay(1)=(1-c)*f(1)
z(1)=c+deltay(1)
if z(1)>1 then let z(1)=1
if z(1)<0 then let z(1)=0
```

```
n=2
for t=1 to tsimu
if not (t>tt(1) and t=tt(n)) then goto 100
deltay(n)=(1-c-z(n-1)*exp(-r*(t-tt(n-1))))*f(n)
z(n)=c+z(n-1)*exp(-r*(t-tt(n-1)))+deltay(n)
if z(n)>1 then let z(n)=1
if z(n)<0 then let z(n)=0
n=n+1
100 if (n>nn) then goto 200
next t
200 for i=1 to nn
RR(i)=p+q/(1-z(i))
next i
print #2, "t (time)        R(t) (Insecticide resistance)"
for i=1 to nn
print #2, tt(i); RR(i)
next i
close #1
close #2
```

R codes for the model above are as follows (insRes.R):

```
# The relationship between the mutation rate y and the dosage of insecticide use x is: y=f(x)≈a+bx
# The total mutation rate, z(t), after the ith insecticide use changes with time t:
# z(t)=z(t_i)exp(-r(t-t_i))+c, t_i≤t<t_i+1
# Insect mutation rate model is:
# Δy(t_1)=(1-c)f(x(t_1)),
# z(t_1)=c+Δy(t_1),i=1;
# Δy(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))+Δy(t_i),t_i≤t<t_i+1, i=2, 3, …
# where Δy(t_i): the rate of newly increased mutant individuals after the ith insecticide use, z(t_i): the total mutation rate
# after the ith insecticide use, t_i: the time of the ith insecticide use, and y(t_i) the theoretical mutation rate of the ith
# insecticide use.
# The relationship between the pest population resistance (e.g., LC50), R(t_i), and the total mutation rate
# after the ith insecticide use z(t_i), is:
# R(t_i)=p+q/(1-z(t_i))
# Insecticide use data in the data file are, e.g., as follows (The file has two rows. The 1st row are values
# for t and the 2nd row are corresponding values for x(t)):
# 5 15 30 35 58 82 120 145 160 175
# 10 70 20 35 40 85 18 62 25 54
# R software platform can be downloaded at: https://mirrors.tuna.tsinghua.edu.cn/CRAN/
a=0.001
b=0.0008
c=0.001
r=0.0001
```

```
p=10
q=5
tsimu=180
# Users should use their own paremetrical values of a, b, c, r, p, q, and tsimu
tx=numeric(nn)
tt=numeric(nn)
xx=numeric(nn)
f=numeric(nn)
deltay=numeric(nn)
z=numeric(nn)
R=numeric(nn)
tx=read.table('D:/Users/Administrator/Documents/data.txt')
# The insecticide use data file, data.txt
nn=length(tx)
tt=tx[1,1:nn]
xx=tx[2,1:nn]
f=a+b*xx
n=1
deltay[1]=(1-c)*f[1]
z[1]=c+(1-c)*f[1]
if (z[1]>1)
z[1]=1
if (z[1]<0)
z[1]=0
n=2
for(t in 1:tsimu){
if ((t>tt[1]) & (t==tt[n])) {
deltay[n]=(1-c-z[n-1]*exp(-r*(t-tt[n-1])))*f[n]
z[n]=c+z[n-1]*exp(-r*(t-tt[n-1]))+deltay[n]
if (z[n]>1)
z[n]=1
if (z[n]<0)
z[n]=0
n=n+1
}
if (n>nn)
break
}
tt=as.numeric(tt)
z=as.numeric(z)
R=p+q/(1-z)
print ("t (time)")
print(tt)
print ("R(t) (Insecticide resistance)")
print(R)
```

```
plot(tt, R, type="o", xlab="t (time)", ylab="R(t) (Insecticide resistance)")
print("End")
```

The GUI (Graphic User Interface) of Matlab, BASIC and R are indicated in Fig. 3, Fig. 4, and Fig. 5.

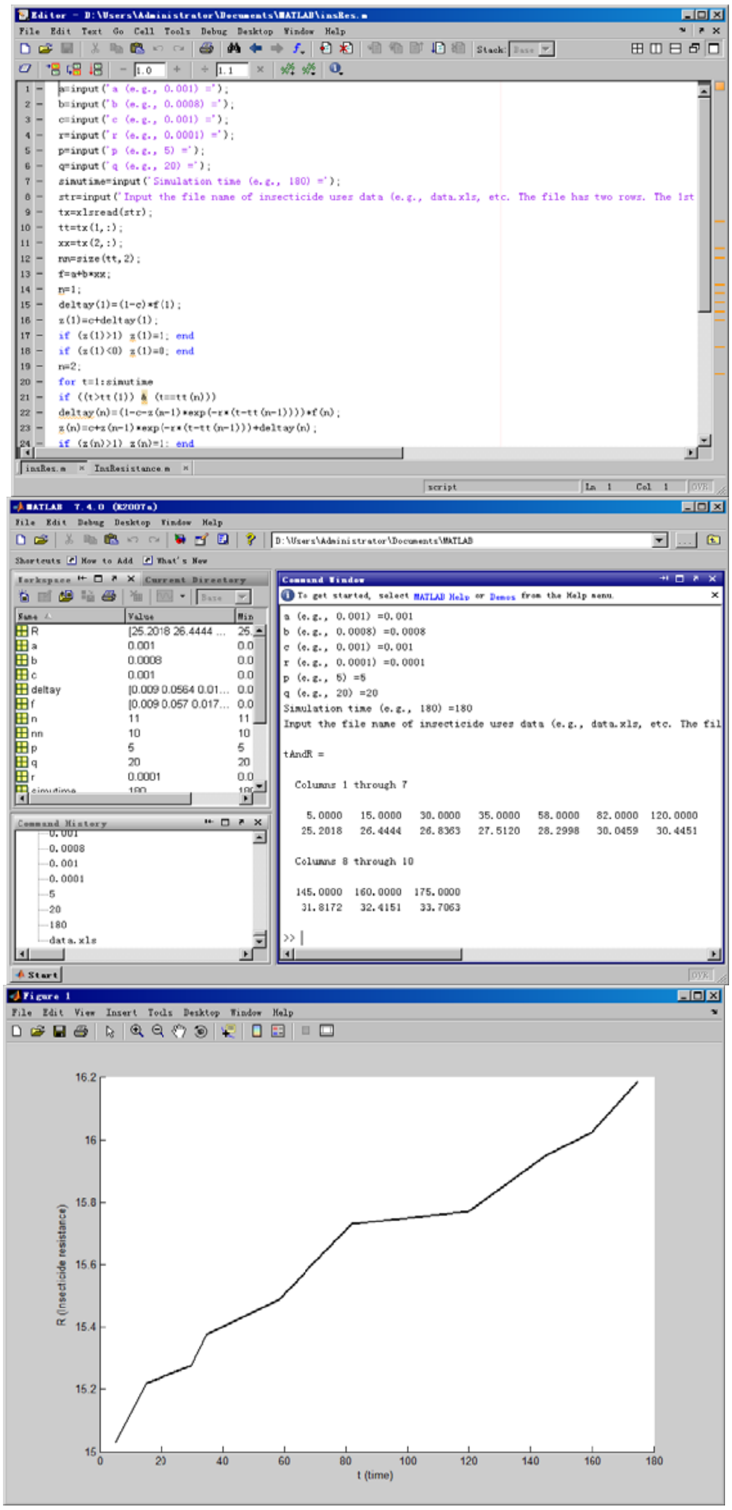


Fig. 3 GUI of Matlab.

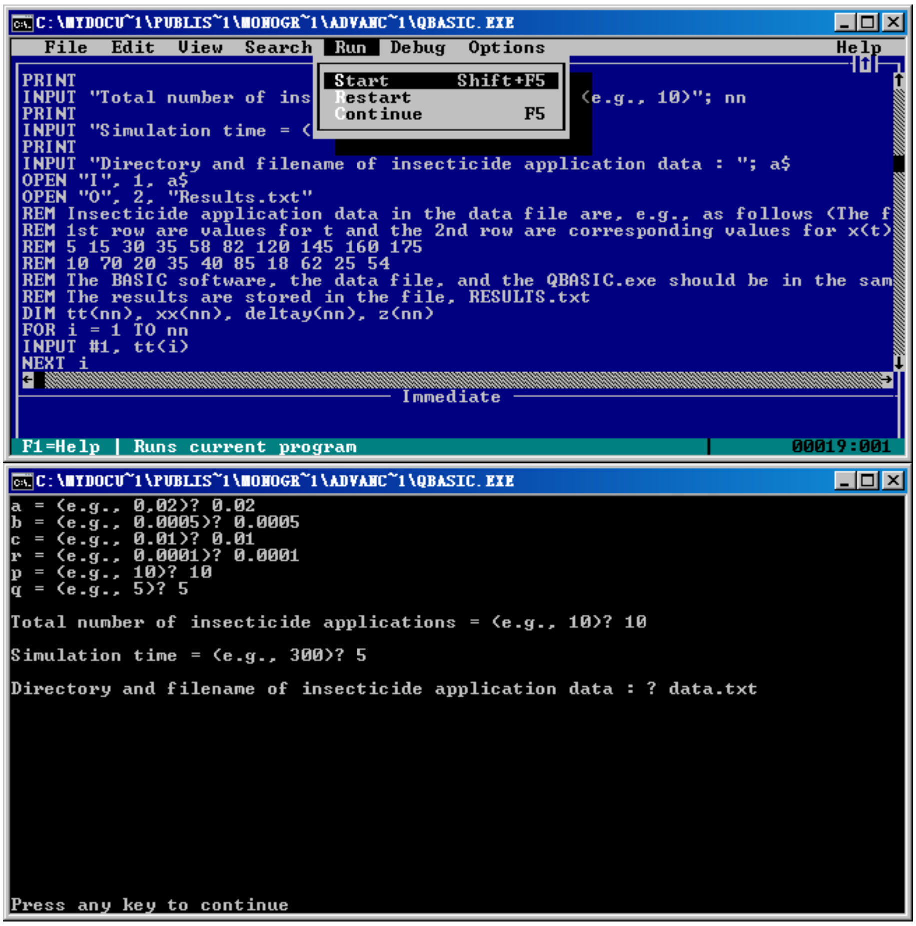
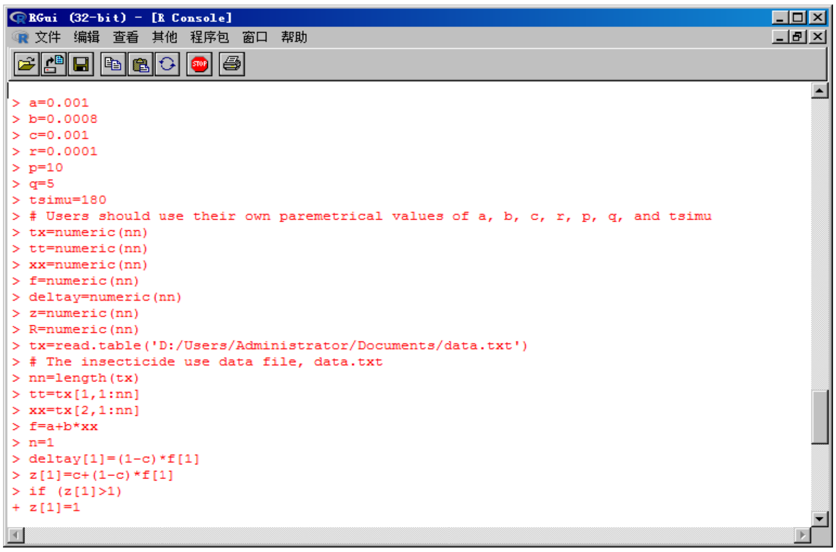


Fig. 4 GUI of BASIC.



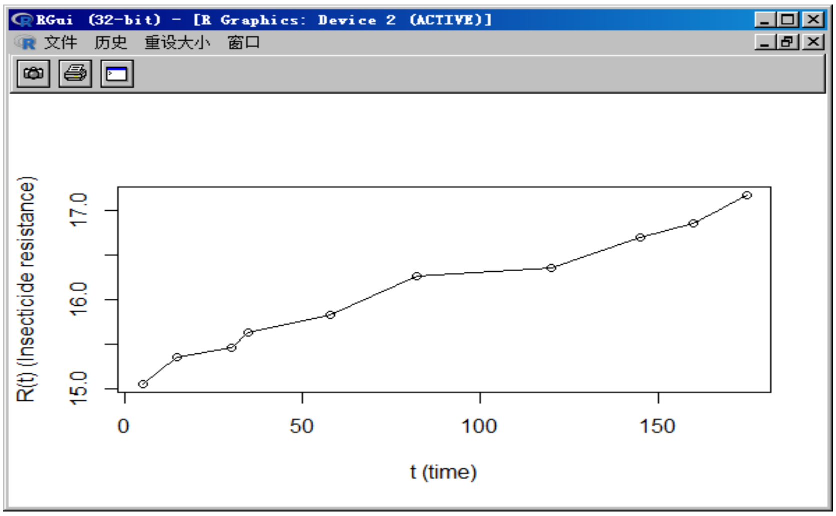


Fig. 5 GUI of R.

3 Sensitivity Analysis

Suppose there are data of insecticide uses as follows:

t	5	15	30	35	58	82	120	145	160	175
x(*t*)	30	90	40	55	60	105	38	82	45	74

The basic parameters are, e.g., as follows: a=0.02, b=0.005, c=0.01, r=0.0005, p=10, q=5. The simulation time, t_{simu}=180.

3.1 Effect of insecticide-resistant individuals' fitness (*r*)

If the environmental fitness of insecticide-resistant individuals does not decrease with time, i.e., r=0, the multiple uses of the insecticide will lead to the continuous increase in insect population's resistance (Fig. 6). The fitness of insecticide-resistant individuals decreases when the insecticide is not applied ($r\neq0$). The lower the fitness of the insecticide-resistant individuals under multiple insecticide uses, the slower the increase of insecticide resistance will be and and even decline (Fig. 6, Table 1).

3.2 Effect of insect individuals' mutagenicity (*b*)

Insect individuals' mutagenicity (b) changes with the types of pesticides and insect species, etc. The greater the mutagenicity is, the more quickly the insecticide resistance will rise (Fig. 6, Table 1).

3.3 Effect of dosage of insecticide use (*x*(*t*))

The greater the insecticide use dosage is, the more quickly the insecticide resistance will increase (Fig. 6, Table 1).

3.4 Effect of insecticide use frequency

The higher the frequency of insecticide uses is, the greater the insecticide resistance will increase (Fig. 6, Table 1).

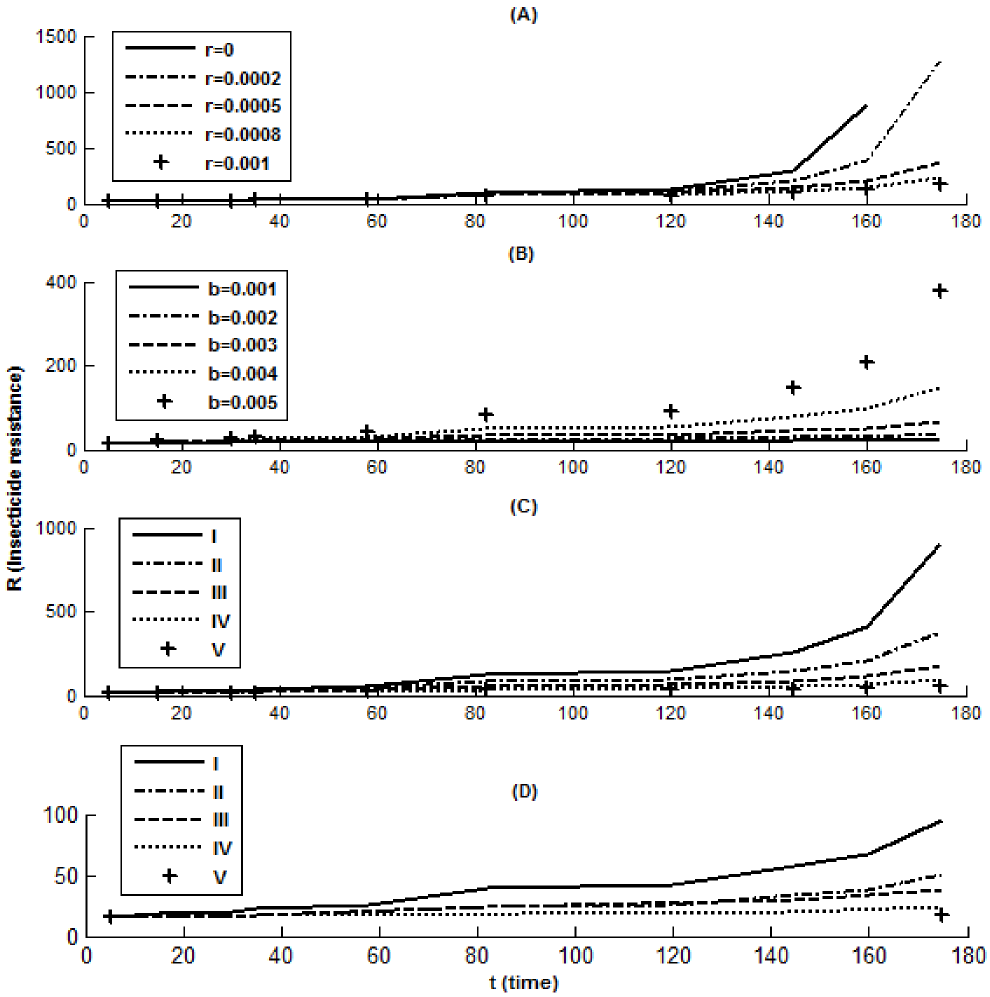


Fig. 6 Development of insecticide resistance ($R(t)$) with time (t). (A) Effect of insecticide-resistant individuals' fitness (r) (a=0.02;b=0.005;c=0.01;p=10;q=5; t_i=[5 15 30 35 58 82 120 145 160 175]; $x(t_i)$=[10 70 20 35 40 85 18 62 25 54]). (B) Effect of insect individuals' mutagenicity (b) (a=0.02; c=0.01; p=10;q=5; r=0.0005; 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]). (C) Effect of dosage of insecticide use ($x(t)$ (a=0.02; b=0.005; c=0.01; p=10;q=5; r=0.0005; t_i=[5 15 30 35 58 82 120 145 160 175]; I: $x(t_i)$=[40 100 50 65 70 115 48 92 55 84]; II: $x(t_i)$=[30 90 40 55 60 105 38 82 45 74]; III: $x(t_i)$=[20 80 30 45 50 95 28 72 35 64]; IV: $x(t_i)$=[10 70 20 35 40 85 18 62 25 54]; V: $x(t_i)$=[5 60 10 25 30 75 8 52 15 44]. **(D)** Effect of insecticide use frequency (a=0.02; b=0.005; c=0.01; p=10; q=5; r=0.0005; I: 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]; II: t_i=[5 30 35 82 120 145 160 175],$x(t_i)$=[10 20 35 85 18 62 25 54]; III: t_i=[5 30 35 82 145 175], $x(t_i)$=[10 20 35 85 62 54]; IV: t_i=[5 35 145 175], $x(t_i)$=[10 35 62 54]; V: t_i=[5 175], $x(t_i)$=[10 54]

Table 1 Sensitivity analysis of the model.

Variable	t	5	15	30	35	58	82	120	145	160	175
	$x(t)$	10	70	20	35	40	85	18	62	25	54
Effect of insecticide-resistant individuals' fitness (r)	r=0	16.08	21.62	25.26	32.32	44.36	91.08	132.50	294.64	885.32	∞
	r=0.0002	16.08	21.62	25.19	32.17	43.56	86.82	111.81	210.02	379.60	1274.29
	r=0.0005	16.08	21.61	25.09	31.95	42.45	81.27	91.50	149.21	209.96	377.73
	r=0.0008	16.08	21.60	24.99	31.74	41.41	76.53	78.17	117.38	148.15	227.48

	r=0.001	16.08	21.60	24.92	31.60	40.77	73.75	71.57	103.42	124.95	181.71
Effect of insect individuals' mutagenicity (b)	$x(t)$	10	70	20	35	40	85	18	62	25	54
	b=0.001	15.32	16.04	16.49	17.10	17.79	18.99	19.57	20.74	21.64	23.02
	b=0.002	15.49	16.93	17.79	19.08	20.66	23.95	25.34	28.90	31.60	36.45
	b=0.003	15.67	18.08	19.50	21.86	24.94	32.61	35.57	44.84	52.29	67.45
	b=0.004	15.87	19.58	21.82	25.88	31.61	48.72	54.56	77.73	98.34	146.26
	b=0.005	16.08	21.61	25.09	31.95	42.45	81.27	91.50	149.21	209.96	377.73
Effect of dosage of insecticide use ($x(t)$)	$x(t)$	40.00	100.00	50.00	65.00	70.00	115.00	48.00	92.00	55.00	84.00
	$R(t)$	16.48	23.65	28.97	39.88	57.57	126.70	142.85	252.87	406.09	902.78
	$x(t)$	30.00	90.00	40.00	55.00	60.00	105.00	38.00	82.00	45.00	74.00
	$R(t)$	16.08	21.61	25.09	31.95	42.45	81.27	91.50	149.21	209.96	377.73
	$x(t)$	20.00	80.00	30.00	45.00	50.00	95.00	28.00	72.00	35.00	64.00
	$R(t)$	15.74	20.00	22.20	26.51	32.77	55.22	60.75	90.86	115.56	180.29
	$x(t)$	10.00	70.00	20.00	35.00	40.00	85.00	18.00	62.00	25.00	54.00
	$R(t)$	15.43	18.71	20.02	22.67	26.37	39.66	42.24	57.97	67.94	94.72
	$x(t)$	5.00	60.00	10.00	25.00	30.00	75.00	8.00	52.00	15.00	44.00
	R(t)	15.29	17.86	18.55	20.15	22.34	30.54	31.48	39.89	43.79	55.58
Effect of insecticide use frequency	$x(t)$	10.00	70.00	20.00	35.00	40.00	85.00	18.00	62.00	25.00	54.00
	$R(t)$	15.43	18.71	20.02	22.67	26.37	39.66	42.24	57.97	67.94	94.72
	$x(t)$	10.00		20.00	35.00		85.00	18.00	62.00	25.00	54.00
	$R(t)$	15.43		16.23	17.83		24.15	25.80	33.70	38.27	50.70
	$x(t)$	10.00		20.00	35.00		85.00		62.00		54.00
	$R(t)$	15.43		16.23	17.83		24.15		30.54		38.78
	$x(t)$	10.00			35.00				62.00		54.00
	$R(t)$	15.43			16.81				20.11		24.31
	$x(t)$	10.00									54.00
	$R(t)$	15.43									17.68

4 Application of Model

Suppose the basic parameters are, e.g., as follows: a=0.001, b=0.001, c=0.01, r=0.0001, p=5, q=20. The simulation time, t_{simu}=200. The assessment of IPM technologies in reducing insecticide resistance in terms of the reduction of insecticide use dosage and frequency of insecticide uses are shown in Tables 2 and 3.

As shown in Table 2, at the time t=100, insecticide resistance will reduce by 55.18% when the dosage is reduced from 180 to 20 by jointly using IPM technologies, while at the time t=200, insecticide resistance will reduce by 83.74% when the dosage is reduced from 180 to 20.

Fixing the dosage $x(t)$=100, insecticide resistance will reduce by 30.74% when the frequency is reduced from 10 to 1 at the time t=100 by jointly using IPM technologies, while insecticide resistance will reduce by 59.09% when the frequency is reduced from 10 to 1 at t=200 (Table 3).

The results show that the insecticide dosage is more important than usage frequency in determining the development of insecticide resistance. It highlights the importance of joint use of reducing insecticide dosage and adopting IPM technologies.

There are nonlinear relationships between insecticide resistance reduction and dosage and frequency of insecticide uses, and the relationships change with time non-linearly.

Table 2 Assessment of insecticide resistance for reduction of insecticide use dosage.

t	20	40	60	80	100	120	140	160	180	200
x(*t*)	180	180	180	180	180	180	180	180	180	180
R(*t*)	29.667	35.48	42.752	51.897	63.475	78.259	97.34	122.32	155.61	201.11
x(*t*)	140	140	140	140	140	140	140	140	140	140
R(*t*)	28.518	32.694	37.668	43.612	50.747	59.36	69.823	82.631	98.464	118.27
R(t) ↓ (%)	3.8718	7.8507	11.892	15.965	20.052	24.149	28.269	32.444	36.725	41.192
x(*t*)	100	100	100	100	100	100	100	100	100	100
R(*t*)	27.472	30.274	33.458	37.085	41.227	45.973	51.43	57.731	65.041	73.571
R(t) ↓ (%)	7.399	14.673	21.738	28.542	35.051	41.256	47.165	52.802	58.203	63.417
x(*t*)	60	60	60	60	60	60	60	60	60	60
R(*t*)	26.514	28.158	29.943	31.885	34.002	36.312	38.837	41.604	44.642	47.985
R(t) ↓ (%)	10.626	20.638	29.961	38.56	46.433	53.6	60.101	65.986	71.312	76.14
x(*t*)	20	20	20	20	20	20	20	20	20	20
R(*t*)	25.635	26.296	26.984	27.701	28.448	29.227	30.039	30.887	31.773	32.7
R(t) ↓ (%)	13.589	25.884	36.881	46.623	55.183	62.654	69.14	74.748	79.582	83.74

Table 3 Assessment of insecticide resistance for reduction of frequency of insecticide uses.

t	20	40	60	80	100	120	140	160	180	200
x(*t*)	100	100	100	100	100	100	100	100	100	100
R(*t*)	27.472	30.274	33.458	37.085	41.227	45.973	51.43	57.731	65.041	73.571
x(*t*)	100	0	100	100	0	100	100	0	100	100
R(*t*)	27.472	27.744	30.583	33.81	34.234	37.97	42.24	42.918	47.915	53.669
R(t) ↓ (%)	0	8.3568	8.5925	8.8307	16.961	17.407	17.869	25.659	26.332	27.052
x(*t*)	100	0	100	0	0	100	0	0	100	100
R(*t*)	27.472	27.744	30.583	30.926	31.277	34.6	35.045	35.503	39.418	43.899
R(t) ↓ (%)	0	8.3568	8.5925	16.607	24.134	24.739	31.858	38.503	39.395	40.332
x(*t*)	100	0	100	0	0	0	0	0	0	100
R(*t*)	27.472	27.744	30.583	30.926	31.277	31.637	32.005	32.383	32.77	36.3
R(t) ↓ (%)	0	8.3568	8.5925	16.607	24.134	31.184	37.769	43.907	49.617	50.66
x(*t*)	0	0	100	0	0	0	0	0	0	0
R(*t*)	25.222	25.449	27.98	28.264	28.553	28.849	29.152	29.461	29.778	30.101
R(t) ↓ (%)	8.1881	15.939	16.373	23.787	30.742	37.247	43.317	48.968	54.218	59.086

5 Discussion

The more reasonable simulation and assessment are dependent upon the more accurate parametrical values in the model. In the practical application, parametrical values can be determined according to field experiments and historical data on insecticide resistance. In addition, the present model can be further improved for better performance. For example, the equations (2), (4), (7) and (8) may be expressed as the more suitable equations in terms of the different mechanisms of insecticide resistance.

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