System Dynamics models to assess the risk of mosquito-borne diseases and to evaluate control policies

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ABSTRACT

The authors built a System Dynamics (SD) model to study the diffusion and control of a disease transmitted by the mosquito Aedes albopictus in Italy. Such arthropod is one of the world’s most invasive species, due to the trade of used tyres, which are a good vehicle of mosquito eggs because they are likely to contain small deposits of water. It is spreading rapidly outside its original regions, into temperate zones, owing to its adaptability to climate changes. An outbreak of Chikungunya in Italy in 2007 proved that Europe is definitely at risk for Aedes-borne diseases.
SD is particularly suitable for the analysis of infectious diseases because it can model properly the feedback effect between the populations of susceptible and infected people. There are also more recent applications to model the more complex mosquito-borne diseases.
Although the present work is meant for an application in Italy, it can be adapted to tackle other mosquito-borne diseases in other countries.

1. Introduction

The mosquito *Aedes (Ae.) albopictus*, commonly known as the “Asian tiger mosquito”, originally a forest-mosquito in the tropical and subtropical regions of Southeast Asia, up to China and Japan, in the 20th century has expanded to other countries.

It received international attention when it appeared in Houston, Texas, in 1986, through importations of used tyres from Japan (Bruce Knudsen, 1995). Then it established in North, Central and South America. In Europe its presence was reported for the first time from Albania in 1979 (Scholte et al, 2007). In Africa, it has been reported from car-tyre import inspections into South Africa and it became established in Cameroon, Equatorial Guinea, Nigeria and Gabon (Scholte et al, 2007). In New Zealand and Australia, the species has been intercepted but it is established only on several of the Torres islands north of Queensland (Scholte et al, 2007). It was first imported into Italy in 1990, again through the global shipping trade of used tyres (Pietrobelli, 2008), through the port of Genova, and since then it has widely spread in Italy. By now it is established in the whole area of Rome (Cignini et al, 2008, Severini et al, 2008), Rome being the first example of extensive colonization of an urban area in Europe. Occasionally, long-distance spread is linked to the importation of ornamental plants, such as

Lucky bamboo, from Ae. Albopictus endemic areas. Local distribution is probably based on passive transport of adult mosquitoes by car or trucks, and on local movement of infested artificial oviposition sites such as used tyres or flowerpots brought from garden centres to gardens (Scholte et al, 2007).

The survival of *Ae. albopictus* in Europe is due to its great adaptability to different climatic conditions and its diffusion mainly to passive transport of eggs or adults. They need water containers, preferably man-made containers and tree-holes, where females may lay eggs, and larvae develop. Temperature must keep between certain limits and there is a threshold on the hours of daylight. From one year to another they survive to lower temperatures. More, its eggs diapause - i.e. undergo a period of suspended development during cold winters, if there are less than 13-14 hours of daylight and temperature is lower than 10°C (Toma et al, 2003) - and disclose in spring, assuring the continuation of the local populations.

Ae. albopictus is a potential vector for the transmission of Dengue, Yellow fever, Encephalites, Chikungunya, Dirofilaria immitis, Dirofilaria repens, Setaria labiatopapillosa and West Nile virus. Dirofilaria immitis, Dirofilaria repens are common in dogs, cattle, equines and pigs, and Setaria labiatopapillosa is common in wild ruminants (Pietrobelli, 2008). The spread of *Ae. albopictus* in Italy has raised concerns about its possible role as a vector for Dirofilaria and Setaria. An outbreak of Chikungunya virus occurred in summer 2007 in the areas of Ravenna, Forlì-Cesena, Rimini and Bologna, with 196 cases plus other sporadic cases. There are fears of outbreaks in Europe (ECDC, 2008).

Control measures can be adopted, to act on larvae or on adult Ae. albopictus. Larval controls aim at the elimination of breeding sites or spraying with conventional larvicides or biological control agents. Adult control measures consist in aerial spraying with insecticides.

Frequency of either larval or adult control measures needs to be optimized.

The EMCA (European Mosquito Control Association) tries to coordinate efforts in Europe.

The urge to monitor and control the development and diffusion of *Ae. albopictus* through suitable mathematical models, data collection and intervention campaigns, is by now widely felt and shared.

Hence this paper aims at building a SD model, by means of the user-friendly software Vensim (Ventana Systems, 2008), to study the development and diffusion of *Ae. albopictus*, also in presence of possible control interventions, in order to give valid support to the definition of control campaigns to adopt.

Such SD model is bound to differ from those built for countries where diseases borne by Ae. Albopictus are endemic. In fact, it has to take into account the diapause phenomenon and, also, the occasional arrival of infected human individuals[1] that can start the spreading of the disease, or of infected eggs/mosquitoes.

2. Data collection

A SD model to study the spreading of a Ae. albopictus borne disease must take into account the difficulty of getting the data necessary for the input. Data vary with places and may change in time, requiring updating through continuous collections**.**

Data on the *Ae. albopictus* life-cycle are collected by various means. Either in laboratory – by growing individuals in cages - or in nature, by means of traps. Qiu et al (2007) report and evaluate various monitoring techniques, targeting resting adults, host-seeking individuals or gravid females. Human bait collections can be used to estimate biting rates (number of bites per human per day) and infection rate.

As far as Roma is concerned, in 2000 the Comune di Roma - the local authority of the city of Rome - initiated a system of ovitraps (egg traps, see Fig.1) to monitor egg-laying rates.

Figure 1. Ovitrap

Ovitraps are 500 ml black plastic flower pots filled with 350 ml water, with a 3x15 cm strip of masonite suspended vertically in the middle of the pot to provide a suitable surface on which mosquitoes can lay eggs . The masonite strips are collected and replaced by new ones weekly, the pots are rinsed and replaced with water, and eggs are counted in order to evaluate the distribution and evolution of *Ae. albopictus* in the area through two measures: the percentage of positive ovitraps (i.e., those containing eggs), and the mean number of eggs found in all the working ovitraps. Such ovitraps were placed in public areas, between March and December at the beginning, then all year round since 2003, because of the increased adaptability of Ae. Albopictus to climate, already mentioned. Currently there are 650 ovitraps in the city of Rome. Toma et al (2003) studied egg hatching rates in Rome. This study, conducted in 2000, used 17312 eggs collected from the ovitraps between the 27^{th} and the 47^{th} week of the year, after keeping them at room temperature for 3 days and finally placing them into

1 the transmission of a disease is not always depending from infected humans; in the case of Dirofilaria, only infected animals can infect the mosquito.

plastic trays containing dechlorinated tap water, trying to reproduce natural conditions. They recorded (see Table 1) a mean hatching rate (MHR) of 65% in week 25, with mean temperature (T) equal to 24.2°C and P (photoperiod or hours of daylight) equal to 15.9 hours; of 21.1% with T=12.3°C and P=10; of 17% with T=18.5°C and P=12.2; greater than 90% in week 35. Very few eggs hatched in the 48th and 49th week and no eggs hatched in the 50th week. The study showed a significant correlation between MHR and T, but not between MHR and rainfall or photoperiod, although egg hatching starts decreasing at P=14, in favour of diapausing, and stops completely if T drops below 10°C. So, P seems to induce diapause.

Table 1. Mean hatching rate (MHR)

MHR (%)	T (C)	P (hours)	week
65	24.2	15.9	25
>90	35th week	13.6	35
decreasing	20.6	13.6	since 36
17	18.5	12.2	40
increasing	15.9	10.5	Weeks 41-45
21.1	12.3	10	47

The authors found positive ovitraps between the 12th and the 52th week of the year. From such data, considering that development time from egg hatching until pupation may be as long as 3 weeks at temperatures between 14°C and 18°C, they assumed that overwintering eggs hatched in the 9th week, with P between 11 and 11.5 and T between 10° and 11°. Adult females survived up to the end of December.

A study carried out by the same authors in 2002-03 showed that around week 37, with P=13, more than 50% eggs started diapausing (Romi et al, 2006). In the period mid-December 2003-mid March 2004, approximately 30% of ovitraps were positive, every week, with a mean number of only 5 eggs per trap, through all the winter, although temperature kept low, reaching also -3°. No eggs hatched until early March and no larvae were found. The explanation for the eggs found may either be that some long-lived females born in November or December survived for at least three months, or that a favourable microclimate (indoor plant cultures, green houses or plant nurseries) allowed the development of at least 1 or 2 generations of mosquitoes (Romi et al, 2006).

Based on the results from the ovitraps, the Comune di Roma launches intervention campaigns in public areas, with the aim of destroying *Ae. Albopictus* larvae. These develop in small water containers such as flower vases, cemetery urns. Citizens are strongly encouraged to destroy potential larvae foci in private areas (gardens and balconies), by removing water from underneath plant containers and pots, and other water containers that might fill with rain.

From literature, in laboratory studies, the period from oviposition to egg hatching varies between a maximum of 6 days at 17° to a minimum of 2 days, at 26° and higher temperatures; mortality depends much on environmental conditions. After 3 months at 25° and RH (relative humidity) of 70-75%, the survival rate was about 50%; at the same temperature and RH of 60-70%, the percentage of egg hatching observed in 2 months was 95%. In three localities of Montana, the mortality of diapausing eggs ranged between 21 and 100%, according if the Ae. albopictus were from Northern Asia and USA or from tropical Asia.

As to the larval and pupal stages, they last, in total, between 20 days (at 14° - 18°) and 6 days at 30°. In field experiments in Singapore, larvae exhibited a mortality of about 80%.

Females live longer than males, usually from 4 to 8 weeks. A strain of females from Calcutta was tested in laboratory over combinations of 3 temperatures and 3 RH and the lowest median survival was of 28.4 days.

The probability of daily survival ranges between 0.71 and 0.88.

The duration of the gonotrophic cycle – interval between two ovipositions - was measured in Vietnam, in an insectary, as of 4.5 – 6 days at 30°; of at least 10 days at 20°.

The occurrence of multiple blood meals per gonotrophic cycle may range to perhaps 20%.

All the previous data are taken from Hawley (1988).

3. SD modelling

System dynamics is an analytical modelling approach whose foundations were laid in the 1950's at MIT by Jay Forrester in his pioneering work on "industrial dynamics" (Forrester 1960, 1961).

SD has been employed for the modelling of diseases for many years (Buhaug et al 1989; Dangerfield 1999). SD has been used widely for modelling the AIDS epidemic (Dangerfield and Roberts 1990; Heidenberger and Flessa 1993; Rauner 2002) and for the sexually transmitted disease chlamydia (Townshend and Turner 2000; Evenden et al 2006). The Vensim model of Evenden et al was used to perform a cost-benefit analysis to quantify the benefits of being able to identify high-risk individuals and target screening programmes at this group.

As to mosquito-borne diseases, mathematical models for malaria date back to Ross (1911). Indeed Ross is seen by many as the founding father of mathematical models of disease. Bailey (1982) recognized the potential for the use of system dynamics for malaria modelling, but in those days the limitations of computer power meant that such models were highly simplified. In recent years, Flessa (1999), published a SD malaria model. The complex nature of the mosquito life cycle, its interaction with the human population, the influence of environmental factors, and the transmisson dynamics of the infection itself, mean that such models must necessarily be very detailed and computer-intensive.

Berchi (2008) developed a model using the SD software Vensim (2008) to capture the life cycle of *Aedes albopictus* and the transmission of Dengue infection in Italy.

SD has two distinct aspects: one qualitative and one quantitative. The qualitative aspect involves the construction of *causal loops* or *influence* diagrams, which depict graphically the way in which the system elements are related. The aim is to enhance the understanding of a problem situation through the structure of the system and the relationships between relevant variables. Discussions with problem owners and other stakeholders allow to identify system elements which are then represented in the form of a causal loop diagram (CLD). In many cases the qualitative analysis of these diagrams is of value in its own right. The understanding and insights that this approach can bring are very useful, even if no further quantitative modelling is carried out.

For quantitative SD modelling, the CLD has to be converted to a *stock-flow diagram*. This model is best conceptualized as a system of water tanks connected by pipes.

The description of a simple model follows, depicting the spread of an infectious disease, known as Susceptible-Infective model (SI).

Figure 2 shows that a susceptible person can become infected through contagion by an infected one and that an infected person recovers after a recovery time. No exits (i.e., no deaths) are considered. So, for example, “new infected” depends on the number of susceptible, the number of infected and the infection rate. It is assumed that the population is homogeneous in terms of behaviour.

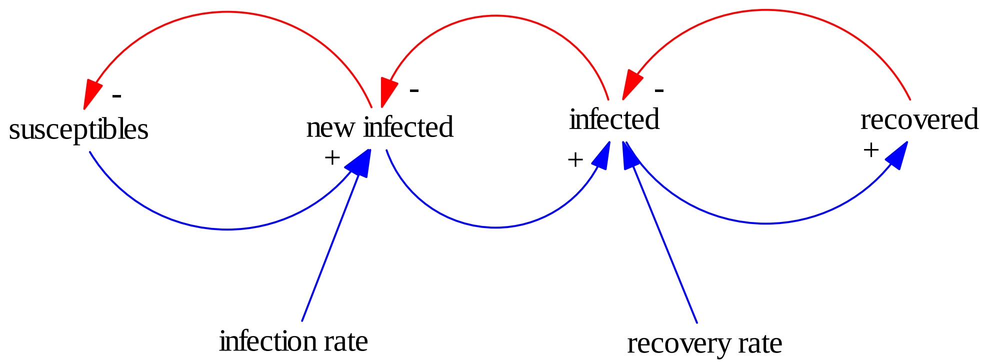

Figure 2. CLD for the simple SI model

The model elements are connected by arrows. The "+" and "–" signs denote the direction of the influence, but not its magnitude. For example, as the infection rate increases, the number of new infected increases, shown by a "+" and, as the new infected increases, the number of infected increases as well. However, as the numbers of recovered increases, the number of infected decreases. This effect is denoted by a "–". In this way complex and informative diagrams can be built to represent and clarify the system being investigated, providing insight into how the various components interact.

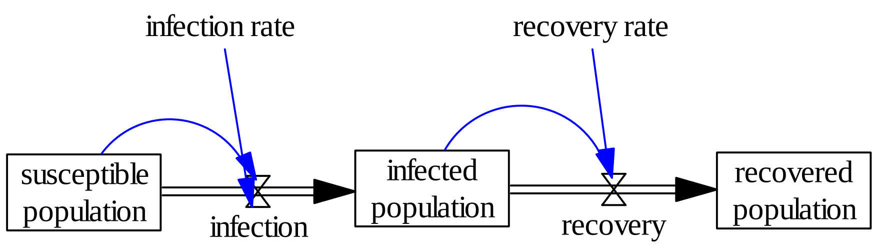

Figure 3. Stock-flow model for the simple SI model

Figure 3 shows the stock-flow diagram constructed from the CLD of Figure 2 in the notation of the software Vensim. Here the "water tanks" (he rectangles) represent stocks or levels (accumulations) of people. The two arrows (pipes) represent infection and recovery, and the valves represent the rate of flow along these pipes.

Some of the original notation from the CLD has been retained, in that "infection rate" and "recovery rate" are now *auxiliary variables* which influence the infected and the recovered people. The form of these influences needs to be quantified and the software allows a variety of ways in which this can be done, ranging from analytical mathematical relationships to graphical functions. The model now needs to be parameterized, by defining the infection rate and the recovery rate and the initial value of the stocks

Then the model is ready to be run or “simulated”. It should be pointed out that although modern SD software does allow limited use of probability distributions, there is generally no variability or stochastic aspect in an SD model.

4. The proposed SD model for Ae. Albopictus – borne diseases

The present work simplifies and improves the above mentioned Berchi’s model, while retaining all its essential components.

The model involves three subsystems: the M*osquito life cycle*, *the Human and Mosquito infection process*, and the *Control strategies.* The infectious process interacts with the vector life cycle. In the infectious process, the number of infectious humans determines the number of infections of mosquitoes which itself determines the number of infections of humans; moreover, for the dengue virus considered here, infected mosquitoes can derive also from eggs layed by infected mosquitos.

The dynamics considers the possibile entrance of an infected human (or mosquito or egg) into a given region. The habits of the vector depend on the environmental characteristics thus the model has to simulate some aspect of the ecological system such as temperature, photoperiod and rainfall.

To represent the dynamics of the Ae. albopictus population, the model analyses the biology of such mosquito. The subsytem depicts the mosquito life-cycle starting from the egg stage, through the larvae and pupae to the growth of new adult female mosquitoes mature for egglaying, after they mate once. In order to be able to lay eggs, females need to have a bloodmeal. Only females have bloodmeals.

Mosquito life cycle

Oviposition is influenced by the probability of finding damp places to lay eggs, which is influenced by the precipitation level. In fact, a female lays her eggs either on flood prone soil or directly on water, then a certain amount of water is required for eggs to hatch and larvae to survive.

Eggs are distinguished into *normal*, and *wintering (diapausing) eggs*, both influenced by the number of eggs layed at each oviposition and by the natural egg mortality rate. Normal eggs hatch into pupae (*summer borning*) after an incubation period (elapsed time between oviposition and hatching), which is dependent on the environmental (temperature and rainfall) and genetic factors. The percentage of wintering eggs depends mainly on photoperiod and their hatching starts on early March, if conditions on temperature and photoperiod are satisfied. The number of new larvae and pupae depends on normal eggs and, immediately after the winter, also on wintering eggs. Larvae mature in water, in a development period that depends on the temperature. The model allows for natural mortality of larvae as well as or mortality due to control measures in private and public soil. The time period necessary for a larva to become mosquito is conditioned by the temperature. Male mosquitoes are distinguished from female ones. After the first coupling, a female mosquito can deposite eggs for her whole life, but before laying eggs, she must take a bloodmeal, every time. Figure 4 depicts the Mosquito life cycle.

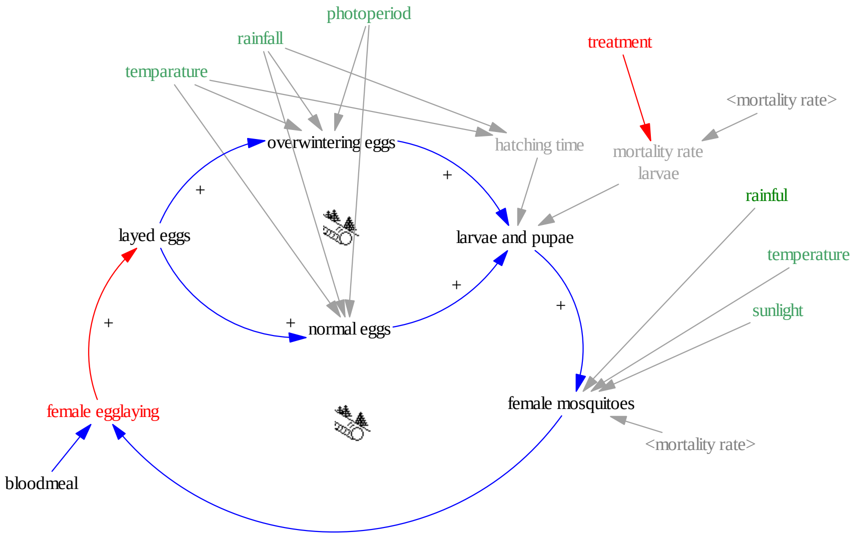

Figure 4. CLD for the Mosquito life cycle

Human and mosquito infection process

The infection process depends on the type of virus considered. In the case of Dengue, a female mosquito gets infected in two ways, either if she bites an infectious human being, or if she develops from an infected pupa. The number of newly infected females depends on the number of non-infected females and the number of infectious human beings. A non-infected human being gets infected if bitten by an infectious mosquito; however, only a percentage of them will indeed get infected. An infected human being develops the virus over an incubation period (the intrinsic incubation period), then becomes infectious. A certain percentage of infectious people recovers and builds up semi-immunity which reduces infectiousness and mortality risk.

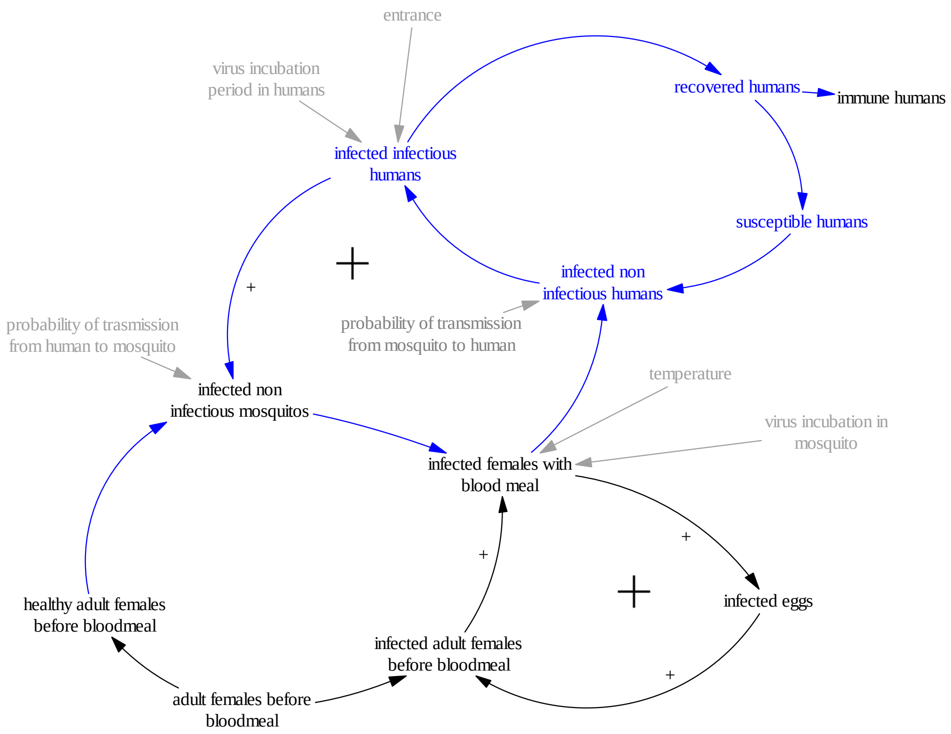

Figure 5. CLD for the Human and Mosquito infection process

As to the *Mosquito to human infection process*, the different stages of susceptible humans, infected non infectious humans, and infected infectious are depicted. The passage from susceptible to infected non infectious is caused by the transmission of the virus through an infected mosquito. This is influenced by the efficacy of transmission from mosquitoes to humans.

As to the *Human to mosquito infection process*, after an infected blood meal, a mosquito can lay either sane or infected eggs. Once ingested by a mosquito, the virus must undergo a development phase within the female mosquito before she gets infected, in a period (the extrinsic incubation period) which depends on the temperature. Eggs become infected if the incubation period is shorter than the deposition period, which is itself influenced by the temperature. In general, except from the first deposition after the infection, an infected female will lay infected eggs which may generate infected larvae and pupae and then mosquitoes.

Control strategies

The control interventions submodel describes the effect of intervention strategies, in particular, larval interventions to control the development of *Ae. albopictus*. More types of interventions can be adopted.

Periodic applications of larvicide or occasional applications in periods of high rainfall are considered here.

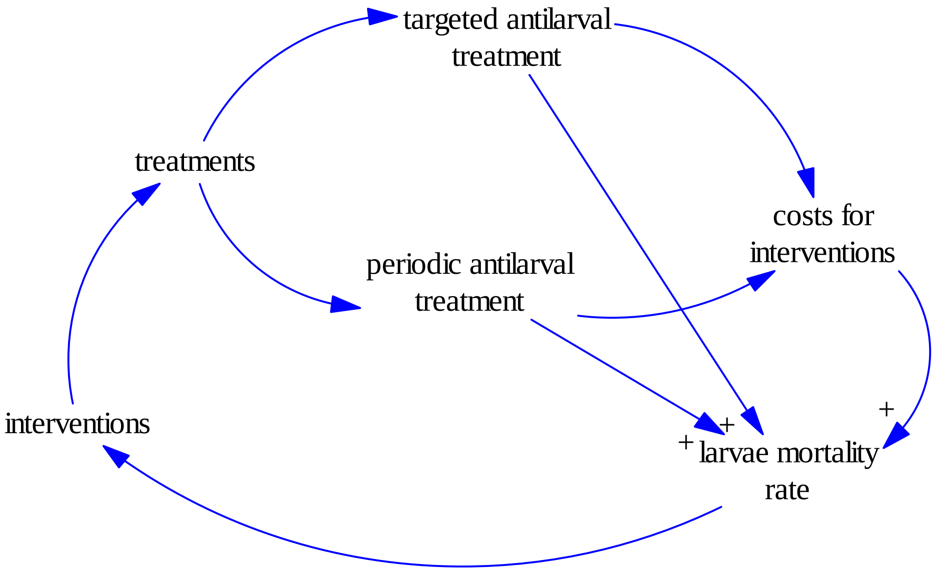

Figure 6. CLD for the Control strategies submodel

The CLDs have been converted into stock-flow diagrams and the SD model has been run for a simulation of 365 days, with time intervals of one day, under different scenarios. Some results are reported in next section.

5. **Results and conclusions**

All scenarios consider a human population of 10000 people, all of them susceptible and a number of 50 winter eggs (all healthy) per person, and the arrival of one infected person on the day 190. The initial number of adult mosquitoes, of larvae and pupae and of normal eggs is 0, because the starting time is set on the first day of the year, which, using the climatic data of Rome in 2002, corresponds to a cold winter day in which only diapausing eggs can survive.

In the first scenario no control strategies are adopted. Figure 7 shows the resulting number of infected adult female mosquitoes and of infected infectious humans.

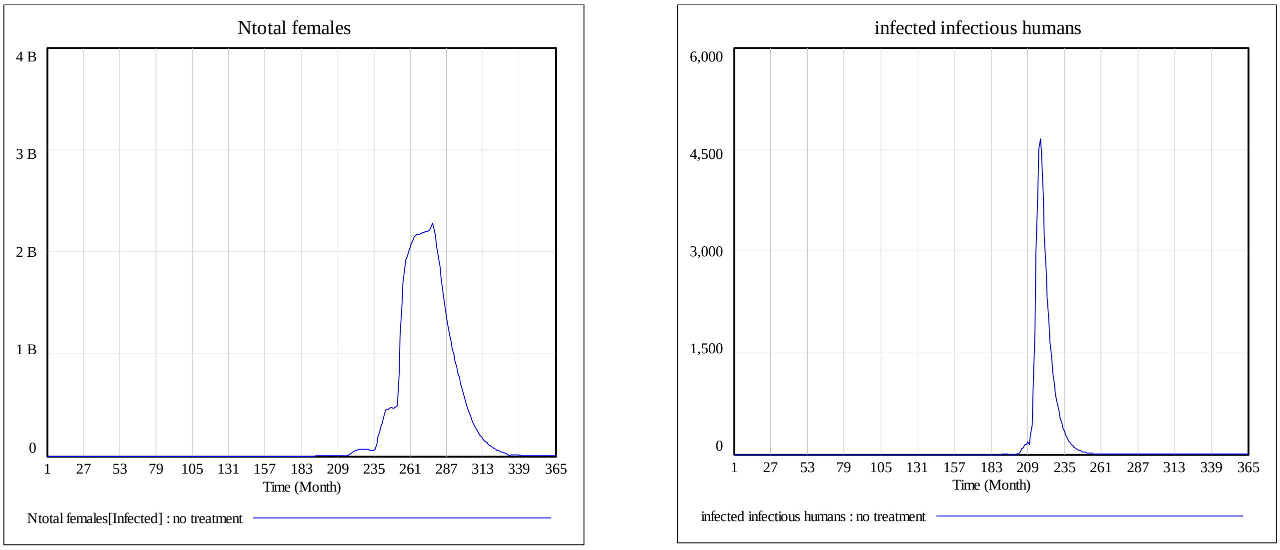

Figure 7. First scenario

In the second scenario, weekly applications of larvicide are considered. The results are shown in Figure 8.

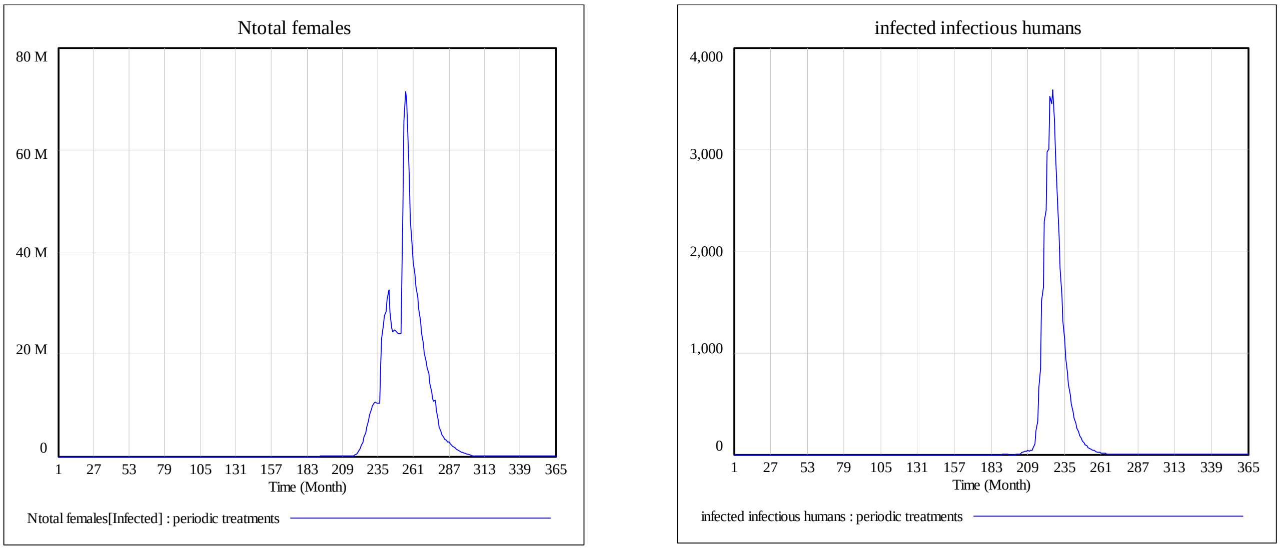

Figure 8. Second scenario

In the third scenario, the application of larvicide depends on rainy days, the related results are given in Figure 9. The third scenario shows a smaller reduction of the number of mosquitoes than the second scenario, in fact rain was rare in the summer period, so few interventions took place in the simulation.

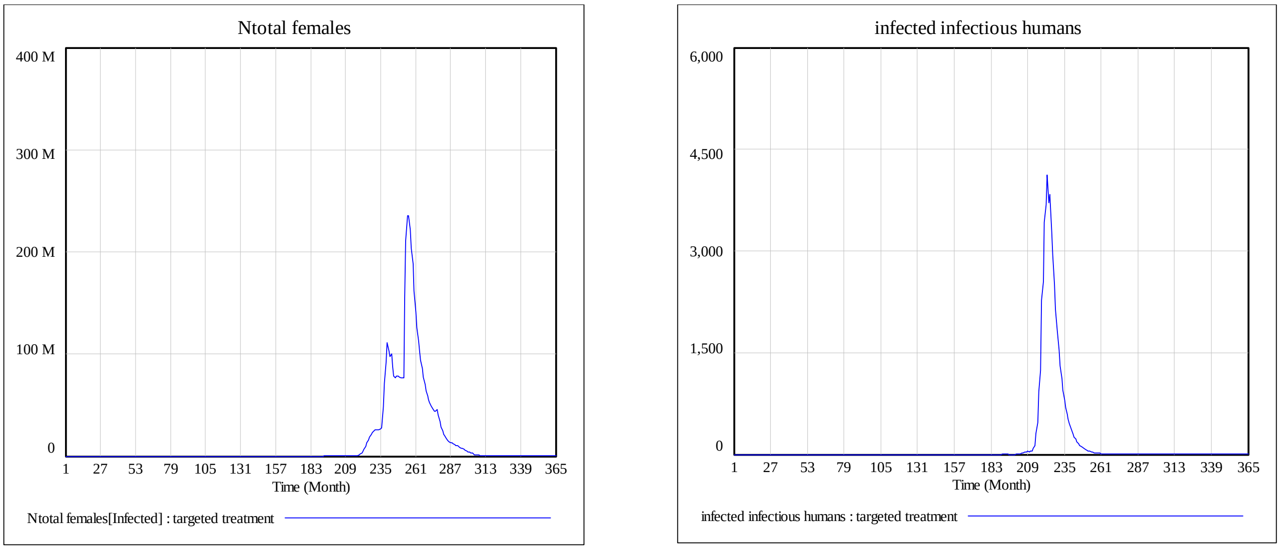

Figure 9. Third scenario

The results obtained look reasonable and promising, yet more work is required for the validation of the model and of its input data.

Nevertheless, we think the model can contribute to stimulate field research to get more reliable and complete data and to educate authorities responsible for health care to the use of models in the choice of intervention campaigns.

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