# MODULE 4.4

## Modeling a Persistent Plague: Malaria

### Download

The text's website has a *malaria* file, which contains the model of this module, available for download for various system dynamics tools.

### Introduction

How important to civilization can a mosquito-borne protozoan be? Unfortunately, we cannot ask the ancient Romans, but we do have some recent evidence that implicates this tiny parasite in the fall of one of the mightiest empires of all time. Excavations in a cemetery near Lugano, Italy, have uncovered at least one infant from AD 450 that yielded the DNA of *Plasmodium falciparum*—the deadliest of all the human malarias. Nearby, 50 other infants, who also showed fingerprints of this parasite, were buried in a relatively short period of time.

The death of many infants would be expected during a malaria epidemic, partially because *falciparum* induces high rates of miscarriages and infant death. The mosquitoes that transmit malaria flourish in marshy areas found in the Tiber River valley; and if malaria swept through Rome, the disease may indeed have contributed to its downfall. Even if Roman troops were not directly affected by disease, disruptions to the production and supply of food and war materials could have drastically impaired the military's ability to protect Rome.

Interestingly, around the time the infant lived, Attila's Huns were pillaging in the north of Italy en route to Rome. Although legend credits Pope Leo the Great with persuading Attila to withdraw, it is more likely that the presence of malaria in the city was even more convincing (Carroll 2001).

Malaria is a very old disease (probably prehistoric), originating in Africa, spreading as humankind migrated to other lands. The disease gets its name from an Italian word for "bad air" (RPH).

After more than 1500 yr, we still have mosquitoes and malaria. In fact, the WHO estimates that malaria sickens 216 million people, killing more than 655,000 of them, each year—that is almost 1800 per day. Most of these fatalities are among African children (WHO, World Malaria Report). In fact, 1 out of 20 African children die of malaria before the age of 5. (NetMark).

*So long as Woman has walked the earth,*
*malaria may have stalked her.*
—Duffy et al.

Pregnant women and their developing young seem to be at special risk from infection, which seems to have been true from the earliest human records (Duffy et al. 2001). *P. falciparum* malaria in pregnant women is associated with high levels of maternal and fetal morbidity and mortality (Desai et al. 2007). The anemia associated with malaria infections results in approximately 10,000 maternal deaths and thousands of low-birth-weight infants. Up to 200,000 of such infants in Africa may die annually (ter Kuile and Rogerson 2008).

## Background Information

A **vector** is an animal that transmits a pathogen, or something that causes a disease, to another animal. Mosquitoes are the only vectors for malaria, but only 60 out of the 380 species of ***Anopheles*** mosquitoes can host malaria-causing ***Plasmodium*** (Ryan 2008).

Three-fifths of the female *Anopheles* mosquitoes, like their sisters of other lines, are dependent on blood meals to feed their maturing eggs. While sipping blood, a *Plasmodium*-infected female mosquito injects thread-shaped, infectious agents called **sporozoites** into her human **host**. Sporozoites circulate for a time and then enter the parenchymal cells of the liver to hide out from the immune system. Here, they live for 1 to 2 weeks, multiplying asexually to produce thousands of offspring, which mature into other invasive cells, **merozoites**. Eventually, all this activity causes the parenchymal cell to break open and release merozoites into the blood. In other malaria-causing parasites, *Plasmodium vivax* and *ovale*, some of the sporozoites become dormant **hypnozoites**. Later, these mature to reinvade other liver cells, where they continue to produce more merozoites, causing recurring bouts with malaria. Interestingly, the most deadly species, *Plasmodium falciparum*, does not produce these hypnozoites (Despommier et al. 2005; NIAID; Wiser).

Merozoites enter red blood cells to feed on the blood. They reproduce asexually to form more merozoites, which invade other red blood cells. This cycle continues unless stopped by the body's defenses or medicine (NIAID).

While in the red blood cells, some merozoites mature into **male** and **female gametocytes**. Upon release, these do not enter the red blood cells, but circulate, awaiting transfer to the mosquito host. The female mosquito takes her blood meal from an infected host and simultaneously sucks up some of the gametocytes.

In the mosquito's stomach, the male gametocyte (sperm) and the female gametocyte (egg) fuse. The resulting **oocyst** divides to produce thousands of sporozoites. The sporozoites migrate to the salivary glands of the mosquito awaiting their

journey into a vertebrate host. Figure 4.4.1 diagrams the life cycle of *Plasmodium falciparum*.

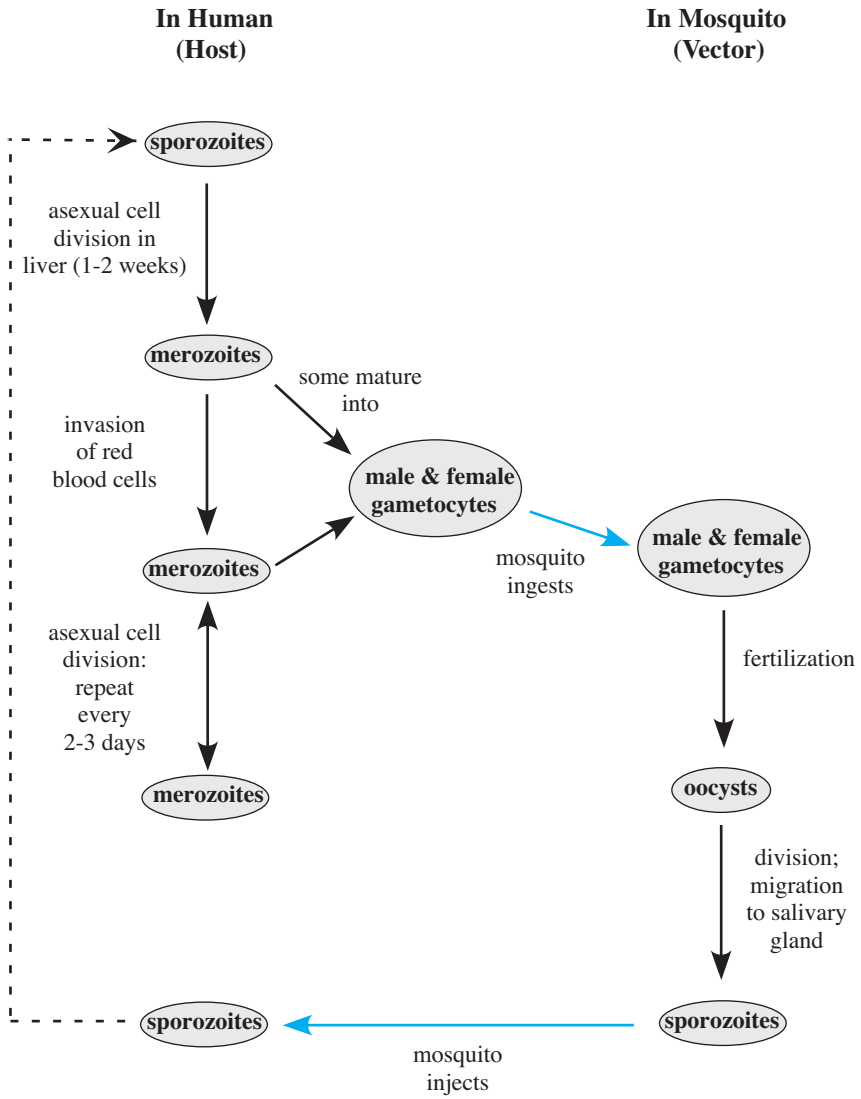


**Figure 4.4.1** Life cycle of *Plasmodium falciparum*

## Analysis of Problem

In the discussion that follows in this module, we consider the modeling process involving malaria (see Module 1.2, "The Modeling Process"). We begin by analyzing the situation to identify the problem and understand its primary questions.

In this problem, we wish to investigate the progress of malaria. In particular, we

consider the relationships between human and *Anopheles* mosquito populations, both of which are necessary for the life cycle of *Plasmodium*. Thus, with a system dynamics model, we wish to study the changing numbers of various categories of humans and mosquitoes as time progresses.

## Formulating a Model: Gather Data

Data on malaria are often difficult to find and may be undependable. Countries with high rates of malaria are also often desperately poor, and the effectiveness of data collection can vary dramatically from year to year. Moreover, climate can play a significant role, with the number of cases of malaria correlating to periods of high rainfall. Also, the values associated with mosquitoes, such as numbers in each category, birth and death rates, bite probabilities, and constants of proportionality, are usually not available.

In a computational science study, such as of malaria, an interdisciplinary team approaches a problem from many directions. "Wet-lab" team members conduct initial experiments and, with their "dry-lab" counterparts, pose questions for the latter to consider in modeling. In formulating a model, the group may uncover the need for additional parameters, such as birth and death rates of anopheline mosquitoes. If not available from other sources, the team may decide to conduct additional experiments to collect data for empirical computations of such values.

Websites for the WHO, the U.S. Central Intelligence Agency (CIA), and other organizations do provide some enlightening and startling data concerning people. For example, the entire population of Malawi lives in malarious areas. In 2012, the population of Malawi was more than 16 million, with a birth rate of 40.42 births/1000 population, a death rate of 12.84 deaths/1000 population, and a life expectancy of only 52.31 years (CIA 2012). According to the Kaiser Family Foundation, in 2010, there were 6,851,108 reported cases of malaria, thousands of which will result in death (KFF 2010). Pregnant women and children under the age of 5 are at particular risk. Infected mothers are more likely to miscarry or to experience intrauterine demise, premature delivery, low-birth-weight neonates, and neonatal death. They are also more likely to develop anemia and/or die during delivery (Schantz-Dunn and Nour 2009).

## Formulating a Model: Make Simplifying Assumptions

For our first model of malaria, we make several simplifying assumptions. We model the serious form of malaria that *Plasmodium falciparum* causes, in which relapses do not occur. In the model, we primarily consider the number of individuals in several categories of humans and mosquitoes and ignore *Plasmodium*.

### Quick Review Question 1

Considering the simplifying assumption in the preceding paragraph, give the major submodels of the malaria model.

Because the life expectancy of a human is much greater than that of a mosquito, we assume that the population of humans is closed with no births, no immigration, and no deaths except from malaria. We presume that as soon as a vector bites a human, the individual becomes a host. No immunity exists for uninfected individuals, and no incubation period occurs. Some human hosts eventually become immune and others die, while still others recover and become susceptible again. We ignore the chance of relapse. Deceased individuals pass from consideration in the model.

Because of their relatively short life expectancy, we do consider mosquito births and deaths. We have the assumption that the death rates for infected and uninfected mosquitoes are identical. Similarly, we assume that all mosquitoes reproduce at the same rate. At birth, a mosquito is uninfected. As a simplification for this first version of the model, we suppose that an infected mosquito immediately becomes a host that can infect humans.

### Quick Review Question 2

Based on these assumptions, list major categories of organisms for a model. In a system dynamics diagram, we represent these categories, which can accumulate individuals, as stocks (box variables).

Also, for simplification in this version of the model, except where relevant interactions between mosquitoes and humans occur, let us assume that the number of organisms in each category (uninfected humans, human hosts, immune humans, uninfected mosquitoes, mosquito vectors) expands or contracts in an unconstrained manner. In such situations, constraints, such as competition for food or predators, do not exist.

## Formulating a Model: Determine Variables and Units

Based on these simplifying assumptions, we monitor three categories of humans, employing the following variables with the basic unit being one person:

***uninfected_humans***, who are susceptible to the disease
***human_hosts***, who have malaria and can infect mosquitoes that bite them
***immune***, who cannot get the disease again

For the mosquito submodel, as with the human submodel, we do not count the number of dead individuals. Consequently, assuming no incubation period for *Plasmodium*, we consider the following two categories of mosquitoes:

***uninfected_mosquitoes***, which do not carry *Plasmodium*
***vectors***, which carry *Plasmodium*

We employ a day as the basic unit of time, ***t.***

### Quick Review Question 3

This question considers the relationships among these categories of humans and mosquitoes. After completing the question, we recommend that you develop a rela-

tionship diagram with stocks (box variables) representing the categories and with appropriate flows. Making the foregoing simplifying assumptions, give the requested flow information by selecting from the categories *uninfected_humans; human_hosts; immune; uninfected_mosquitoes; vectors;* and undesignated "clouds," such as for deceased humans, dead mosquitoes, and unborn mosquitoes:

**a.** Destination(s) of flow(s) from *uninfected_humans*
**b.** Source(s) of flow(s) to *uninfected_humans*
**c.** Destination(s) of flow(s) from *human_hosts*
**d.** Source(s) of flow(s) to *immune*
**e.** Source(s) of flow(s) to undesignated "cloud(s)" for deceased humans
**f.** Destination(s) of flow(s) from *uninfected_mosquitoes*
**g.** Source(s) of flow(s) to *uninfected_mosquitoes*
**h.** Source(s) of flow(s) to *vectors*
**i.** Destination(s) of flow(s) from *vectors*
**j.** Source(s) of flow(s) to undesignated "cloud(s)" for dead mosquitoes

## Formulating a Model: Establish Relationships

Based on biology of the organisms and the simplifying assumptions, Figure 4.4.2 presents a relationship diagram with the two major submodels for humans and mosquitoes, stocks (box variables) representing the three human and two mosquito categories, and appropriate flows between stocks. Arrows (connectors) represent the

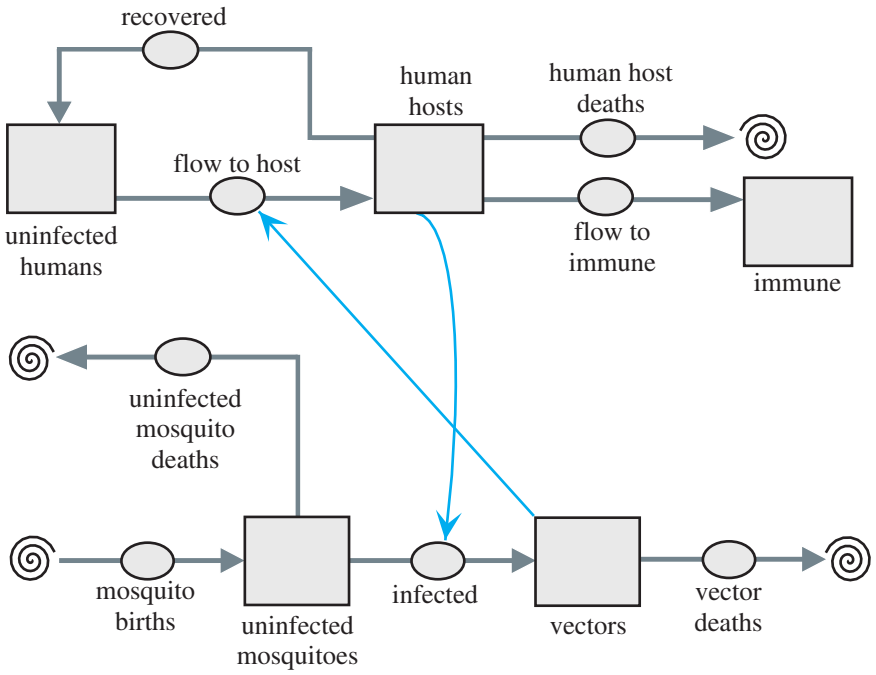


**Figure 4.4.2** Relationship diagram

impact of one population on the other. For example, the infected mosquito category (*vectors*) is a necessary component in an uninfected human becoming infected, a member of *human_hosts*. Similarly, for an uninfected mosquito to become to a vector, the former must bite a person in *human_hosts*.

### Quick Review Question 4

One of the simplifying assumptions is that, except where interactions between mosquitoes and humans occur, the number of organisms in a category (stock or box variable in Figure 4.4.2) exhibits unconstrained expansion or contraction. Give requested differential equations that utilize this assumption. Incorporate additional proportionality constants as needed.

**a.** *d*(*immune*)/*dt*
**b.** *d*(*deceased_humans*)/*dt*
**c.** rate of change from *human_hosts* to *uninfected_humans*
**d.** *d*(deceased_vectors)/*dt*

## Formulating a Model: Determine Equations and Functions

Because we assume unconstrained growth or decay except where interactions between mosquitoes and humans occur, the following flow equations with constants of proportionalities in boldface correspond to proportionalities:

*flow_to_immune* = ***immunity_rate*** * *human_hosts*
*human_host_deaths* = ***malaria_induced_death_rate*** * *human_hosts*
*recovered* = ***recovery_rate*** * *human_hosts*
*mosquito_births* = ***mosquito_birth_rate*** * *mosquitoes*, where *mosquitoes* = *uninfected_mosquitoes* + *vectors*
*uninfected_mosquito_deaths* = ***mosquito_death_rate*** * *uninfected_mosquitoes*
*vector_deaths* = ***mosquito_death_rate*** * *vectors*

Because only uninfected mosquitoes are born and both categories of mosquitoes reproduce, *mosquito_births* is proportional to the total number of mosquitoes. Moreover, we assume that the death rate is the same for uninfected mosquitoes and vectors, so the last two equations have the same constant of proportionality, *mosquito_death_rate*.

### Quick Review Question 5

Suppose for a simulation that the change in time ($\Delta t$) from one time step to another is 0.1 da.

**a.** Give the unit of measure for *d*(*immune*)/*dt*.
**b.** If at day 6 *immunity_rate* is 0.2, *human_hosts* is 500, and *immune* is 400, using the technique discussed in the section on "Difference Equation" from Module 2.2, "Unconstrained Growth and Decay," estimate the number of im-

mune people at day 6.1. (This technique is Euler's method, which Module 6.2 considers in greater detail.)

For uninfected humans, we have individuals entering from and exiting to the population of human hosts. The differential equation contains a positive term for a growth component with constant *recovery_rate* while subtracting a decay term, as follows:

$$d(uninfected\_humans)/dt = (recovery\_rate)(human\_hosts) - (transmission\_constant)(uninfected\_humans) \quad (1)$$

We can break *transmission_constant* into two factors, the probability that a human is bitten by a mosquito (***prob_bit***) and the probability that a mosquito is a vector (***prob_vector***). The product of these two probabilities forms the transmission constant. For example, if the probability that someone is bitten by a mosquito is 60% = 0.60 and the probability that a mosquito is a vector is 20% = 0.20, then the probability that a human is bitten by a vector is (0.60)(0.20) = 0.12 = 12%. With no presumed immunity, the transmission constant is equal to this probability. Thus, the following differential equation reflects a refinement of Equation 1:

$$d(uninfected\_humans)/dt = (recovery\_rate)(human\_hosts) - (prob\_bit)(prob\_vector)(uninfected\_humans) \quad (2)$$

The probability of a vector is the quotient of the number of vectors (*vectors*) and the total number of mosquitoes (*mosquitoes*). Thus, we have the following equation:

$$prob\_vector = vectors/mosquitoes$$

Substituting into Equation 2, the rate of change of *uninfected_humans* is as follows:

$$d(uninfected\_humans)/dt = (recovery\_rate)(human\_hosts) - (prob\_bit)(vectors)(uninfected\_humans)/mosquitoes$$

Similar to the situation for humans, the rate of change from uninfected mosquito to vector is the product of a rate and *uninfected_mosquitoes*. Assuming that an uninfected mosquito that bites a human host always becomes infected, we again break the rate into two factors, the probability that the mosquito bites a human (***prob_bite_human***) and the probability that a human is a host (***prob_host***). Thus, the differential equation for the rate of change from uninfected to infected mosquito (*vector_formation*) is as follows:

$$d(vector\_formation)/dt = flow\_to\_host = (prob\_bite\_human)(prob\_host)(uninfected\_mosquitoes) \quad (3)$$

The probability that a mosquito is a vector (*prob_vector*) and the probability that a human is a host (*prob_host*) are the connections between the models for humans and mosquitoes. For ***humans***, being the total number of humans (*uninfected_humans* + *human_hosts* + *immune*), we have the following identities:

$$prob\_host = human\_hosts/humans$$
$$= human\_hosts/(uninfected\_humans + human\_hosts + immune)$$

## Solving the Model

We can use a system dynamic tool to help model the spread of malaria, perform a simulation, and generate graphs and tables of the results. Figure 4.4.3 pictures a human submodel of the malaria model. A converter/variable, *humans*, stores the sum of the quantities in the three stocks (box variables) for humans. Other converters/variables store constants of proportionality and probabilities. For example, *immunity_rate* might store the constant 0.01 to indicate that the rate at which human hosts become immune from malaria is 1% a day. An initial value 1 for *human_hosts* would indicate that the human population has one human host at the start of the simulation.

### Quick Review Question 6

Consider Figure 4.4.3.

**a.** Give the number of terms in the differential equation for $d(human\_hosts)/dt$.
**b.** Give the number of these terms that contribute to an increase in *human_hosts*.

The mosquito submodel in Figure 4.4.4 also has four flows, with associated converters/variables for constants of proportionality and probabilities. Similar to the human submodel, a converter/variable, *mosquitoes*, contains the sum of the populations for *uninfected_mosquitoes* and *vectors*.

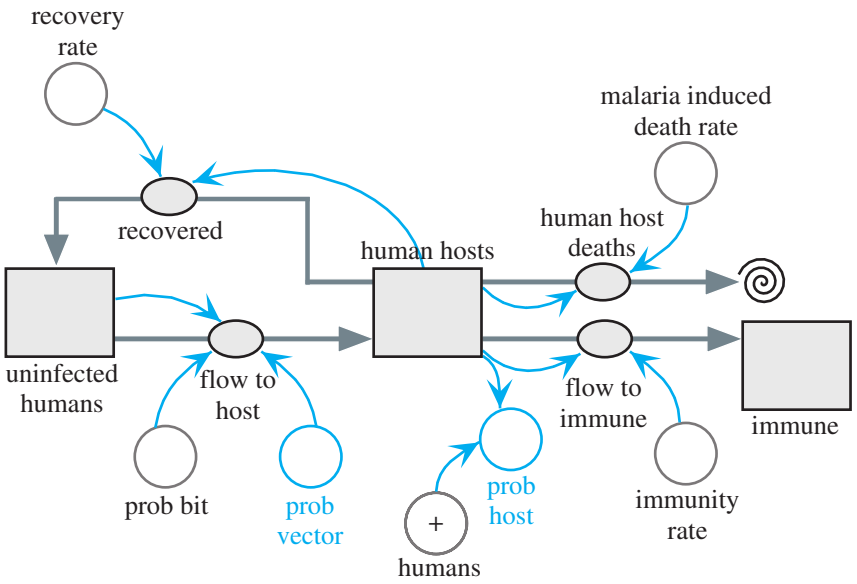


**Figure 4.4.3** Human submodel for a closed system

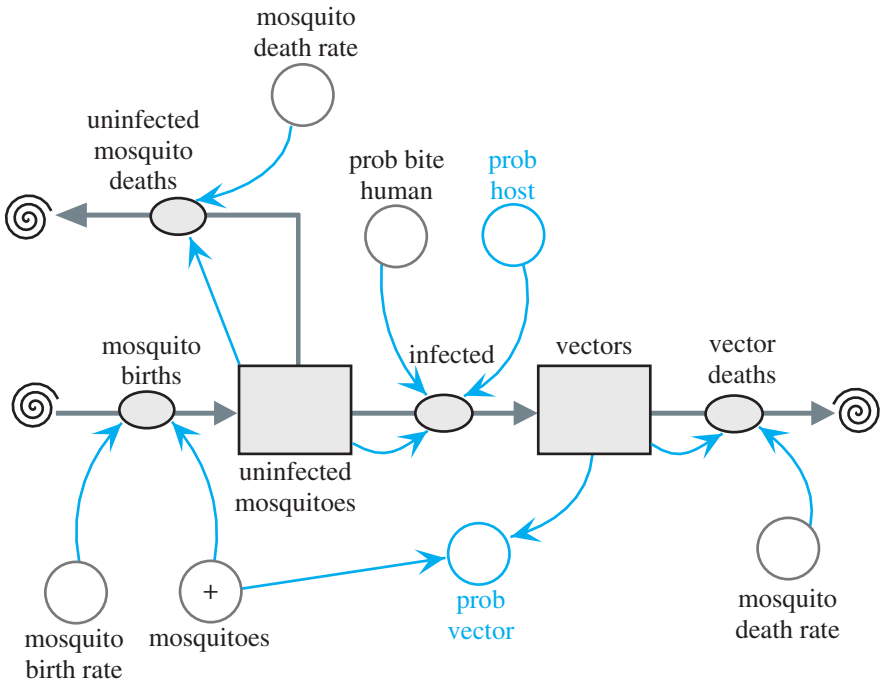


**Figure 4.4.4** Mosquito submodel

Converters/variables for the probability of a vector (*prob_vector*) and the probability of a host (*prob_host*) appear in both submodels and in color in the figures. We calculate *prob_vector* in the mosquito submodel and use it in the human submodel. Symmetrically, the calculation for *prob_host* is in the human submodel, while the mosquito submodel employs the result.

## Quick Review Question 7

Give the difference equation to estimate *vectors*(*t*) using the technique discussed in the section "Difference Equation" from Module 2.2, "Unconstrained Growth and Decay."

We specify a simulation length of 200 days and $\Delta t = 0.0625$ days with Euler's method for the integration technique. Equation Set 4.4.1 shows parameters for one run of the simulation. We begin with equal numbers of uninfected mosquitoes and humans (300), no vectors or immune humans, and one human host. (However, we could change the units and consider, for example, the number of humans in the thousands and the number of mosquitoes in the millions.) From such a small incidence, we hope to observe the dramatic spread of the disease to become an epidemic. In this run of the simulation, for humans we make the rates of immunity, recovery to being susceptible once more, and malaria death be 1%, 30%, and 0.5% per day, respectively. We give the probability that a human is bitten by a mosquito or that a mos-

quito bites a human as 30%/day. For a constant number of mosquitoes, we make their birth and death rates equal, in this case 1%/day.

### Equation Set 4.4.1

Parameters for one run of the simulation:

*uninfected_humans*(0) = 300
*human_hosts*(0) = 1
*immune*(0) = 0
*prob_bit* = 0.3
*recovery_rate* = 0.3
*immunity_rate* = 0.01
*malaria_induced_death_rate* = 0.005
*mosquito_birth_rate* = 0.01
*mosquito_death_rate* = 0.01
*vectors*(0) = 0
*uninfected_mosquitoes*(0) = 300
*prob_bite_human* = 0.3

## Verifying and Interpreting the Model's Solution

Figure 4.4.5 presents the graphs of the five stocks, and a table of values with a reporting interval of 1 day appears in Table 4.4.1. Over 80 days, we observe a dramatic drop from 300 to a minimum of about 24 uninfected mosquitoes and a corresponding rise from 0 to a maximum of about 276 vectors. Afterward, the number of uninfected mosquitoes begins to increase, while the number of vectors drops. With equal birth and death rates, the population of mosquitoes holds constant at 300, which helps to verify the solution.

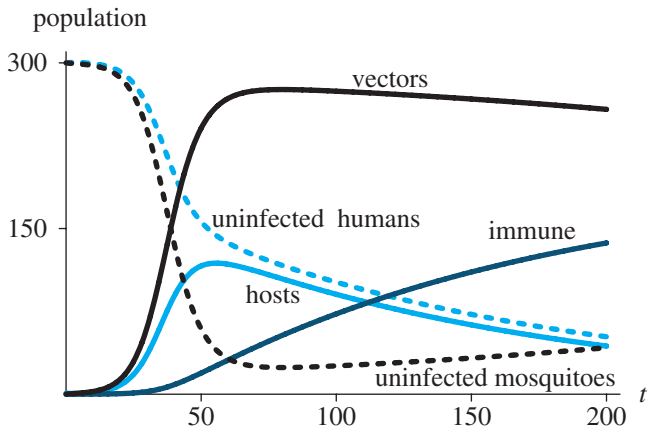


**Figure 4.4.5** Graphs resulting from simulation with parameters of Equation Set 4.4.1 and time, *t* (da)

**Table 4.4.1**
Table of Values Corresponding to Graphs of Figure 4.4.5

| *Time* | *Uninfected Humans* | *Human Hosts* | *Immune* | *Uninfected Mosquitoes* | *Vectors* |
|---|---|---|---|---|---|
| 0 | 300.00 | 1.00 | 0.00 | 300.00 | 0.00 |
| 10 | 299.34 | 1.53 | 0.09 | 297.52 | 2.48 |
| 20 | 292.08 | 8.20 | 0.48 | 286.58 | 13.42 |
| 30 | 261.42 | 35.96 | 2.41 | 239.30 | 60.70 |
| 40 | 199.40 | 88.69 | 8.61 | 136.33 | 163.67 |
| 50 | 156.09 | 116.17 | 19.16 | 59.11 | 240.89 |
| 60 | 136.89 | 117.66 | 30.97 | 32.17 | 267.83 |
| 70 | 125.57 | 111.74 | 42.46 | 25.29 | 274.71 |
| 80 | 116.63 | 104.46 | 53.28 | 24.15 | 275.85 |
| 90 | 108.70 | 97.25 | 63.36 | 24.65 | 275.35 |
| 100 | 101.44 | 90.44 | 72.75 | 25.65 | 274.35 |
| 110 | 94.72 | 84.08 | 81.47 | 26.86 | 273.14 |
| 120 | 88.48 | 78.16 | 89.58 | 28.19 | 271.81 |
| 130 | 82.67 | 72.65 | 97.12 | 29.62 | 270.38 |
| 140 | 77.28 | 67.53 | 104.13 | 31.13 | 268.87 |
| 150 | 72.27 | 62.77 | 110.64 | 32.73 | 267.27 |
| 160 | 67.61 | 58.35 | 116.69 | 34.41 | 265.59 |
| 170 | 63.27 | 54.25 | 122.32 | 36.19 | 263.81 |
| 180 | 59.24 | 50.43 | 127.56 | 38.06 | 261.94 |
| 190 | 55.49 | 46.88 | 132.42 | 40.03 | 259.97 |
| 200 | 52.00 | 43.58 | 136.94 | 42.10 | 257.90 |

Trailing the rapid increase in the number of vectors is a fast decrease in the number of uninfected humans and quick increase in the number of human hosts over about a 25-day period. The number of hosts reaches a maximum of about 119 about day 55. Then, the number of hosts gradually falls, while the number of uninfected humans continues declining, but not as rapidly. Eventually, the two graphs appear almost parallel, while the graph of the number of immune humans increases in a concave-down fashion.

Extending the length of the simulation to 1500 days, we obtain the graphs of Figure 4.4.6. The numbers of uninfected humans and human hosts approach zero, and most of the surviving humans are immune. The total number of humans is reduced by about one-third to around 200. With the number of vectors tending to zero, the vast majority of the mosquitoes are uninfected. Because most humans are immune and almost no mosquito carries *Plasmodium*, malaria is virtually eradicated.

The results seem reasonable under the assumptions and simplifications. However, considerations suggest several stages of refinement.

We have extended the length of the simulation to more than 4 years and presumed no births or deaths from causes other than malaria for humans. Also, we have not considered the incubation period for *Plasmodium*.

For another model we might consider a different form of malaria, in which an individual could have a relapse of the disease. Moreover, expectant mothers tend to have lower-birth-weight children and more miscarriages, which affects the birth and death rates for humans. Also, data show that children have a higher death rate from

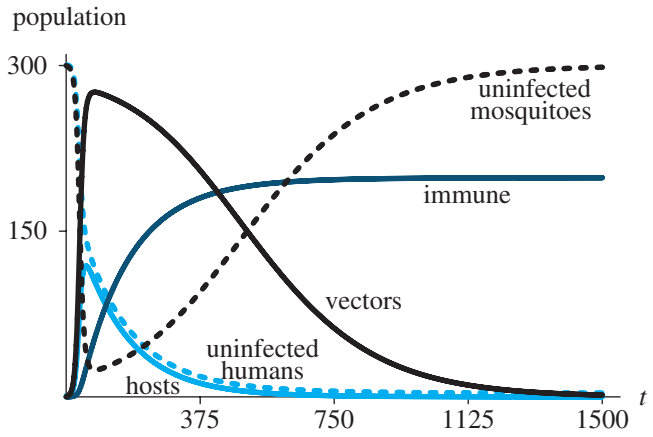


**Figure 4.4.6** Simulation run for 1500 da

malaria than older humans. Consequently, other model refinements could involve expanding the number of human categories with varying death rates. Various projects consider such refinements.

## Exercises

1. Discuss possible factors that could contribute to the situation in which 90% of malaria cases occur in Africa, south of the Sahara.
2. Give a differential equation for the rate of change of *human_hosts*.
3. Give a differential equation for the rate of change of *uninfected_mosquitoes*.
4. Give a differential equation for the rate of change of *vectors*.

## Projects

*For additional projects, see Module 7.11, "Fueling Our Cells—Carbohydrate Metabolism"; Module 7.14, "Control Issues: The Operon Model"; and Module 7.15, "Troubling Signals: Colon Cancer."*

1. Run the simulation for the following situations. Describe and explain the long-term results.
   - **a.** Various initial values of stocks (box variables)
   - **b.** Slightly higher birth rate than death rate for mosquitoes
   - **c.** No human host and one vector
   - **d.** Zero death rate for humans
   - **e.** Probability that a human is bitten reduced by a factor of 10 to 3%
   - **f.** Probability that a mosquito bites a human reduced by a factor of 10 to 3%
2. Refine the malaria model of this module to accommodate human births and deaths.

3. Refine the malaria model of Project 2 of this module to include a stock (box variable) of tainted mosquitoes, who are infected but not yet vectors. In these mosquitoes, the *Plasmodium* protozoans are in incubation.
4. Develop an alternative implementation of the model for Project 3 that employs a conveyor for the tainted mosquitoes. Because we are considering births and deaths for mosquitoes, the inflow multiplier from the conveyor to the stock of vectors is not 1. However, the value is not 1 – *mosquito_death_rate*, which is 0.99 for a death rate of 0.01, because the inflow multiplier applies only to the number exiting the conveyor at that time step, not over the period of incubation. Consequently, you must employ the actual, accumulated survival rate over the period of incubation as a multiplier. You can use mathematics or your system dynamics tool to compute the actual survival rate for the number exiting the conveyor.

   Because we only remove mosquitoes from the conveyor at the end of the incubation period, using the number in the conveyor to calculate the total number of mosquitoes, *mosquitoes*, results in an overestimate for *mosquitoes*. Thus, for this project, assume a constant number of mosquitoes, so *mosquitoes* is the sum of the initial values of the various mosquito stocks.
5. Develop an alternative implementation of the model for Project 3 that employs a separate stock (block variable) for each day of incubation. A portion (*mosquito_death_rate*) of the mosquitoes is siphoned off each day, and the remainder is transferred to the next day's stock or, after the final day of incubation, to the stock *vector*.
6. Model malaria caused by *Plasmodium vivax* or *ovale* in which a human host can go into remission and have relapses.
7. Refine one of the previous models to reflect a seasonal increase in the number of mosquitoes, such as in a rainy season (see Project 1 in Module 4.2, "Predator-Prey Model").
8. Using one of the previous models, consider the effect on the epidemic of distribution of a prophylactic drug, such as Malazone, which travelers take to prevent malaria. Suppose everyone in the population takes the drug. Investigate varying degrees of effectiveness. Such drugs are expensive, especially relative to the economy of populations in which malaria thrives. Discuss the practicality of such treatments.
9. Using one of the previous models, consider the effect on the epidemic of using insecticides to control the mosquito population. Investigate varying degrees of insecticide effectiveness. Discuss the practicality of such an approach relative to the ecosystem.
10. Starting with the model from Project 8, consider the effect on the epidemic of a combined approach consisting of distribution of a prophylactic drug, mosquito netting, and use of insect repellant and insecticides.
11. Refine a malaria model of Projects 2–5 to consider that a person does not obtain permanent, complete immunity from malaria, but only temporary, partial immunity.
12. Refine a malaria model by expanding the number of human categories with varying contraction and death rates. In particular, data shows that *falciparum* is lethal to children under 5 years old. Each day, approximately 3000

children under the age of 5 die from malaria. In some of the worst areas, it is estimated that more than 40% of the toddlers die from the disease. More than 30% of the children in Africa get malaria by time they are 3 months old. However, approximately, one-eighth of the children in some countries of sub-Saharan Africa are born with sickle cell anemia, which makes it more difficult for them to contract malaria.

**13.** Because mothers are more likely to suffer malarial relapses during pregnancy, malaria is an important cause of low weight births and stillbirths. More than half of the miscarriages in endemic areas are caused by malaria. Adjust the model for Project 12 to reflect this information.

**14.** Adjust one of the earlier models to have constrained growth with a carrying capacity for humans and a carrying capacity for mosquitoes. Examine and discuss the effects of these changes. A logistic equation can model such constrained growth (see Module 2.3, "Constrained Growth").

**15.** Obtain information and data about another infections disease, where the disease spreads through a vector. Model at least one aspect of the spread of the disease, starting with one infected individual in a particular area. Run the model for various scenarios, produce graphs and tables, and discuss the results. The following are some suggested diseases: West Nile virus, Lyme disease, Chagas' disease, bubonic plague, typhus.

**16.** Repeat Project 16 for a zoonotic disease, which can spread from one animal species to another. The following are some suggested diseases: Nipah virus, hantavirus, avian flu, rabies, tularemia.

## Answers to Quick Review Questions

**1.** humans and mosquitoes

**2.** uninfected humans, human hosts, immune humans, uninfected mosquitoes, mosquito vectors

**3.** **a.** *human_hosts*
**b.** *human_hosts*
**c.** *uninfected_humans*, *immune*, and undesignated "cloud" for deceased humans
**d.** *human_hosts*
**e.** *human_hosts*
**f.** *vectors* and undesignated "cloud" for dead mosquitoes
**g.** undesignated "cloud" for unborn mosquitoes
**h.** *uninfected_mosquitoes*
**i.** undesignated "cloud" for dead mosquitoes
**j.** *uninfected_mosquitoes* and *vectors*

**4.** **a.** *d*(*immune*)/*dt* = *immunity_rate* * *human_hosts*
**b.** *d*(deceased_humans)/*dt* = *malaria_induced_death_rate* * *human_hosts*
**c.** rate of change from *human_hosts* to *uninfected_humans* = *recovery_rate* * *human_hosts*
**d.** *d*(deceased_vectors)/*dt* = *mosquito_death_rate* * *vectors*

**5.** **a.** people per day

**b.** 410 because *immune*(6.1) = *immune*(6) + *immunity_rate* * *human_hosts*(6) * $\Delta t$ = 400 + (0.2)(500)(0.1) = 400 + 10 = 410

**6. a.** 4, one for each flow entering or leaving the stock *human_hosts*

**b.** 1, because only one flow enters the stock *human_hosts*.

**7.** *vectors*($t$) = *vectors*($t - \Delta t$) + (*infected* – *vector_deaths*) * $\Delta t$

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