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A Mathematical model of cutaneous leishmaniasis

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**A MATHEMATICAL MODEL
OF
CUTANEOUS LEISHMANIASIS**

THESIS REPORT PRESENTED TO THE
SCHOOL OF MATHEMATICAL SCIENCES
ROCHESTER INSTITUTE OF TECHNOLOGY

IN FULFILLMENT OF THE
REQUIREMENTS FOR THE DEGREE
MASTER OF SCIENCE IN APPLIED &
COMPUTATIONAL MATHEMATICS

SUBMITTED BY

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Abstract

A SIS model for Cutaneous Leishmaniasis is developed and analyzed. The model contains a human population of incidental hosts, along with animals that are the reservoir hosts and the sandfly vector. Reproductive rates for the persistence of the infection are derived from the model. Conditions for the existence of endemic and disease-free equilibrium are obtained. The stability analysis of the disease-free equilibrium is investigated and numerical simulations for the model are provided.

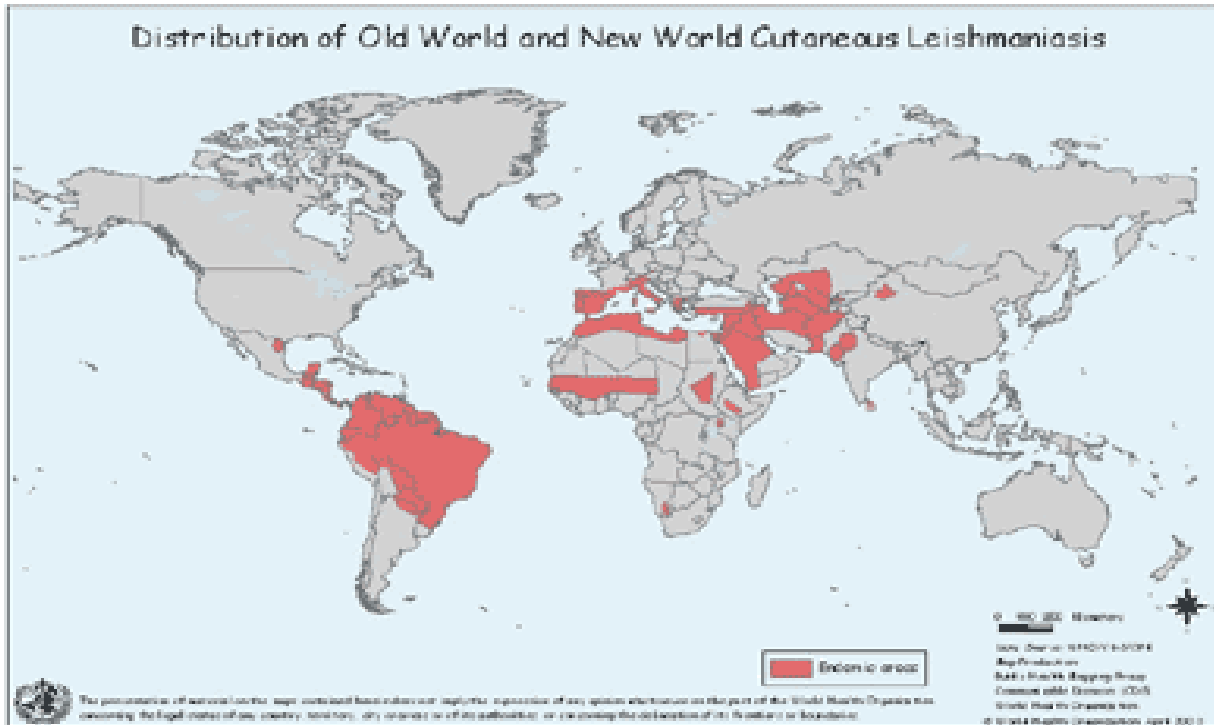
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1. INTRODUCTION

1.1. LEISHMANIASIS

Leishmaniasis is a parasitic disease transmitted by the bite of infected female phlebotomine sandflies. The disease is endemic in 88 countries throughout Africa, Asia, Europe, and North and South America [1], the geographic distribution is shown in the figure below. There are an estimated 12 million cases worldwide, with 1.5 to 2 million new cases each year. Although the incidence of leishmaniasis is greater in the Old World(the Eastern Hemisphere) than in the New World(the Western Hemisphere), the U.S. traveler is most likely to contract this disease in Latin America. Fifty to 100 cases of New World cutaneous leishmaniasis are diagnosed each year in the United States. They are contracted mainly in Peru and Brazil, although the disease is endemic and can be contracted in any country from Mexico to Argentina, except Uruguay and Chile.[2] There also is an endemic focus in Texas. Leishmaniasis is a disease associated with rural areas and poverty, but it has adapted to the urban environment as well.



Courtesy: WHO

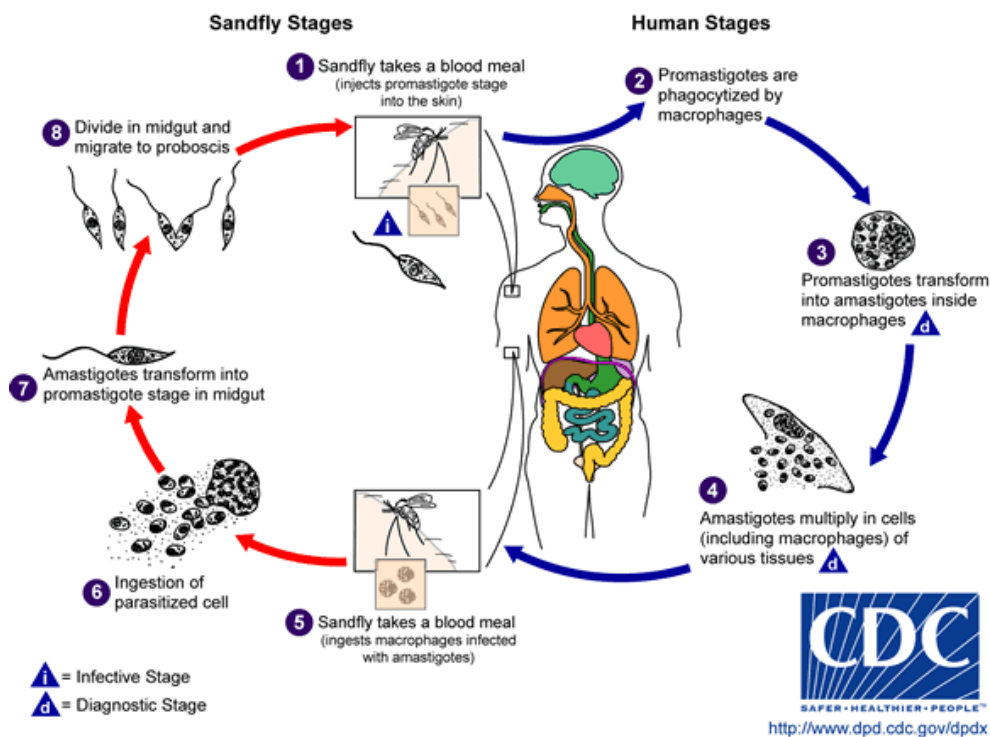
Fig 1. Distribution of Leishmaniasis.

In World War II, there was a high incidence of leishmaniasis and sandfly fever in troops deployed to the Persian Gulf region. In the Gulf War (1990 to 1991), approximately 697,000 U.S. troops were deployed in this region. Only 19 cases of cutaneous leishmaniasis and 12 cases of visceral disease were diagnosed in this group. The Improvement came about because of the use of insecticides and repellents, lower transmission rates in the summer, and more time spent in urban areas.[3],[4] About 150 cases of leishmaniasis have reportedly been diagnosed in U.S. soldiers serving in Iraq in 2003, and more are expected.[5] Preliminary data on 22 cases of cutaneous leishmaniasis contracted by American troops in Afghanistan, Kuwait, and Iraq and treated at Walter Reed Army Medical Center between August 2002 and September 2003 were recently released.[6] The majority of these persons were infected with *Leishmania major* in urban areas of Iraq after a median period of deployment of 60 days.

The Leishmania protozoan was first described in 1903 by Leishman and Donovan, working separately.[2] Since then, this organism has been found to be a complex grouping of species, at least 20 of which cause infections in humans. Some species cause visceral leishmaniasis, some cause cutaneous disease, and some cause both. Visceral leishmaniasis is a systemic infection characterized by fever, weight loss, and hepatosplenomegaly, and it is usually fatal without treatment. This article focuses on cutaneous leishmaniasis, the more common form of the disease.

1.2. CUTANEOUS LEISHMANIASIS

Cutaneous leishmaniasis occurs in the New World and the Old World. Old World disease primarily is caused by *Leishmania tropica* in urban areas and *Leishmania major* in dry desert areas. The two subgenera of interest in Latin America are *Leishmania leishmania* (e.g., *Leishmania mexicana*, *Leishmania amazonensis*, *Leishmania chagasi*) and *Leishmania viannia* (e.g., *Leishmania panamensis*, *Leishmania braziliensis*, *Leishmania guyanensis*). The incubation period is two to eight weeks, although longer periods have been noted. The disease begins as an erythematous papule at the site of the sandfly bite on exposed parts of the body. The papule increases in size and becomes a nodule. It eventually ulcerates and crusts over. The border is usually raised and distinct. There may be multiple lesions, especially when the patient has encountered a nest of sandflies. The ulcer is typically large but painless unless there is secondary bacterial or fungal infection. The life cycle of cutaneous leishmaniasis is fully described in the figure below.



Courtesy: CDC

Fig 2. Life cycle of cutaneous leishmaniasis.

Old World leishmaniasis and *L. Mexicana* lesions tend to heal spontaneously in months, but *L. braziliensis* may take years to heal. After healing, a depressed scar remains that is usually round but can be irregular. **Figure 3** shows a typical leishmaniasis lesion before treatment. Satellite lesions with a nodular lymphangitis resembling sporotrichosis have been described.



Fig 3. Cutaneous leishmaniasis in a young patient.

Cutaneous leishmaniasis can become disseminated (diffuse cutaneous leishmaniasis), especially in immunosuppressed persons. This illness can go on for years and does not heal spontaneously. Patients with human immunodeficiency virus (HIV) infection are particularly susceptible. Other unusual types of cutaneous disease include leishmaniasis recidivans, in which small nodules develop around a healed scar, and post-kala-azar dermal leishmaniasis, in which widespread cutaneous lesions arise after a visceral infection. These conditions occur primarily in the Old World. When physicians assess a patient with suspected leishmaniasis in the United States, the travel and military histories are most important. Patients who served in the military in the Middle East can return with this infection.

Treatment with antimonials will heal lesions faster and prevent relapse, local dissemination, mucosal disease (usually), and transmission. Not all lesions require treatment. Old World disease tends to be self-healing, and systemic treatment seldom is used. New World lesions more often require systemic treatment. The main reasons to treat cutaneous leishmaniasis are cosmetically unacceptable lesions, chronic lesions, large lesions, lesions in immunosuppressed patients, lesions over joints, mucosal disease, multiple lesions, nodular lymphangitis and Worsening lesions etc. Pentavalent antimony remains the treatment of choice. It is thought to work by inhibition of adenosine triphosphate synthesis. The antimonial agent used in the United States is sodium stibogluconate (Pentostam).

Prevention

Vaccine development is under way. The combination of killed promastigotes plus bacilli Calmette-Guérin vaccine is being tested in Iran, Sudan, and Ecuador.[20] Avoiding sandflies is important but difficult, because they have adapted to urban environments. The use of insecticides in endemic areas is important for travelers. House and space spraying have reduced sandfly populations, and fine-weave pyrethroid-impregnated bednets have been used in Burkina Faso, Sudan, and Columbia. Destruction of rodent reservoirs by pumping insecticides into rodent burrows has had limited success.[7].

A recent randomized study in Venezuela evaluated the effectiveness of pyrethroidimpregnated curtains in an urban area with an incidence of cutaneous leishmaniasis of 4 percent. In 569 homes, 2,913 inhabitants were included in this study. Use of the curtains reduced the sandfly population and, 12 months after the installation of these curtains, the incidence of cutaneous leishmaniasis dropped to zero.[21] [SOR B, single RCT].

1.3. RESERVOIRS

The previous models mostly contains only the interaction between the Humans and sandflies or animals and sandflies. But in reality humans are mainly the incidental hosts, sandflies are the carrier vectors and the animals are the main reservoirs of the disease. Hence for more accurate functioning of the model it is required to consider all the three groups. The following tables show different reservoirs in different regions.

Old world cutaneous leishmaniasis (zoonotic cutaneous leishmaniasis)

Type of disease	Species	Localities	Main vectors	Main reservoirs
Oriental sore and recidiva	Leishmania (Leishmania) tropica	India	Phlebotomus sergenti	Dog
		Former Soviet Union (urban)	P. Sergenti	Humans
		Iran	Phlebotomus ansarii	Dog
		Mediterranean basin	P. Sergenti	Humans
Phlebotomus perfiliewi				
Oriental sore and oronasal	Leishmania (Leishmania) major	Former Soviet Union (rural)	Phlebotomus papatasi	Gerbils
		Saudi Arabia, Central Asia	P. papatasi	Gerbils,merions
		Mediterranean basin	P. papatasi	Gerbils,merions
		Sudan	P. papatasi	Rodents
		Senegal	Phlebotomus duboscqi	Rodents
	India	Phlebotomus saheli	Rodents	
	Leishmania (Leishmania) tropica complex	Namibia	Phlebotomus rossi	Hyrax
Single sore and diffusa	Leishmania (Leishmania) aethiopica	Ethiopia	Phlebotomus longipes	Hyrax
		Kenya	Phlebotomus pedifer	Hyrax. Cricetomys

Table a

New World cutaneous mucocutaneous leishmaniasis

Type of disease	Species	Localities	Main vectors	Main reservoirs
Simple cutaneous and diffusa	Leishmania (Leishmania) mexicana	Mexico, Guatemala, Belize	Lutzomyia olmeca	Forest rodents
	Leishmania (Leishmania) Mexicana complex	Trinidad	Lutzomyia flaviscutellata	Forest rodents
		Texas	Lutzomyia anthropophora	Neotoma micropis
	Leishmania (Leishmania) amazonensis	Brazil (Amazon basin)	Lutzomyia flaviscutellata	Forest rodents
	Leishmania (Leishmania) garnhami	Venezuela	Lutzomyia townsendi	Opossum
	Leishmania (Viannia) naiffi	Brazil(pará)	Lutzomyia paraensis	Armadillo
	Leishmania (Viannia) lainsoni	Brazil(pará), Peru	Lutzomyia ubiquitalis	Paca
Espundia	Leishmania (Viannia) braziliensis	Brazil	Lutzomyia wellcomei	Forest rodents
		Brazilian Amazon	Lutzomyia wellcomei	
			Lutzomyia squamiventris	
Plan bois	Leishmania (Viannia) guyanensis	Guyanas	Lutzomyia umbratilis	Sloths, ant-eaters
		Northern Brazil	Lutzomyia whitmani	Rodents
			Lutzomyia anduzei	Rodents
Simple sore or pian bois	Leishmania (Viannia) panamensis	Panama	Lutzomyia trapidoi	Sloths
		Costa Rica	Lutzomyia ylephiletor	Monkeys
	Leishmania (Viannia) colombiensis	Colombia	Lutzomyia hartmanni	Sloths
	Leishmania (Viannia) shawi	Brazil(pará)	Lutzomyia whitmani	Sloths, monkeys, Coatimundi
Uta	Leishmania (Viannia)	Peru(west of Andes)	Lutzomyia verrucarum	Dog

Table b

2. THE MODEL

2.1. THE BASIC MODEL USED

It is possible to mathematically model the progress of most infectious diseases to discover the likely outcome of an epidemic. This is done using some basic assumptions and some simple mathematics to find parameters for various infectious diseases.

The SIS model [28] is the simplest for many infectious diseases. Standard convention labels these three compartments S, I and S. Therefore, this model is called the SIS model. The model is given by the following differential equations:

$$\frac{dS}{dt} = -\beta SI + \gamma I$$

$$\frac{dI}{dt} = \beta SI - \gamma I$$

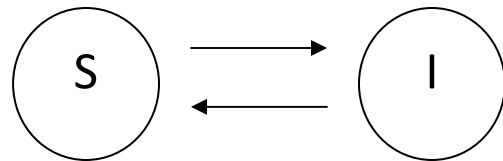


Fig 4. Interactions in a SIS model

Where,

S : The proportion of the population who are susceptible to the disease (neither immune nor infected).

I : The proportion of the population who are infectious to the disease.

β : The Contact Rate.

γ : The Recovery Rate.

From the above differential equations we observe that:

$$\frac{dS}{dt} + \frac{dI}{dt} = 0$$

$S(t) + I(t) = Constant = N(\text{Total Population}).$

The **basic reproduction number**(R_0) is an important parameter that gives, the average number of other individuals each infected individual will infect in a population that has no immunity to the disease. If $R_0 > 1$, the infection will be able to spread in a population. Large values of R_0 may indicate the possibility of a major epidemic. If $R_0 < 1$, the infection will die out in the long run (provided infection rates are constant). From the above differential equations we get,

$$R_0 = \beta/\gamma.$$

2.2. OVERALL STRUCTURE OF THE MODEL

The proposed model, by means of system analysis is a reference framework for the modeling including the interrelationships among the three subsystems that intervene in the transmission dynamics, human population, sandfly population and animal population.

The Human population subsystem is divided into two:

1. **The susceptible human:** Who is susceptible to the disease (neither immune nor infected). Even the recovered human comes in this category.
2. **The infected human:** Who is infected by the disease, by the bite of infected sandfly. They can infect the susceptible sandfly in turn.

The Sandfly population subsystem is divided into two:

1. **The susceptible sandfly:** Which is susceptible to the disease (neither immune nor infected). Even the recovered sandfly comes in this category.
2. **The infected sandfly:** Which is infected by the disease, after biting infected human or infected animal.

The Animal population subsystem is divided into two:

1. **The susceptible animal:** Which is susceptible to the disease (neither immune nor infected). Even the recovered animal comes in this category.
2. **The infected animal:** Which is infected by the disease, by the bite of infected sandfly. They can infect the susceptible sandfly in turn.

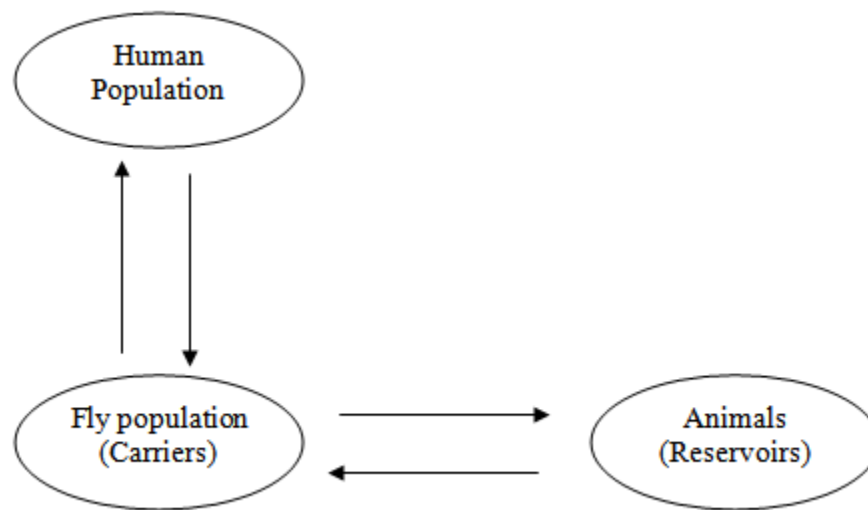


Fig 5. Interactions in Cutaneous leishmaniasis

2.3. ASSUMPTIONS

Based on transmission dynamics of the disease the overall structure of the model is divided into three groups, namely Human population (the incidental hosts), Sandfly population (the vector) and Animal population (the main reservoirs). A number of assumptions are required for the construction of the model. The following are the assumptions in each group considered in constructing the required model.

HUMAN POPULATION:

- Flies bite them at a constant rate(α_H).
- There is no birth and death within this period.
- They recover from the infected population to become susceptible again.
- They can get infected from the flies or infect the flies.
- They won't die of the disease.
- Population remains constant throughout.

SANDBLY POPULATION:

- They bite the Human and Animal population at different rates.
- They recover, if they eject infection completely, to become susceptible again.
- They birth and death rates are same.
- They can infect both Human and Animal population.
- They can get infected from both Human and Animal population.
- They won't die of the disease.
- Population remains constant throughout

ANIMAL POPULATION:

- Flies bite them at a constant rate(α_A).
- They give birth and die at same rates.
- They recover from the infected population to become susceptible again.
- They can get infected from the flies or infect the files.
- They won't die of the disease.
- Population remains constant throughout

2.4. DERIVATION OF THE MODEL

HUMAN POPULATION :(SIS MODEL)

Humans are the incidental hosts. Humans are called susceptible if they can become infected as a result of being bitten by infected vectors. Their transition from susceptible to infected depends on the rate at which the sandflies are biting them, the probability that these bites will lead to an infection and the fraction of blood meals taken from susceptible. Humans are called infectious if they are infected and can transmit the infection to the vector. Infective humans upon recovery will transition to the susceptible class. Since there is no birth or death, the total population, N_H , at any time is constant and is given by $N_H = S_H(t) + I_H(t)$. The following differential equations model the rates of change in the susceptible and infectious populations.

$$\frac{dS_H}{dt} = -\alpha_H P_H \frac{S_H}{N_H} I_F + \gamma_H I_H$$

$$\frac{dI_H}{dt} = \alpha_H P_H \frac{S_H}{N_H} I_F - \gamma_H I_H$$

where,

$S_H =$ Susceptible human population

$I_H =$ Infected human population

$N_H =$ Total human population

$I_F =$ Infected sandfly population

$\alpha_H =$ Sand fly biting rate of Human Population

$P_H =$ Probability of infecting

$\gamma_H =$ Recovery rate of human population

SANDBLY POPULATION :(SIS MODEL)

Sandflies are the disease carriers. Sandflies are called susceptible if they can become infected as a result of biting an infected human or animal. Their transition from susceptible to infected depends on the rate at which the sandflies are biting them, the probability that these bites will lead to an infection and the fraction of blood meals taken from susceptible. Sandflies are called infectious if they are infected and can transmit the infection. Infective Sandflies upon recovery will transition to the susceptible class. Since the birth or death rates are same, the total population (N_F), at any time is constant and is given by $N_F = S_F(t) + I_F(t)$. The following differential equations model the rates of change in the susceptible and infectious populations.

$$\frac{dS_F}{dt} = - \left[\alpha_H P_{FH} \frac{I_H}{N_H} + \alpha_A P_{FA} \frac{I_A}{N_A} \right] S_F + B_F N_F - D_F S_F + \gamma_F I_F$$

$$\frac{dI_F}{dt} = \left[\alpha_H P_{FH} \frac{I_H}{N_H} + \alpha_A P_{FA} \frac{I_A}{N_A} \right] S_F - D_F I_F - \gamma_F I_F$$

where,

$S_F =$ Susceptible sandfly population

$I_F =$ Infected sandfly population

$N_F =$ Total sandfly population

$I_H =$ Infected human population

$I_A =$ Infected Animal population

$N_A =$ Total Animal population

$\alpha_A =$ Sand fly biting rate of Animal Population

$P_{FH} =$ Probability of infecting by biting human

$P_{FA} =$ Probability of infecting by biting Animal

$B_F =$ Birth rate of sandfly population

$D_F =$ death rate of sandfly population

$\gamma_F =$ Recovery rate of sandfly population

ANIMAL POPULATION: (SIS MODEL)

Animals are the main reservoirs. Animals are called susceptible if they can become infected as a result of being bitten by infected vectors. Their transition from susceptible to infected depends on the rate at which the sandflies are biting them, the probability that these bites will lead to an infection and the fraction of blood meals taken from susceptible. Animals are called infectious if they are infected and can transmit the infection to the vector. Infective Animals upon recovery will transition to the susceptible class. Since the birth or death rates are same, the total population, N_A , at any time is constant and is given by $N_A = S_A(t) + I_A(t)$. The following differential equations model the rates of change in the susceptible and infectious populations.

$$\frac{dS_A}{dt} = -\alpha_A P_A \frac{S_A}{N_A} I_F + \gamma_A I_A + B_A N_A - D_A S_A$$

$$\frac{dI_A}{dt} = \alpha_A P_A \frac{S_A}{N_A} I_F - \gamma_A I_A - D_A I_A$$

where,

$S_A =$ Susceptible Animal population

$I_A =$ Infected Animal population

$N_A =$ Total Animal population

$I_F =$ Infected sandfly population

$\alpha_A =$ Sand fly biting rate of Animal Population

$P_A =$ Probability of infecting

$\gamma_A =$ Recovery rate of Animal population

$B_A =$ Birth rate of Animal population

$D_A =$ death rate of Animal population

3. ANALYSIS OF THE MATHEMATICAL MODEL

To analyze the model provided in the previous chapter we focus our attention on the infective equations only. The system of infective equations is given as follows:

$$\frac{dI_H}{dt} = \alpha_H P_H \frac{S_H}{N_H} I_F - \gamma_H I_H \quad (1a)$$

$$\frac{dI_F}{dt} = \left[\alpha_H P_{FH} \frac{I_H}{N_H} + \alpha_A P_{FA} \frac{I_A}{N_A} \right] S_F - D_F I_F - \gamma_F I_F \quad (1b)$$

$$\frac{dI_A}{dt} = \alpha_A P_A \frac{S_A}{N_A} I_F - \gamma_A I_A - D_A I_A. \quad (1c)$$

3.1. BASIC REPRODUCTION RATIO

We recall here that the basic reproduction number (R_0) is the average number of individuals infected by introducing a single infected case into a susceptible population. To obtain the reproduction number for the model we normalized the system (1) by defining the following dimensionless variables:

$$U_H = \frac{S_H}{N_H}, \quad V_H = \frac{I_H}{N_H}, \quad U_F = \frac{S_F}{N_F}, \quad V_F = \frac{I_F}{N_F}, \quad U_A = \frac{S_A}{N_A} \text{ and } V_A = \frac{I_A}{N_A}. \quad (2)$$

Substituting the quantities given in equation (2) into the system (1), we obtain the normalized system

$$\frac{dV_H}{dt} = \gamma_H [\xi_H U_H V_F - V_H] \quad (3a)$$

$$\frac{dV_F}{dt} = (D_F + \gamma_F) [U_F (\xi_{FH} V_H + \xi_{FA} V_A) - V_F] \quad (3b)$$

$$\frac{dV_A}{dt} = (D_A + \gamma_A) \gamma_H [\xi_A U_A V_F - V_A], \quad (3c)$$

where,

$$\xi_H = \frac{\alpha_H P_H N_F}{\gamma_H N_H}, \quad \xi_{FH} = \frac{\alpha_H P_{FH}}{(\gamma_F + D_F)}, \quad \xi_{FA} = \frac{\alpha_A P_{FA}}{(\gamma_F + D_F)} \text{ and } \xi_A = \frac{\alpha_A P_A N_F}{(\gamma_A + D_A) N_A}.$$

Let R_{OA} denote the number of Secondary cases in Animals that we expect to be produced by introducing a single infected animal into a wholly susceptible population. We can observed from the system (3) that a single infected animal will infect $\frac{\alpha_A P_A N_F}{(\gamma_A + D_A) N_A}$ sandflies, which will then infect $\frac{\alpha_A P_{FA}}{(\gamma_F + D_F)}$ animals. This is simply the product of the parameters ξ_A and ξ_{FA} . Thus

$$R_{OA} = \frac{\alpha_A \alpha_A P_A P_{FA} N_F}{(\gamma_F + D_F)(\gamma_A + D_A) N_A} = \xi_A \xi_{FA}.$$

Similarly let R_{OH} denote the number of Secondary cases in humans that we expect to be produced by introducing a single infected human into a wholly susceptible population. We can also observe from the system (3) that a single infected human will infect $\frac{\alpha_H P_H N_F}{\gamma_H N_H}$ sandflies, which leads to $\frac{\alpha_H P_{FH}}{(\gamma_F + D_F)}$ infected humans. Again, this is just the product of the parameters ξ_H and ξ_{FH} . Thus

$$R_{OH} = \frac{\alpha_H \alpha_H P_H P_{FH} N_F}{(\gamma_F + D_F) \gamma_H N_H} = \xi_H \xi_{FH}.$$

The total reproduction number (R_O) of the model is given by: $R_O = R_{OA} + R_{OH}$.

3.2. EXISTENCE OF NONTRIVIAL EQUILIBRIUM SOLUTION

In this section, we show that in addition to the disease free equilibrium, the model possesses two endemic equilibriums. To achieve this we remark that all total populations are constant and therefore.

$$S_H = N_H - I_H, \quad S_F = N_F - I_F \quad \text{and} \quad S_A = N_A - I_A . \quad (4)$$

Substituting the variables of equation (4) into the infective system (1) we obtain the following system of equations

$$\frac{dI_H}{dt} = \alpha_H P_H \frac{(N_H - I_H)}{N_H} I_F - \gamma_H I_H \quad (5a)$$

$$\frac{dI_F}{dt} = \left[\alpha_H P_{FH} \frac{I_H}{N_H} + \alpha_A P_{FA} \frac{I_A}{N_A} \right] (N_F - I_F) - D_F I_F - \gamma_F I_F \quad (5b)$$

$$\frac{dI_A}{dt} = \alpha_A P_A \frac{(N_A - I_A)}{N_A} I_F - \gamma_A I_A - D_A I_A . \quad (5c)$$

To normalize the system (5), we use the following variables which are obtained by dividing the variables in equation (4) by their corresponding total populations:

$$U_H = 1 - V_H, \quad U_F = 1 - V_F \quad \text{and} \quad U_A = 1 - V_A . \quad (6)$$

Substituting (6) into the system (5) we obtain

$$\frac{dV_H}{dt} = \gamma_H [\xi_H (1 - V_H) V_F - V_H] \quad (7a)$$

$$\frac{dV_F}{dt} = (D_F + \gamma_F) [(1 - V_F) (\xi_{FH} V_H + \xi_{FA} V_A) - V_F] \quad (7b)$$

$$\frac{dV_A}{dt} = (D_A + \gamma_A) [\xi_A (1 - V_A) V_F - V_A] . \quad (7c)$$

To find the equilibrium solutions of the system (7) we set

$$\frac{dV_H}{dt} = 0, \quad \frac{dV_A}{dt} = 0 \quad \text{and} \quad \frac{dV_F}{dt} = 0.$$

Therefore,

$$\gamma_H[\xi_H(1 - V_H)V_F - V_H] = 0 \quad (8a)$$

$$(D_F + \gamma_F)[(1 - V_F)(\xi_{FH}V_H + \xi_{FA}V_A) - V_F] = 0 \quad (8b)$$

$$(D_A + \gamma_A)[\xi_A(1 - V_A)V_F - V_A] = 0. \quad (8c)$$

Solving the system of equations (7) simultaneously for V_H , V_A and V_F we obtain

$$V_H = \frac{\xi_H V_F}{1 + \xi_H V_F}, \quad (9)$$

$$V_A = \frac{\xi_A V_F}{1 + \xi_A V_F}, \quad (10)$$

and
$$V_F = \frac{\xi_{FA}V_A + \xi_{FH}V_H}{1 + \xi_{FH}V_H + \xi_{FA}V_A}. \quad (11)$$

We can rewrite the equation (11) in the form

$$\frac{V_F}{1 - V_F} = \xi_{FH}V_H + \xi_{FA}V_A \quad (12)$$

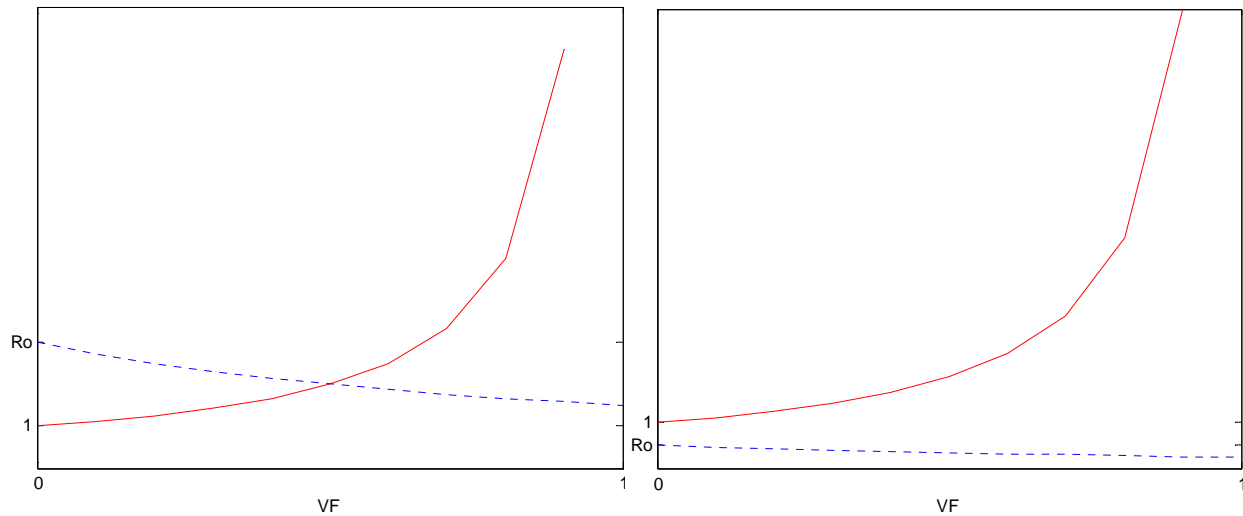
Substituting equations (9) and (10) into equation (12) we get

$$\frac{V_F}{1 - V_F} = \frac{\xi_{FH}\xi_H V_F}{1 + \xi_H V_F} + \frac{\xi_{FA}\xi_A V_F}{1 + \xi_A V_F} \quad (13)$$

It is clear from equation (13) that $V_F = 0$, which therefore imply that $V_H = V_A = 0$. This is the trivial equilibrium solution for the system (7). To obtain the non-trivial equilibrium solutions, we factor out V_F from equation (13) to obtain

$$\frac{1}{1 - V_F} = \frac{\xi_{FH}\xi_H}{1 + \xi_H V_F} + \frac{\xi_{FA}\xi_A}{1 + \xi_A V_F} \quad (14)$$

We can easily see that equation (14) is quadratic in the variable V_F . This implies that V_F has two non-zero solutions. The system (7) therefore possesses two non-trivial equilibrium solutions. The figures below show the behavior of the equation (14).



In the above figures the solid line and the dash line represents the right hand and left hand side of equation (14) respectively. We can clearly see from the above figures that if $R_0 > 1$ there exists a non trivial equilibrium solution. If $R_0 < 1$ then there is only one equilibrium solution which is the trivial case. In the subsequent section, we analyze the stability of the trivial equilibrium.

3.3. STABILITY ANALYSIS OF THE TRIVIAL EQUILIBRIUM SOLUTION

Stability analysis is a widely used tool to study the performance of dynamical systems at equilibria. To show that the trivial solution is stable, we developed the following theorem

Theorem:

If $R_0 < 1$, then the equilibrium solution of the system is a global attractor (i.e. asymptotically stable).

Proof:

We define a Lyapunov function for the system of equation (7) by

$$\varphi(V_A, V_H, V_F) = \max \left\{ \frac{V_A}{\xi_A(1 - V_A)}, \frac{V_H}{\xi_H(1 - V_H)}, V_F \right\}.$$

Clearly since V_A, V_H and V_F all are positive in the system of equations (7), it is clear that the function, $\varphi(V_A, V_H, V_F)$ is positive definite. We proceed with the proof as follows:

CASE I:

Suppose that,

$$\varphi(V_A, V_H, V_F) = \frac{V_A}{\xi_A(1 - V_A)}.$$

Differentiating the above equation, we obtain

$$\varphi'(V_A, V_H, V_F) = \frac{V_A'}{\xi_A(1 - V_A)^2}.$$

Substituting equation (7c) in the above equation, we obtain

$$\varphi'(V_A, V_H, V_F) = \frac{(D_A + \gamma_A)[\xi_A(1 - V_A)V_F - V_A]}{\xi_A(1 - V_A)^2}.$$

Rewriting the above equation, we obtain

$$\varphi'(V_A, V_H, V_F) = \frac{(D_A + \gamma_A)}{(1 - V_A)} \left[V_F - \frac{V_A}{\xi_A(1 - V_A)} \right] < 0.$$

CASE II:

Suppose that,

$$\varphi(V_A, V_H, V_F) = \frac{V_H}{\xi_H(1 - V_H)}$$

Similarly differentiating the above equation we get

$$\varphi'(V_A, V_H, V_F) = \frac{\gamma_H}{(1 - V_H)} \left[V_F - \frac{V_H}{\xi_H(1 - V_H)} \right] < 0.$$

CASE III:

Suppose that,

$$\varphi(V_A, V_H, V_F) = V_F.$$

Then, we have

$$V_F > \frac{V_A}{\xi_A(1 - V_A)}.$$

$$\xi_A V_F > \frac{V_A}{(1 - V_A)} > V_A.$$

$$\xi_{FA} \xi_A V_F > \frac{\xi_{FA} V_A}{(1 - V_A)} > \xi_{FA} V_A. \quad (15)$$

Similarly

$$\xi_{FH}\xi_H V_F > \frac{\xi_{FH}V_H}{(1-V_H)} > \xi_{FH}V_H. \quad (16)$$

Adding the inequality equation (15) and (16), we obtain

$$\xi_{FA}\xi_A V_F + \xi_{FH}\xi_H V_F > \xi_{FA}V_A + \xi_{FH}V_H$$

Or

$$R_O V_F > \xi_{FA}V_A + \xi_{FH}V_H. \quad (17)$$

Recall that,

$$\varphi(V_A, V_H, V_F) = V_F.$$

Differentiating the above equation, we obtain

$$\varphi'(V_A, V_H, V_F) = V_F'.$$

Substituting for V_F' using equation (7b), we obtain

$$\varphi'(V_A, V_H, V_F) = (D_F + \gamma_F)[(1 - V_F)(\xi_{FH}V_H + \xi_{FA}V_A) - V_F]. \quad (18)$$

Substituting equation (17) in equation (18), we obtain

$$\varphi'(V_A, V_H, V_F) < (D_F + \gamma_F)[(1 - V_F)R_O V_F - V_F].$$

If $R_O < 1$, then we have

$$\varphi'(V_A, V_H, V_F) < 0.$$

From the above three cases we see that $\varphi'(V_A, V_H, V_F) < 0$ and therefore the trivial equilibrium is a global attractor.

4. RESULTS

In order to analyze the model performance, we simulated a virus infection scenario. The data required to simulate the model are indicated below.

4.1. PARAMETER ESTIMATES

Human and Animal Recovery Rate:

A prospective longitudinal survey of cutaneous leishmaniasis (*Leishmania peruviana*) was carried out in Peru on a study population of 4716 persons living in 38 villages (Departments of Lima, Ancash and Piura). Demographic and clinical data were collected from all individuals and a Montenegro skin test (MST) was carried out on 72% (3418) of the study population. Each household was revisited at 3-monthly intervals for up to 2 years to detect new leishmaniasis cases; 497 people received a second MST at the end of the study. The results from the survey indicated that recovery rate of human is 1.2/year [33].

A similar survey of canine American cutaneous leishmaniasis(ACL) was investigated in Huánuco, Peru. Over a three-year period 1,022 dogs were surveyed, and the results from the survey indicated that recovery of dogs vary between 4.6 - 5.4 /year [34]. We therefore take the recovery rate for dogs to be 5/year for our simulations. The death and birth rate of dogs are considered to be 1per year.

Biting Rate of Sandfly:

The life span of an adult sandfly is 2 weeks. The sandfly will take 2 blood meals during the life span. So we assumed that on average the biting rate of sandfly is 1/14 per day (both humans and animals).

Populations:

The total population of humans, sandflies and animals are assumed to be constant during the virus infection scenario. The population of each is assumed to be 5000.

Probabilities of Infection:

The probability that a bite from an infected sandfly translates to an infection is assumed to be 0.3 for human and 0.25 for animals. The probability that a sandfly becomes infected from biting an infectious human or animal is assumed to be 0.25.

Sandfly Birth and Recovery Rate

An infected sandfly becomes susceptible if it ingests all promastigotes by taking a blood meal. We hereby assume a recovery rate of 1/14 per day. The birth and death rate of sandfly is considered to be 1/14 per day.

4.2. SIMULATION

We will use the above parameters to run simulations for the following three cases: various biting rates of sandfly, human recovery rates and animal recovery rates. In all three cases we provide results for the infective populations only and results for the infective populations combined with the susceptible populations.

CASE 1:

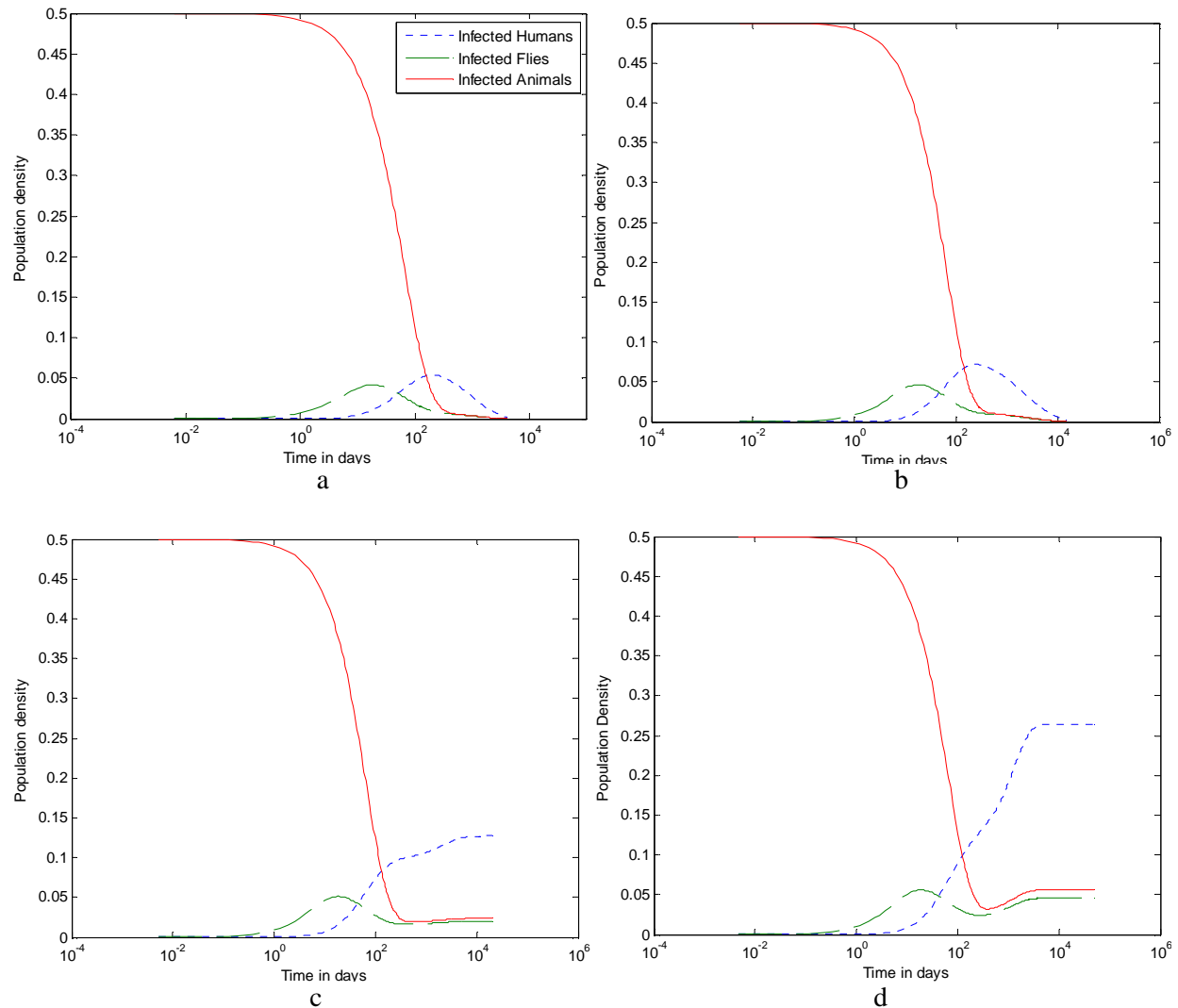


Fig 6. Varying the biting rate of Sandfly (α) for infective populations. In graphs a, b, c, & d, we set $\alpha = 0.9/14$, $1/14$, $1.1/14$ and $1.2/14$ respectively

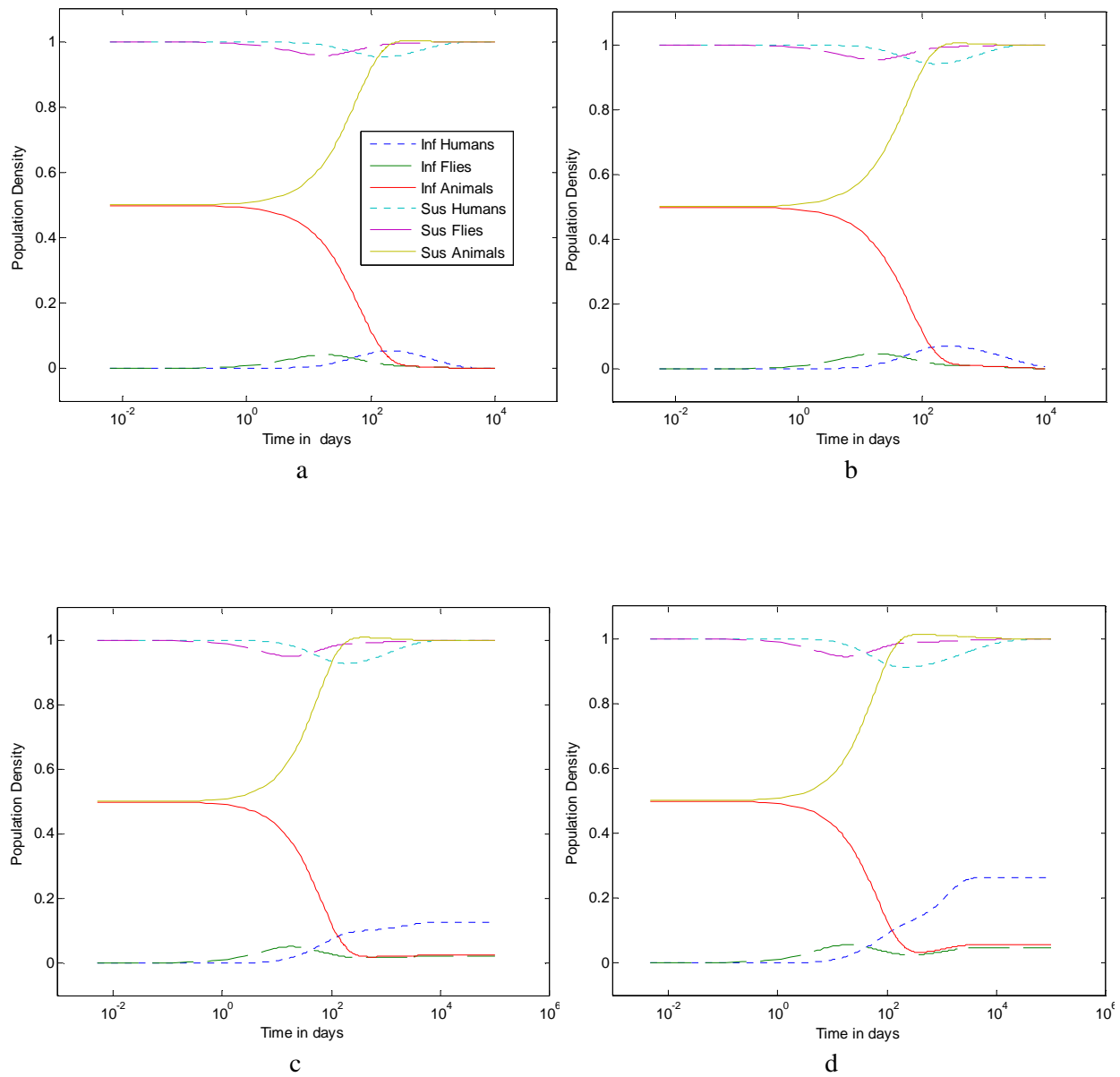


Fig 7. Varying the biting rate of Sandfly (α), for infective and susceptible populations. Here $\alpha = 0.9/14, 1/14, 1.1/14$ and $1.2/14$ per day in graphs a, b, c and d respectively

For the parameters used here it is clear from Figures 6 (a-b) and 7(a-b) that for small sandfly biting rates the disease is in recession. However as the biting rates increases, Figures 6(c-d) and 7(c-d), the disease becomes endemic. We remark here that the reproduction number for the model R_0 is given by $R_0 = R_{OH} + R_{OA}$. Clearly it can be seen from Table 1 that for small biting rates $R_0 < 1$, that the disease is in recession and for high biting rates $R_0 > 1$, the disease is endemic.

Biting Rates(α)	Animal Reproduction Number(R_{OA})	Human Reproduction Number(R_{OH})	Total Reproduction Number(R_0)
0.9/14	0.11	0.66	0.77
1/14	0.14	0.81	0.95
1.1/14	0.16	0.99	1.15
1.2/14	0.20	1.17	1.37

Table1. Varying the biting rates of sandfly

CASE 2:

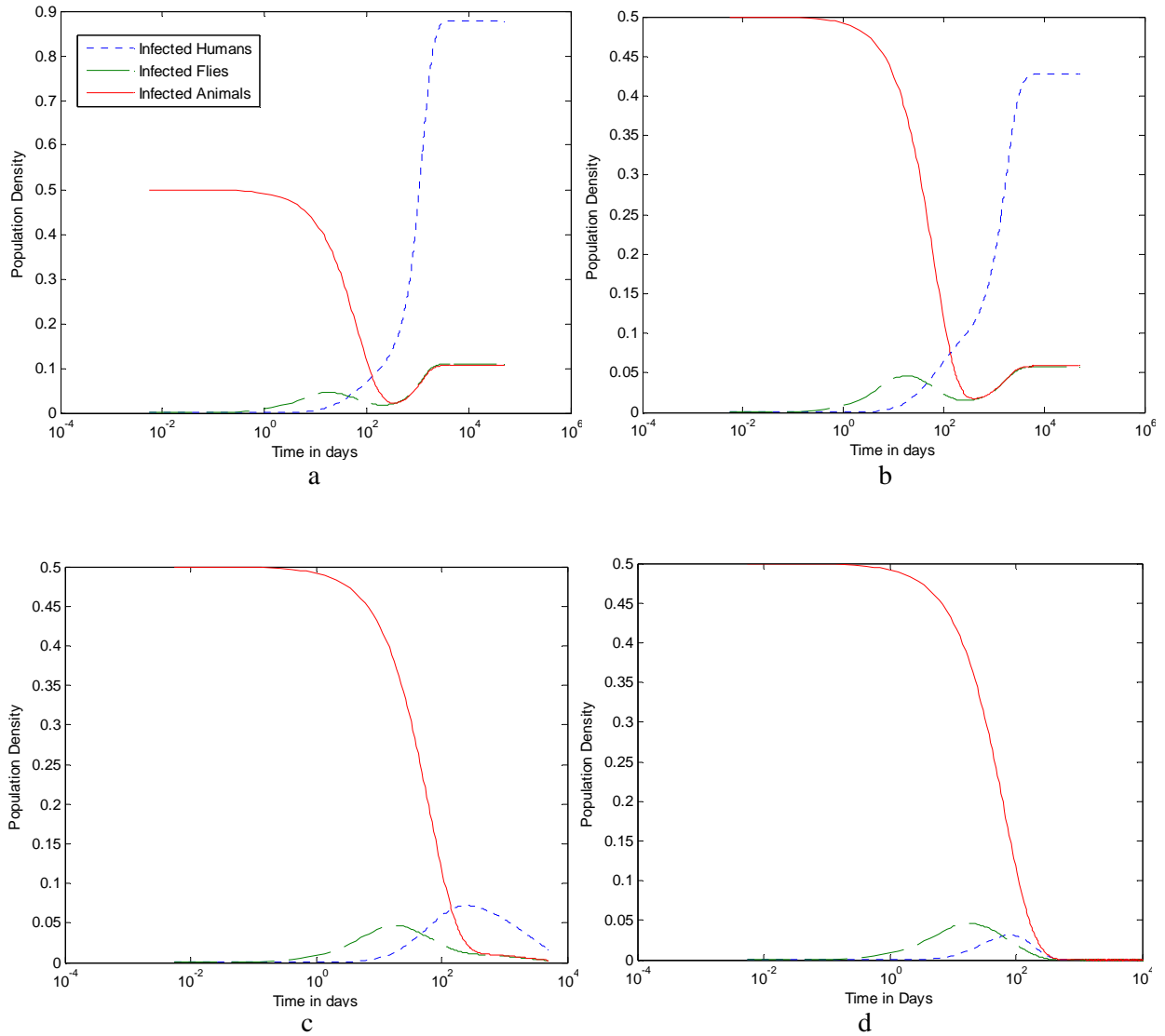


Fig 8. Varying the recovery rate of Humans (γ_h) for only infective equations of human, sandfly and animal populations with respect to time,, here $\gamma_h = 0.12, 0.6, 1.2$ and 6 per year for a, b, c and respectively.

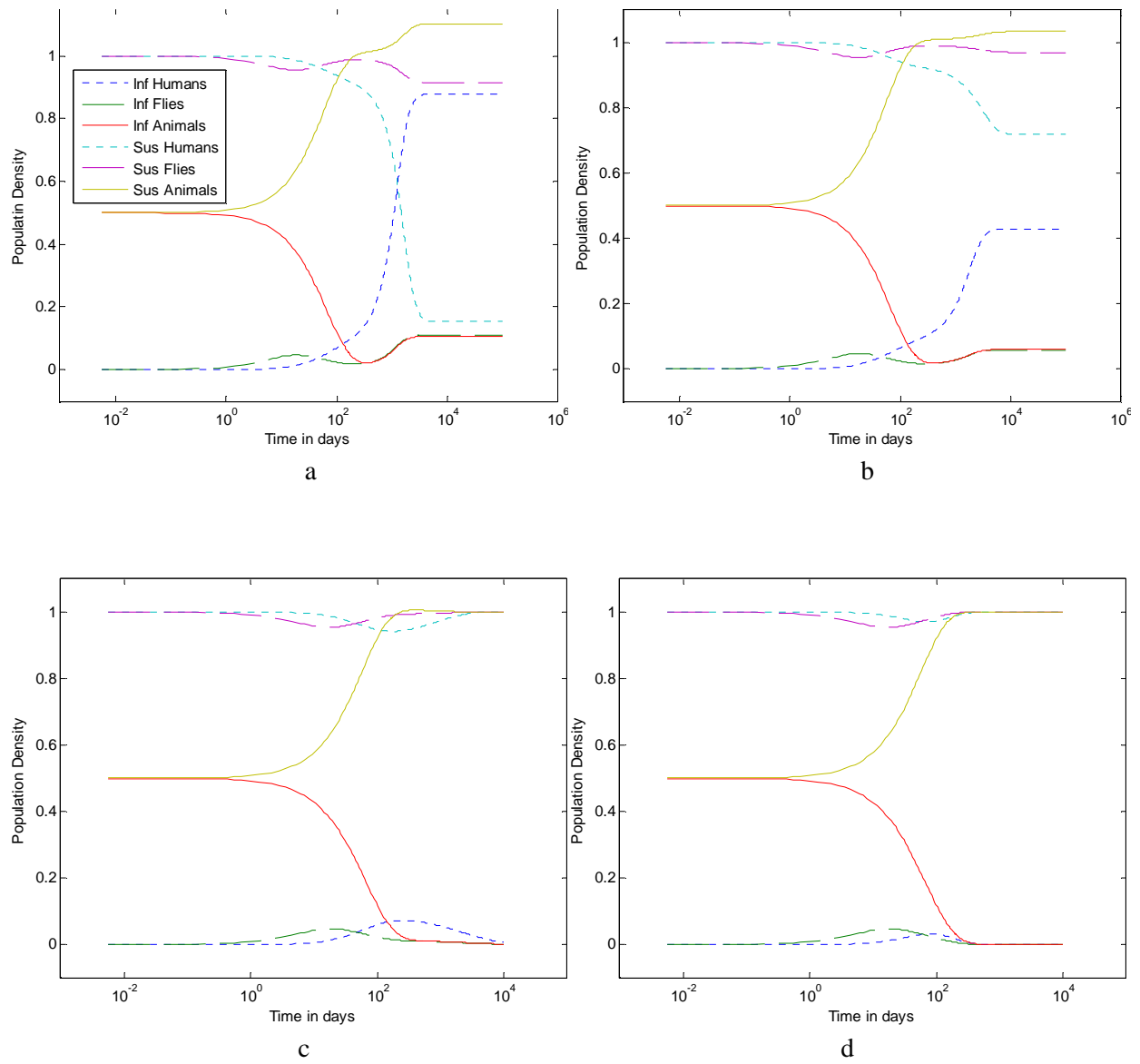


Fig 9. Varying the recovery rate of Humans (γ_h) for infective and susceptible populations. Here $\gamma_h = 0.12, 0.6, 1.2$ and 6 per year in graphs a, b, c and d respectively.

From Figures 8 (a-b) and 9 (a-b), we notice that the disease is persistent when the recovery rate is very low. Given higher recovery rates, Figures 8(c-d) and 9 (c-d) show the disease receding. Hence we notice that as the recovery rate of the human increases the model becomes more stable. Clearly Table 2 shows high recovery rates $R_0 < 1$, the disease is in recession and for low recovery rates $R_0 > 1$, the disease is endemic.

Recovery Rate of Humans(γ_h)	Animal Reproduction Number(R_{OA})	Human Reproduction Number(R_{OH})	Total Reproduction Number(R_0)
0.12	0.14	8.15	8.29
0.6	0.14	1.63	1.77
1.2	0.14	0.81	0.95
6.0	0.14	0.16	0.30

Table2. Varying the Recovery Rate of Humans(γ_h).

CASE 3:

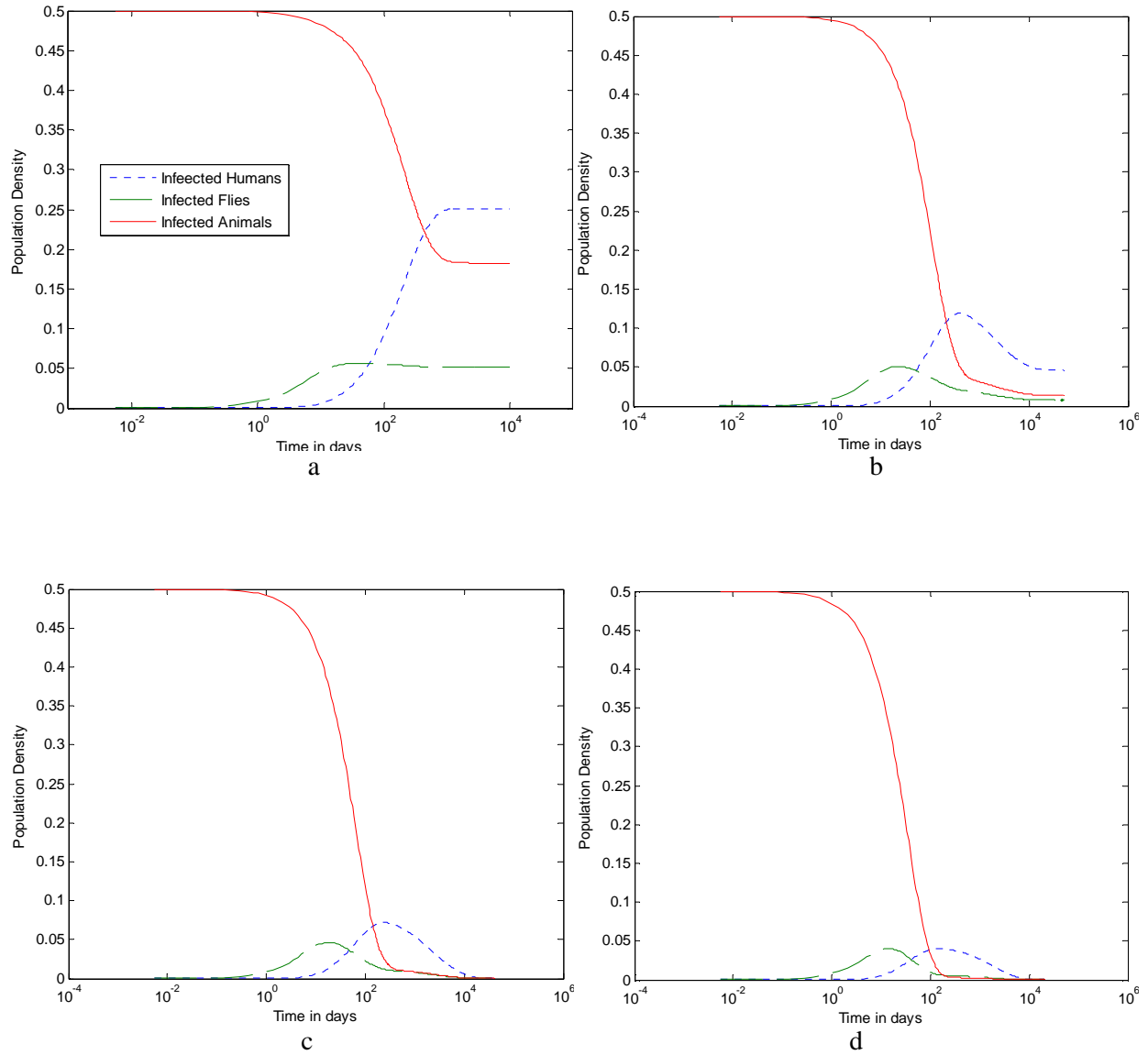


Fig 10. Changes in infective population by varying the recovery rate of Animals (γ_a) for only infective equations of human, sandfly and animal populations with respect to time., here $\gamma_a = 0.5, 2.5, 5$ and 10 per year for a, b, c and d respectively.

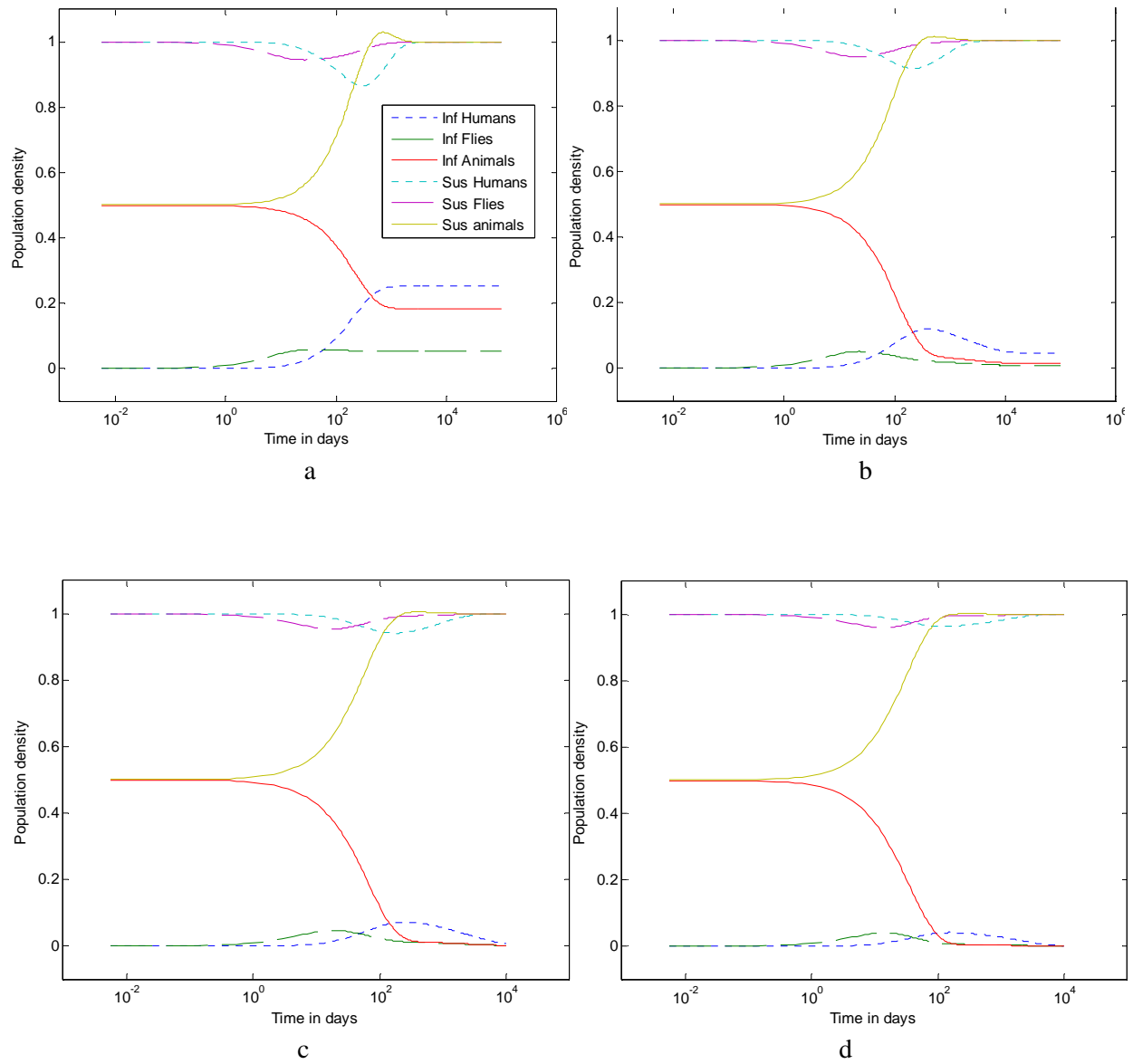


Fig 11. Changes in infective and susceptible populations by varying the recovery rate of Animals (γ_a) . Here $\gamma_a = 0.5, 2.5, 5$ and 10 per year in graph a, b, c and d respectively.

The effect of varying the animal recovery rates is similar to the human case. In Figures 10 (a-b) and 11 (a-b), we observed that the disease is endemic when the recovery rate is low. Figures 10(c-d) and 11 (c-d) show the disease receding when the animal recovery rate is high. Again we can see from Table 3 that when the recovery rates is high, $R_0 < 1$, the disease is in recession and for low recovery rates $R_0 > 1$, the disease is endemic.

Recovery Rate of Humans(γ_h)	Animal Reproduction Number(R_{OA})	Human Reproduction Number(R_{OH})	Total Reproduction Number(R_0)
0.5	0.54	0.81	1.34
2.5	0.23	0.81	1.04
5.0	0.14	0.81	0.95
10	0.07	0.81	0.88

Table3. Varying the Recovery Rate of Animals (γ_a).

4.3. NUMERICAL THRESHOLD CONDITIONS

For the parameters used in the simulations, the model shows that the disease is in recession for the following threshold values:

Human population

Biting rates till it increases to 1.04.

Probability of infection of humans till it increases to 0.32.

Population till it decreases to 4696.

Recovery rate till it decreases to 1.13/365.

Sandfly Population

Probability of infection sandfly from Human till it increases to 0.26.

Probability of infection sandfly from Animal till it increases to 0.34.

Population till it increases to 5277.

Recovery rate till it decreases to 0.9.

Death rate till it decreases to 0.9.

Animal Population

Biting rates increases of = 1.17.

Probability of infection till increase = 0.34.

Population till it decreases to 3645.

Recovery rate till it decreases to 3.3/365.

5. CONCLUSIONS

In this thesis, we have developed a heuristic SIS model for the transmission of Cutaneous Leishmaniasis which can also be used to study other vector borne diseases. The model incorporates both host and reservoir populations in addition to the vector populations. Analysis of the model shows that the disease free equilibrium is stable if the total reproduction number is less than one. The behavior of the disease under various conditions has been studied and the simulations show that the disease is endemic if reproduction number is greater than one and is in recession otherwise.

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