ສຶກສາແບບຈຳລອງທາງຄະນິດສາດສຳລັບການແຕ່ກະຈາຍຂອງ ເຊື້ອພະຍາດຊິສໂຕໂຊມາຍ ແມ່ຂອງກີ: ໃນ ສປປ ລາວ

Mathematical Study of Schistosoma Mekongi Models: Application to Laos

ໂດຍ: ນາງ ສຸກຣະດາ ຫຸ່ນລະຫວັ່ນ

ວິທະຍານິພົນລະດັບປະລິນຍາໂທ

ຫຼັກສູດປະລິນຍາໂທວິທະຍາສາດ ສາຂາ ຄະນິດສາດນຳໃຊ້

ມະຫາວິທະຍາໄລແຫ່ງຊາດ

2018

ສຶກສາແບບຈຳລອງທາງຄະນິດສາດສຳລັບການແຜ່ກະຈາຍ ຂອງເຊື້ອພະຍາດຊິສໂຕໂຊມາແມ່ຂອງກີ: ໃນ ສປປ ລາວ

Mathematical Study of Schistosoma Mekongi Models: Application to Laos

ວິທະຍານິພົນປະລິນຍາໂທວິທະຍາສາດ ສາຂາ ຄະນິດສາດນຳໃຊ້

ຊື່ ແລະ ນາມສະກຸນ ນັກສຶກສາ: ນາງ ສຸກສະດາ ທຸ່ນສະຫວັດດີ

ຊື່ ແລະ ນາມສະກຸນ ອາຈານທີ່ປຶກສາ: ປອ. ຜຸຍ ສຸກສົມຫວັງ

ສົກສຶກສາ 2017-2018

ວິທະຍານິພົນນີ້ຮັບຮອງໂດຍ:

1. ອາຈານທີ່ປຶກສາ:

ປອ. ຜຸຍ ສຸກສົມຫວັງ

ວັນທີ: 31/7/2018

ລາຍເຊັ້ນ: .....

2. ຄະນະກຳມະການປ້ອງກັນວິທະຍານິພົນ:

ຮສ. ປທ. ສັກມອນ ສິຣິສັກ (ປະທານ) .....

ປອ. ຜຸຍ ສຸກສົມຫວັງ (ຮອງປະທານ) .....

ປອ. ລີຊັດເຕີ ລີເລ່ຍນູ (ກຳມະການ) .....

3. ຄະນະບໍດີຄະນະວິທະຍາສາດທຳມະຊາດ:

ວັນທີ: 02 AUG 2018

ລາຍເຊັ້ນ: .....ຮສ.ປອ.ບຸນຜັນ ຕົ້ນແພງ

Mathematical study of Schistosoma Mekongi models: Application to Laos

Souksada Tounsavathdy

Master of Sciences
Mathematics

Faculty of Natural Sciences
National University of Laos

2018

Mathematical study of Schistosoma Mekongi models: Application to Laos

Master of Sciences
Mathematics

Souksada Tounsavathdy

Supervised by:

Dr. Phoui Souksomvang

Prof. Dr. Youcef Mammeri, University of Picardie Jules Verne, Amiens, France

Prof. Dr. Joaquim M.C Correia, University of Evora, Portugal

Edited by:

Assoc. Prof. Sackmone Sirisack

Period of Dissertation: October 2017 to May 2018

Dissertation Certification:

Supervised by:

Dr. Phoui Soksomvang .....

Prof. Dr. Youcef Mammeri .....

Prof. Dr. Joaquim M.C Correia .....

Edited by:

Assoc.Prof. Sackmone Sirisack .....

Prepared by:

Souksada Tounsavathdy

This thesis was defended on July 17, 2018 at National University of Laos

Committee:

Assoc. Prof. Sackmone Sirisack .....

Dr. Lisatteur Lilianou .....

Dr. Phoui Souksomvang .....

Dean of Faculty of Natural Sciences
National University of Laos
Date: 02 AUG 2018

Signature

Assoc.Prot.Dr.Bounphanh TONPHENG

Abstract:
We study different models of Schistosomiasis transmission a water borne disease. Modeling tools as well as analysis of differential equations are presented and various scenarios are simulated (with Python).

Keywords:
Schistosomiasis, Macdonald, Ross, Cauchy problem, Equilibrium, Stability, Progressive wave, Python.

Acknowledgements

First and foremost, I would like to express my deep gratitude to Dr. Phoui Souksomvang and Prof. Dr. Youcef Mammeri who are my local and foreign dissertation supervisors respectively, for their patient guidance, enthusiastic encouragement. That is to say, this work would have been impossible without their kind support. Besides, I would also express my great appreciation to Prof. Joaquim M.C Correia and Ass. Prof. Sackmone Sirisack who have encouraged me to study master and exchange in University of Evora, Portugal under European Union Programme, Erasmus Mundus EMMA-EAST 2014.

I would also like to extend my thanks to all the teachers of Department of Mathematics, Faculty of Natural Sciences for their effort to offer the effective courses, especially my seniors namely, Bouasy Doungsavanh Khankham Vongsavang who always give me the favor whenever I meet the problems on my work.

Finally, I could not forget to thank my parents, whose love are with me in whatever I pursue, they give me infinite spirit.

Contents

Chapter 1

Introduction

Schistosoma mekongi is first reported in 1957 and prevalent in the Mekong river basin from the Khong district in southern Laos to Kratie province in northern Cambodia. The total population at risk for schistosomiasis mekongi is estimated as 60,000 in Laos. Schistosoma mekongi can be parasitic in various mammalian hosts such as humans, dogs, and pigs. Neotricula aperta, an aquatic snail is known to be the intermediate host of S. mekongi. It was observed that the water level of the Mekong river fluctuates seasonally; the period of low water lasts from February to May, while that of high water lasts from June to January. The transmission of S. mekongi from snails to humans occurs during the low water period because water contact of humans is practicable.

Mathematical models are useful to predict the effect of various control measures on suppression of infectious diseases. Macdonald (Macdonald, 1965) proposed a first mathematical model for the transmission of schistosomiasis, and thereafter a number of mathematical models for schistosomiasis transmission have been published. Chan et al. (Chan et al., 1995) constructed an age-structured model for schistosoma mansoni transmission to predict the prevalence and morbidity for the long-term consequences of drug treatment. Ishikawa et al. (Ishikawa, Ohmae, Pangilinan, Redulla, & Matsuda, 2006) developed a model of schistosoma japonicum transmission that took account of a seasonal variation of snail density to predict the effect of control measures in the Philippines. They previously proposed a mathematical model for the transmission of S. mekongi in Cambodia that was described by a system of partial differential equations of time and age, which was aimed at estimating the coverage rate and range of ages in targeted mass treatment to interrupt schistosomiasis transmission.

Objectives

Our aims are:

- In terms of mathematics: to familiarize with modeling and standard tools for the analysis of differential equations;
- In terms of scientific computing: to simulate various scenarios of transmission with Python;

- In terms of biology: to understand the water borne disease (Schistosomiasis) transmission.

Relative Researches

Some researches about Schistosoma mekongi occuring in the south of Laos were performed. In particular, we may cite:

1. K. Fukuhara, S. Phompida, S. Insisiengmay, M. Kirinoki, Y. Chigusa, S. Nakamura, H. Matsuda, and H. Ishikawa, *Analysis of the effectiveness of control measures against Schistosoma mekongi using an intraand inter-village model in Champasak Province, Lao PDR*, Parasitology International 60,4 (2011) 452-445.

2. N. Hisakane, M. Kirinoki, Y. Chigusa, M. Sinuon, D. Sochea, H. Matsuda, and H. Ishikawa, *The evaluation of control measures against Schistosoma mekongi in Cambodia by a mathematical model*, Parasitology International 57,3 (2008) 379-385.

Methodology

The methodology used in this dissertation is based on the following strategy:

- Existence and uniqueness are established according to the Cauchy-Lipschitz theorem:

  Theorem 1.0.1 ***(Cauchy-Lipschitz, Picard-Lindelöf)*** *Let $f : I \times \mathbb{R}^n$ a continuous function and locally Lipschitz with respect to the second variable (for $||u-v|| \leq \delta$, $||f(t,u) - f(t,v)|| \leq L||u-v||$). Then there exits $T > 0$ and a unique solution of the differential equation*

  $$u'(t) = f(t, u(t)),$$

  of class $\mathcal{C}^1$ on $]0, T[$ with $u(0) = u_0$. Moreover if $f \in \mathcal{C}^k$ then $u \in \mathcal{C}^{k+1}$.

- The stability of equilibrium (stationary point such that $f(u^*) = 0$) with respect to sign of the eigenvalues of Jacobian matrix $Jf(u^*)$ thanks to the Routh-Hurwitz theorem:

  Theorem 1.0.2 ***(Routh-Hurwitz)*** *Let u^* an equilibrium.*

  1. *If every eigenvalue of $Jf(u^*)$ has a negative real part, then $\lim_{t\to+\infty} u(t) = u^*$ (u^* is said asymptotically stable).*
  2. *If there is one eigenvalue of $Jf(u^*)$ with a positive real part, then u^* is said unstable.*

- Numerical simulations with Python.

Details about these theorems and Python codes are provided inside the appendices.

Chapter 2

Description of the Schistosomiasis

Human schistosomiasis is a family of diseases caused primarily by five species of genus *Schistosoma* flatworms. The parasites, schistosomes, have to go through an intermediate host (snails in most cases) to complete their life cycle: from eggs, to miracidia, to cercaria, finally to adult worms. The aldult worms inhabit the blood vessels lining either in the bladder or intestine, depending on the species of worm. The worms are also known as blood flukes.

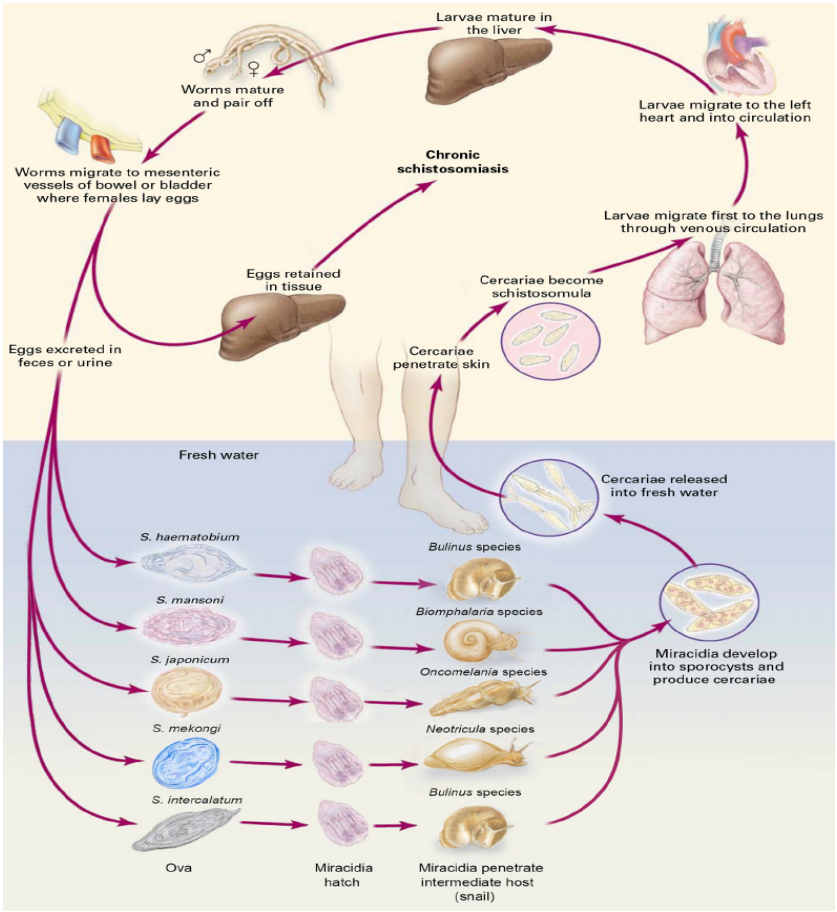


Figure 2.1: The Life Cycle of Schistosomiasis (Li et al., 2000).

The worldwide prevalence of schistosomal infections has not been measured credibly. A figure conventionally cited is 200 million people. Except for imported case, the disease is virtually unknown in the rich countries of the world. There is little doubt that all schistosomes cause considerable pathological change in a comparatively large proportion of the population. Evidences suggest that only a proportion of affected people die from the disease. The absence of quantitative information on health fairly reflects the information available.

Schistosomiasis is characterized by a long-term disability and is thought to significantly impede the advancement of many underdeveloped countries where the disease is endemic. Due to successful control projects, the distribution of schistosomiasis has changed in the last 50 years. However, the total number of people infected or at risk of infection has not changed (Chitsulo, Engels, Montresor, & Savioli, 2000; Ghiboda, Engels, & Berquist, 2000). The public health impact and magnitude of the problem are evident from information available from the World Health Organization (Organization, 1993): more than 600 million people in 74 countries are at risk and more than 200 million people are infected (increased from 114 million in 1974). Mortality exceeds 100,000 annually. Schistosomiasis remains formidable to humans because of the complexities of parasitic adjustment to two or more different hosts (Garrett, 1994; McNeill, 1977). The persistence of a schistosomiasis infection in a locality depends on a complex cycle involving humans and possibly additional mammalian species (definite hosts), certain parasitic flatworms (schistosomes), and particular species of snails (intermediate hosts). The adult schistosome worms mate heterosexually. The paired adults reproduce in the blood vessels of a human or mammalian host. The fertilized eggs pass from the blood into the intestine or bladder and are voided with the feces or urine.

Because of low hygienic standards, some of the eggs are deposited in fresh water where small ciliated larvae (miracidia) emerge and enter a molluscan host. By asexual reproduction in the snail, thousands of a second larval form, cercariae, are produced. When mature, the cercariae enter a free-swimming stage and on contact with a human, they rapidly penetrate the skin and mature into juvenile schistosomes. This is followed by pairing with the opposite sex, copulation, and oviposition which begins the cycle over again.

Human schistosomiasis is caused by five species of flatworms: *Schistosoma Mansoni, Schistosoma Intercalatum, Schistosoma Japonicum, Schistosoma Mekongi, and Schistosoma Haematobium*. The three most widespread are Schistosoma Japonicum which is found in several Asian countries, Schistosoma Haematobium which is present in much of Africa and the Middle East, and Schistosoma Mansoni which is prevalent in much of Africa, the Caribbean, and South America. It is well known that Schistosoma Japonicum has multiple mammalian definite hosts (Li et al., 2000; Wu & Feng, 2002).

Schistosoma Mekongi

Schistosoma Mekongi is first reported in 1957 and prevalent in the Mekong River basin from the Khong district in southern Laos to Kratie province in northern Cambodia. The total population at risk for schistosomiasis mekongi is estimated as 60,000 in Laos and 80,000 in Cambodia. Schistosoma mekongi can be parasitic in various mammalian hosts

such as humans, dogs, and pigs. *Neotricula aperta, an aquatic snail* is known to be the intermediate host of S. mekongi. It was observed that the water level of the Mekong River fluctuates seasonally; the period of low water lasts from February to May, while that of high water lasts from June to January. The transmission of S. mekongi from snails to humans occurs during the low water period because water contact of humans is practicable.

Figure 2.2: Neotricula Aperta and Aquatic Snail.

In Cambodia, a control program of annual mass drug administration was initiated by the Ministry of Health and Médecins Sans Frontières in 1995 (present program conductor: National Center for Parasitology, Entomology and Malaria Control). Sasakawa Memorial Health Foundation (SMHF) joined the cooperative program in 1997, and mainly took charge of examination of animal reservoirs, serodiagnostic surveys, and evaluation of morbidity using ultrasound. The control programs in Cambodia are considered to be successful because of the low level of detection of egg positive cases in recent years, although there remains a high positive rate in several villages where S. mekongi is endemic. In Laos, the average prevalence of schistosomiasis mekongi among the villages decreased to less than 1 percent after six courses of mass treatment with praziquantel during a 10-year control program, which resulted in a cessation of the control program in 1999. Thereafter, the resurgence of schistosomiasis in the Khong district of Laos was confirmed by epidemiological surveys by WHO in 2003, and it was revealed that the prevalence was restored to 20-50 percent in the same area. The situation of re-emergence of Schistosoma mekongi in Laos indicates the necessity for the continuation of both surveillance and control programs, which are required in order to adopt more cost-effective measures.

Chapter 3

Study of Time Dependent Models

3.1 The Macdonald Model

This model was introduced by Macdonald (Macdonald, 1965) in 1965. It is the first mathematical model for the transmission of Schistosomiasis. The transmission of Schistosomiasis can be thought of as a closed loop, in which infection travels from definitive hosts to snails and back again (see Figure 3.1). Any such closed feedback loop which exhibits stability, here the existence of endemic Schistosomiasis, has to have a nonlinear transfer somewhere in the cycle. The first of these statements is trite; the second shows the power of mathematics in demonstrating the consequences of such simple statements. The concrete meaning of a nonlinear transfer is that there must at some stage be a density dependent effect, an interaction between infective units, which reduces the infectivity of each individual as the overall level of infection increases a manifestation of diminishing returns. Since these effects are responsible for the stability of the cycle, it is extremely important to represent them faithfully in any model: indeed, the correct specification of the density dependent effects is likely to be the most critical part of the modeling process.

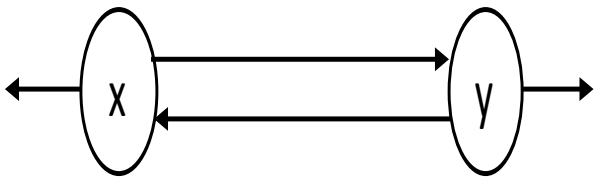


Figure 3.1: Compartimental representation of Macdonald's model.

In terms of mathematics, the variation of the total number of infected snails (s_i) due to the number of parasites (p) is solution of the following ordinary differential equation (Macdonald, 1965; Barbour, 1994):

$$p'(t) = \alpha\delta\left(\frac{s_i(t)}{s}\right)h - \gamma p(t) \tag{3.1}$$

$$s_i'(t) = \beta p(t)\left(1 - \frac{s_i(t)}{s}\right) - \mu s_i(t) \tag{3.2}$$

$$h'(t) = 0. \tag{3.3}$$

Parameters appearing in these equations are sum up into Table 3.1.

Symbol	Description
p	total number of parasite
s_i	total number of infected snails
h	a total number of definitive hosts
s	total number of snail
α	rate of exposure to water
β	force of infection
μ	death rate of the snails
σ	density of definitive hosts
δ	density of snails
γ	death rate of parasite
$s - s_i$	total number of non-inflected snails

Table 3.1: Parameters of the Macdonald model.

Let

$$x = \frac{p}{h} = \frac{\text{number of parasites}}{\text{number of definitive hosts}}$$

be the average parasistes burden in the definitive hosts, and

$$y = \frac{s_I}{s} = \frac{\text{number of infected snails}}{\text{number of snails}}$$

be the prevalence of infection in the population of snails. Then we obtain

$$x'(t) = \alpha\delta y(t) - \gamma x(t) \tag{3.4}$$

$$y'(t) = \beta\frac{\sigma}{\delta}x(t)(1 - y(t)) - \mu y(t). \tag{3.5}$$

3.1.1 Qualitative Study

Since there is no explicit solution, we study the qualitative properties of the solution of the differential equation.

Theorem 3.1.1 *Let (x_0, y_0) be non negative. Then there exits $T > 0$ and a unique solution of the differential equation $(x, y) \in \mathcal{C}([0, T]; \mathbb{R}) \times \mathcal{C}([0, T]; \mathbb{R})$ associated to the initial datum (x_0, y_0).*

Proof: We rewrite (3.4) and (3.5) as

$$u'(t) = f(t, u(t)),$$

where

$$u = \begin{pmatrix} x \\ y \end{pmatrix}, f(t,u) = \begin{pmatrix} \alpha\delta y - \gamma x \\ \beta\frac{\sigma}{\delta}x(1-y) - \mu y \end{pmatrix}.$$

The function f is $\mathcal{C}^\infty$ in particular f is locally Lipschitz with respect to u. The Cauchy-Lipschitz theorem B.1.3 allows to conclude. □

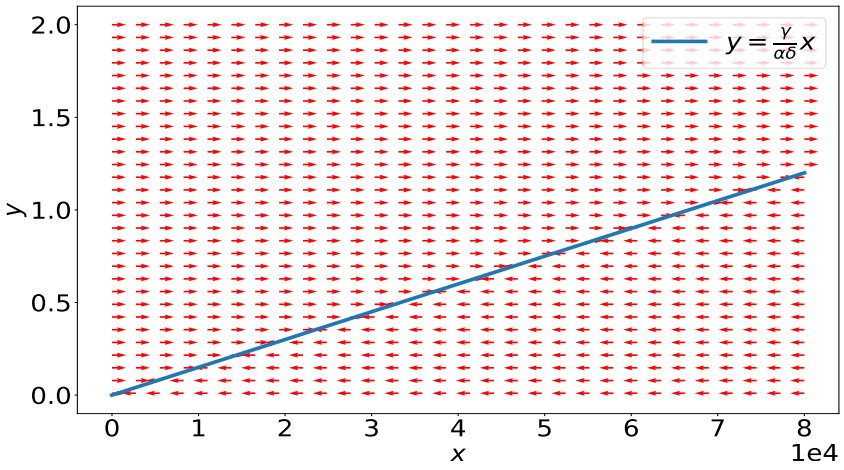
Corollary 3.1.2 *Let $(x_0, y_0) > 0$. Then the solution $(x(t), y(t))$ remains positive and bounded for all the time. In particular, the solution id global in time, i.e. $T = +\infty$.*

Proof: The proof bases on the phase portrait (Figure 3.2C) using that the function $(0, 0)$ is solution and the uniqueness given by the previous theorem noticing that

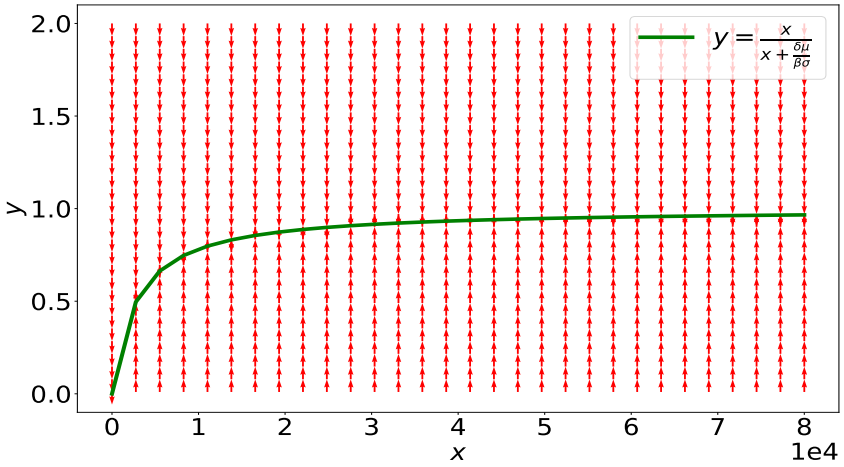
$$\begin{aligned} x' &= \alpha\beta y - \gamma x > 0 \text{ if } y > \frac{\gamma x}{\alpha\delta} \quad \text{(Fig. 3.2A)} \\ y' &= \beta\frac{\sigma x}{\delta}(1-y) - \mu y > 0 \text{ if } y < \frac{x}{x + \frac{\delta\mu}{\beta\sigma}} \quad \text{(Fig. 3.2B).} \end{aligned}$$

□

A.



B.



C.

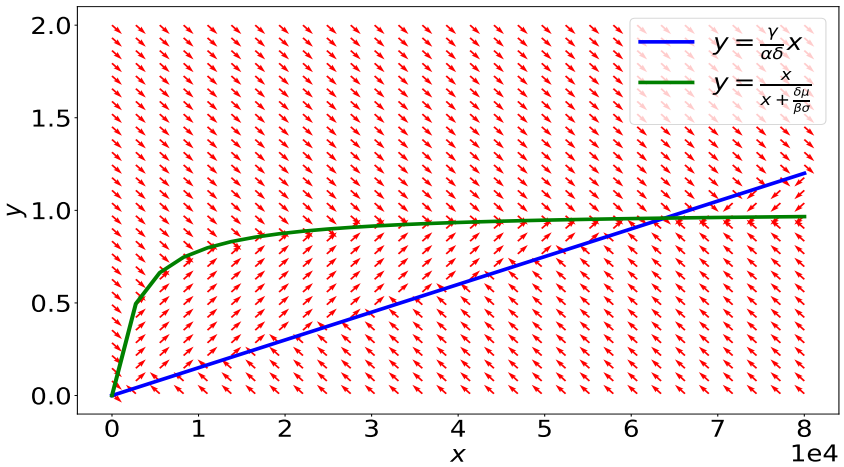


Figure 3.2: Phase portrait of Macdonald's model.

Knowing that the initial value problem is well posed, we compute the equilibrium. The equilibrium (x^*, y^*) are the solution of

$$\begin{cases} \alpha\delta y^* - \gamma x^* = 0 \\ \beta\frac{\sigma}{\delta}x^*(1-y^*) - \mu y^* = 0 \end{cases} \Leftrightarrow \begin{cases} y^* = \frac{\gamma}{\alpha\delta}x^* \\ y^* = \frac{x^*}{x^* + \frac{\delta\mu}{\beta\sigma}} \end{cases}$$

Then

$$\frac{\gamma}{\alpha\delta}x^* = \frac{x^*}{x^* + \frac{\delta\mu}{\beta\sigma}}$$

We have

$$x^* = 0, x^* = \frac{\alpha\delta}{\gamma} - \frac{\delta\mu}{\beta\sigma}$$

which is of biological interest if $\frac{\alpha\delta}{\gamma} - \frac{\delta\mu}{\beta\gamma} \geq 0$.
The Jacobian is defined for $(x, y)'(t) = \begin{pmatrix} f(x,y) \\ g(x,y) \end{pmatrix}$ by

$$J(x^*, y^*) = \begin{pmatrix} \frac{\partial f}{\partial x} & \frac{\partial f}{\partial y} \\ \frac{\partial g}{\partial x} & \frac{\partial g}{\partial y} \end{pmatrix} = \begin{pmatrix} -\gamma & \alpha\delta \\ \frac{\beta\gamma}{\delta}(1-y^*) & -\frac{\beta\gamma}{\delta}x^* - \mu \end{pmatrix}.$$

We deduce for the first equilibrium $(0, 0)$

$$J(0,0) = \begin{pmatrix} -\gamma & \alpha\delta \\ \frac{\beta\sigma}{\delta} & -\mu \end{pmatrix},$$

and

$$\begin{aligned} \mathrm{tr}J(0,0) &= -(\gamma + \mu) < 0 \\ \det J(0,0) &= \gamma\mu - \alpha\beta\sigma \end{aligned}$$

The Routh-Hurwitz theorem B.2.2 implies that the equilibruim $(0, 0)$ is

1. a saddle point if $\det J(0,0) < 0$,
2. asymptotically stable if $\det J(0,0) > 0$, i.e. $\gamma\mu - \alpha\beta\sigma > 0 \quad (A)$

Moreover, since

$$(\mathrm{tr}J)^2 - 4\det J > 0 \Leftrightarrow (\gamma + \mu)^2 - 4(\gamma\mu - \alpha\beta\sigma) > 0,$$

the equilibrium $(0, 0)$ is a stable focus.
Similarly for the positive equilibrium

$$(x^*, y^*) = \left(\frac{\alpha\delta}{\gamma} - \frac{\delta\mu}{\beta\sigma}, 1 - \frac{\gamma\mu}{\alpha\beta\sigma}\right),$$

we have

$$J(x^*, y*) = \begin{pmatrix} -\gamma & \alpha\delta \\ \frac{\gamma\mu}{\alpha\delta} & -\frac{\beta\sigma x^*}{\delta} - \mu \end{pmatrix}.$$

Here

$$\mathrm{tr}J = -(\gamma+\mu) - \frac{\beta\gamma}{\delta}x^* < 0$$
$$\det J = \gamma\left(\frac{\beta\sigma}{\delta}x^* + \mu\right) - \gamma\mu = \frac{\gamma\beta\sigma}{\delta}x^* > 0 \quad (B)$$

and (x^*, y^*) is asymptotically stable.
Moreover, since

$$(\mathrm{tr}J)^2 - 4\det J > 0$$
$$\left((\gamma+\mu) + \frac{\beta\sigma}{\delta}x^*\right)^2 - 4\frac{\gamma\beta\sigma}{\delta}x^* = \left(\gamma - \frac{\beta\sigma}{\delta}x^*\right)^2 + \delta\mu\gamma + \mu^2$$

and (x^*, y^*) is a stable focus.
This study can be summarized in terms of basic reproduction number as follows.

Theorem 3.1.3 *Let R_0 be the basic reproduction number defined as*

$$R_0 = \frac{\alpha\beta\sigma}{\gamma\mu}.$$

1. *If $R_0 > 1$, the disease is endemic.*
2. *If $R_0 \leq 1$, the disease disapears.*

Proof: It is enough to rewrite the conditions (A) and (B) as

(A) $\gamma\mu - \alpha\beta\sigma > 0 \Leftrightarrow \frac{\alpha\beta\sigma}{\gamma\mu} < 1$

(B) $\frac{\gamma\beta\sigma}{\delta}x^* = \frac{\gamma\beta\sigma}{\delta}\left(\frac{\alpha\delta}{\gamma} - \frac{\delta\mu}{\beta\sigma}\right) > 0 \Leftrightarrow \frac{\alpha\beta\sigma}{\gamma\mu} > 1.$

□

3.1.2 Numerical Simulations

The values of parameters are chosen from (Hisakane et al., 2008) reflecting data from North of Cambodia.

α	rate of exposure to water	1
β	force of infection	10^{-4}
μ	death rate of the snails	7×10^{-3}
σ	density of definitive hosts	1
δ	density of snails	40
γ	death rate of parasite	6×10^{-4}

Simulations are made during 25 years with a time step equal to 1 day. Figure 3.3 represents the evolution with respect to day of x and y. Here $R_0 = \frac{\alpha\beta\sigma}{\gamma\mu} = \frac{1\times10^{-4}\times1}{6\times10^{-4}\times7\times10^{-3}} = \frac{1000}{42} > 1$ and the epidemic occurs.

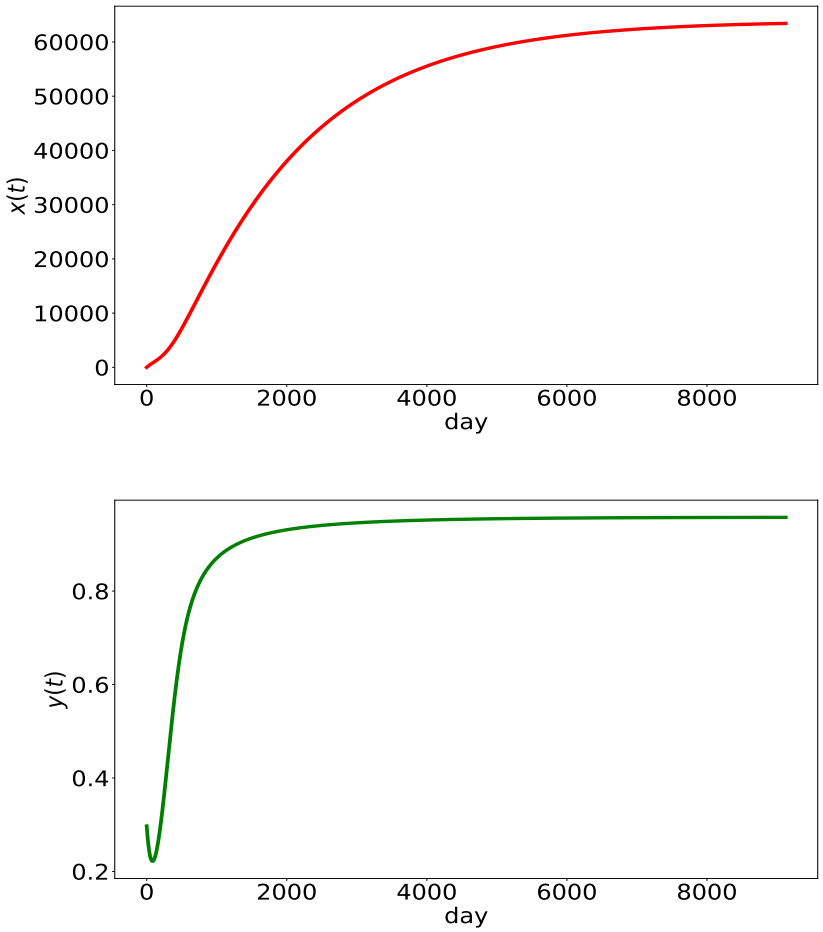


Figure 3.3: Evolution with respect to day of x and y.

To control the epidemic, it is necessary to provide $R_0 = \frac{\alpha\beta\sigma}{\gamma\mu}$ smaller than 1. To do that, it is allowed to:

- increase μ using pesticides to reduce the number of snails;
- increase γ by killing parasites inside hosts with drugs;
- decrease α by change the behavior of people who should avoid contact with dirty water.

In Figure 3.4, we show the value of equilibrium (x^*, y^*) for different values of μ. We notice that when $R_0 < 1$, the disease disappears.

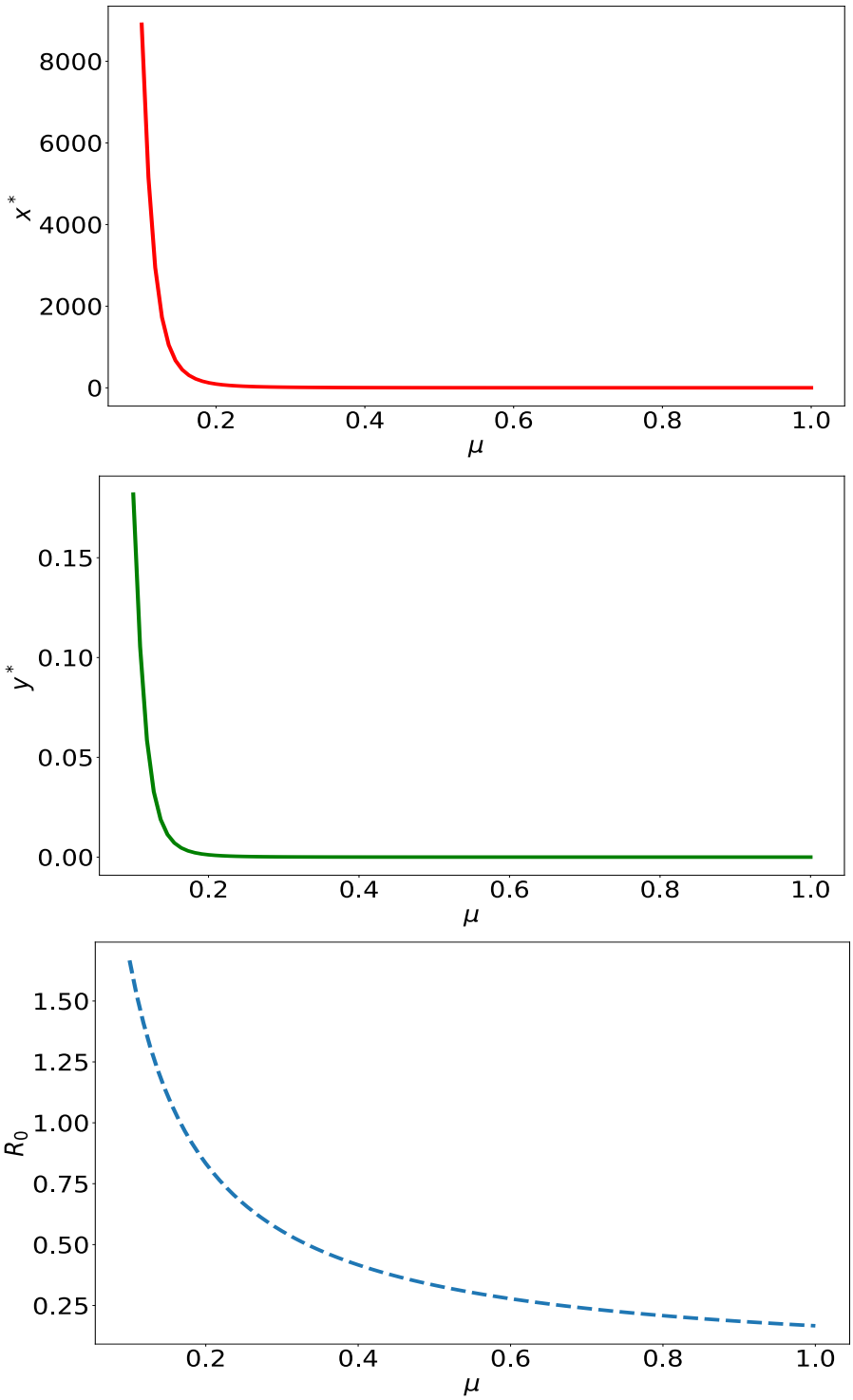


Figure 3.4: Bifuraction with respect to μ the mortality rate of snails.

3.2 Ross'Model

Suppose that the definitive hosts, like the snails, come only in two sorts, infected and uninfected, with the infectivity of an infected definitive host not being influenced by the number of times he may subsequently have been infected or by his current parasite burden. Assume also that infected definitive hosts have a *per capita* recovery rate of g, which is fixed, whatever the infection history of the host. This might, for instance, plausibly be the case with perfect concomitant immunity. Upon recovery, the definitive host is taken to become once more normally susceptible to infection. Host lifetimes are tacitly assumed to be negative exponentially distributed, mortality being exactly compensated by births of new susceptibles, the mortality rate being subsumed into the recovery rate g. Once again, these assumptions are highly oversimplified, but present a feasible starting point for models incorporating density-dependent effects arising in the human host.

Reasoning in the same way as for Macdonald's model, we translate these model assumptions into a system of ordinary differential equations. The relevant variables for the transmission are now J, the number of infected hosts, and Y, the number of infected snails and satisfy the following differential equations (Macdonald, 1965; Barbour, 1994):

$$J'(t) = a\delta\frac{Y(t)}{N}(H - J(t)) - gJ(t) \tag{3.6}$$

$$Y'(t) = bJ(t)\left(1 - \frac{Y(t)}{N}\right) - \mu Y(t) \tag{3.7}$$

Parameters appearing in these equations are sum up into Table 3.2.

Symbol	Description
H	total number of definitive hosts
N	total number of snail
a	rate of incidence for one single definitive host
b	rate of snail infections
g	recovery rate for definitive host infections
μ	death rate of the snails
σ	density of infinitive hosts
δ	density of snails

Table 3.2: Parameters of the Ross model.

Consider

$$x = \frac{J}{H} = \frac{\text{number of parasites}}{\text{number of definitive hosts}}$$

the average parasistes burden in the definitive hosts, and

$$y = \frac{Y}{N} = \frac{\text{number of infected snails}}{\text{number of snails}}$$

the prevalence of infection in the population of snails provides

$$x'(t) = a\delta y(t)(1 - x(t)) - gx(t) \tag{3.8}$$

$$y'(t) = b\frac{\sigma}{\delta}x(t)(1 - y(t)) - \mu y(t). \tag{3.9}$$

3.2.1 Qualitative Study

Theorem 3.2.1 *Let (x_0, y_0) be non negative. Then there exits $T > 0$ and a unique solution of the differential equation $(x, y) \in \mathcal{C}([0, T]; \mathbb{R}) \times \mathcal{C}([0, T]; \mathbb{R})$ associated to the initial datum (x_0, y_0).*

Proof: We rewrite (3.8) and (3.9) as

$$u'(t) = f(t, u(t)),$$

where

$$u = \begin{pmatrix} x \\ y \end{pmatrix}, f(t, u) = \begin{pmatrix} a\delta y(1-x) - gx \\ b\frac{\sigma}{\delta}x(1-y) - \mu y \end{pmatrix}.$$

The function f is $\mathcal{C}^\infty$ in particular f is locally Lipschitz with respect to u. The Cauchy-Lipschitz theorem B.1.3 allows to conclude.

□

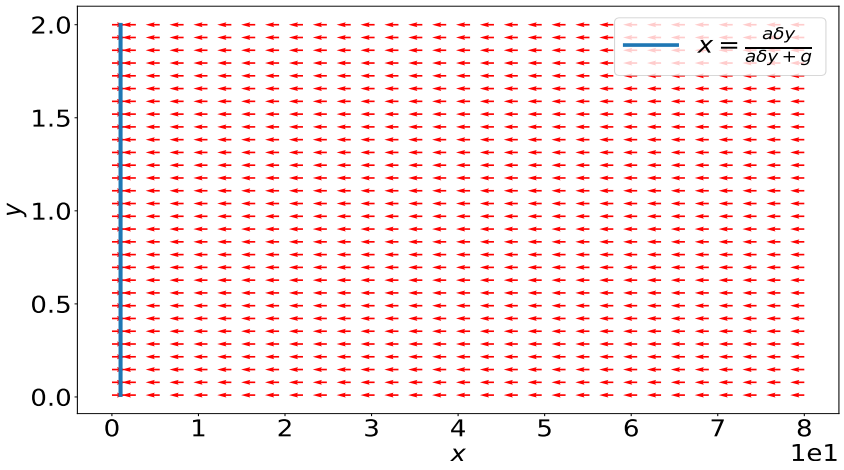
Corollary 3.2.2 *Let $(x_0, y_0) > 0$. Then the solution $(x(t), y(t))$ remains positive and bounded for all the time. In particular, the solution id global in time, i.e. $T = +\infty$.*

Proof: The proof bases on the phase portrait (Figure 3.5C) using that the function $(0, 0)$ is solution and the uniqueness given by the previous theorem. We note that

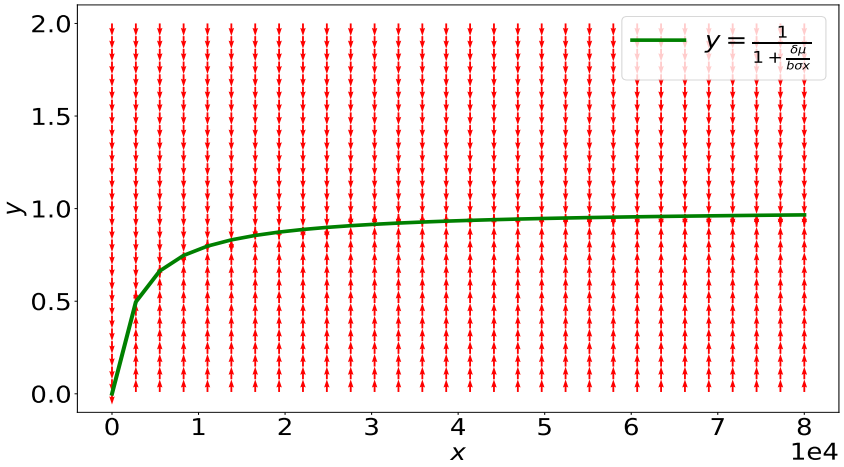
$$a\delta y(1-x) - gx > 0 \text{ if } x < \frac{a\delta y}{a\delta y + g} \text{ and } x \neq 1 \text{ (Fig. 3.5A)}$$
$$b\frac{\sigma}{\delta}x(1-y) - \mu y > 0 \text{ if } y < \frac{1}{1 + \frac{\mu\delta}{b\sigma x}} \text{ and } y \neq 1 \text{ (Fig. 3.5B).}$$

□

A.



B.



C.

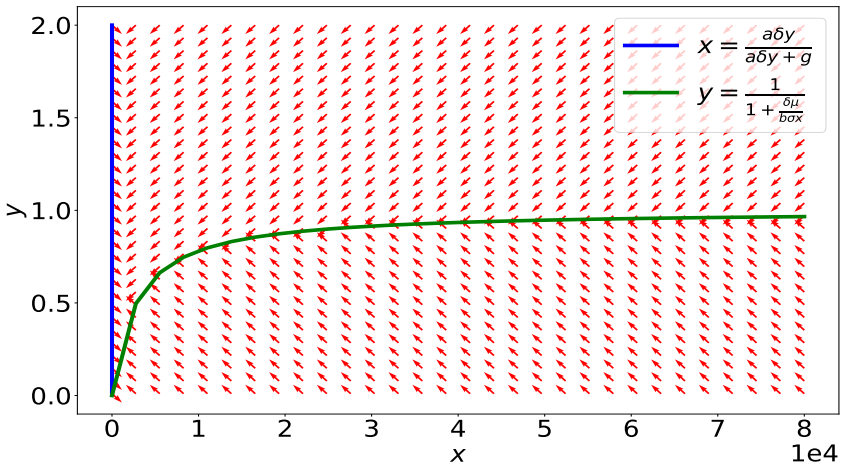


Figure 3.5: Phase portrait of Ross' model.

The equilibrium (x^*, y^*) are the solution of

$$\begin{cases} a\delta y^*(1-x^*) - gx^* = 0 \\ b\frac{\sigma}{\delta}x^*(1-y^*) - \mu y^* = 0 \end{cases}$$

which gives

$$\begin{cases} x^* = \frac{a\sigma y}{a\sigma y + g} \text{ and } x^* \neq 1 \\ y* = \frac{1}{1+\frac{\mu\delta}{b\sigma x}} \text{ and } y^* \neq 1. \end{cases}$$

The Jacobian is for $(x,y)'(t) = \begin{pmatrix} f(x,y) \\ g(x,y) \end{pmatrix}$

$$J(x^*, y^*) = \begin{pmatrix} \frac{\partial f}{\partial x} & \frac{\partial f}{\partial y} \\ \frac{\partial g}{\partial x} & \frac{\partial g}{\partial y} \end{pmatrix} = \begin{pmatrix} -a\delta y - g & a\delta(1-x) \\ b\frac{\sigma}{\delta}(1-y) & -b\frac{\sigma}{\delta}x - \mu \end{pmatrix}.$$

Then

$$J(0,0) = \begin{pmatrix} -g & a\delta \\ b\frac{\sigma}{\delta} & -\mu \end{pmatrix},$$

and

$$\begin{aligned} \mathrm{tr}J(0,0) =& -(g+\mu) < 0 \\ \det J(0,0) =& g\mu - ab\sigma. \end{aligned}$$

The equilibruim $(0,0)$ is

1. a saddle point if $\det J(0,0) < 0$
2. asymptotically stable if $\det J(0,0) > 0$, i.e. $g\mu - ab\sigma > 0 \quad$ (C).

Moreover, since

$$(\mathrm{tr}J)^2 - 4\det J > 0 \Leftrightarrow (g+\mu)^2 - 4(g\mu - ab\sigma) > 0,$$

$(0,0)$ is a stable focus.

Theorem 3.2.3 *Let R_0 be the basic reproduction number defined as*

$$R_0 = \frac{ab\sigma}{g\mu}.$$

1. *If $R_0 > 1$, the disease is endemic.*
2. *If $R_0 \leq 1$, the disease disappears.*

Proof: It is enough to rewrite the conditions (C)

$$g\mu - ab\sigma > 0 \Leftrightarrow \frac{ab\sigma}{g\mu} < 1.$$

□

3.2.2 Numerical Simulations

The values of parameters are chosen from (Hisakane et al., 2008) reflecting data from North of Cambodia.

a	rate of incidence for one single definitive host	1
b	rate of snail infections	10^{-4}
μ	death rate of the snails	7×10^{-3}
σ	density of definitive hosts	1
δ	density of snails	40
g	recovery rate for definitive host infections	5×10^{-4}

Simulations are made during 25 years with a time step equal to 1 day. Figure 3.6 represents the evolution with respect to day of x and y. Here $R_0 = \frac{ab\sigma}{g\mu} = \frac{1\times10^{-4}\times1}{5\times10^{-4}\times7\times10^{-3}} = \frac{1000}{35} > 1$ and the epidemic occurs.

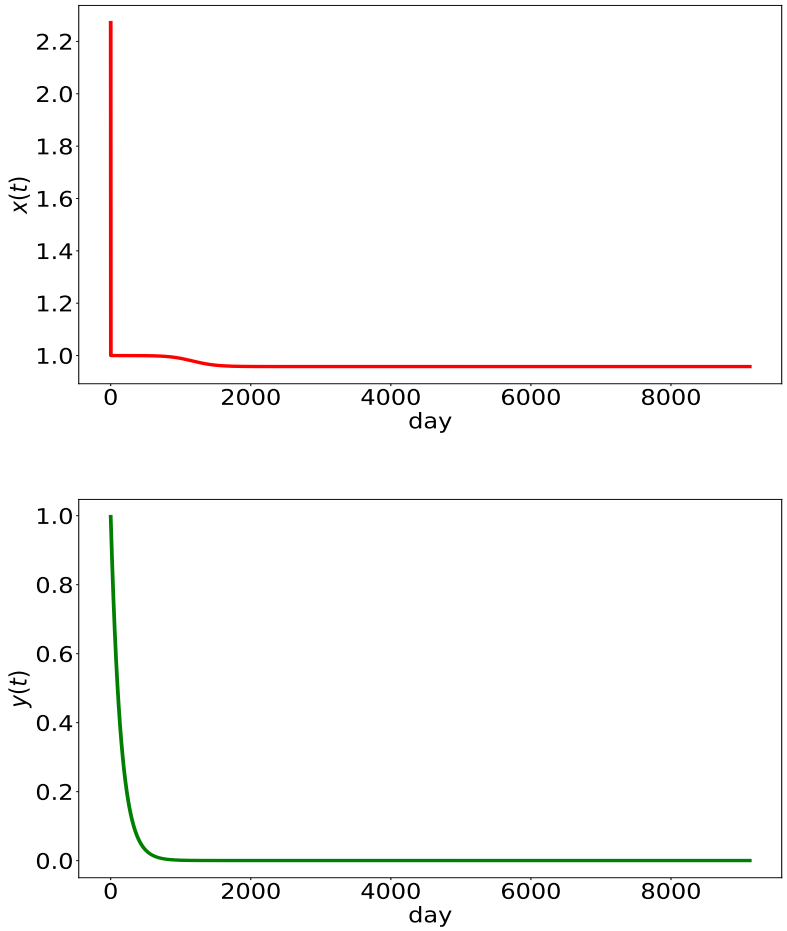


Figure 3.6: Evolution with respect to day of x and y.

To control the epidemic, it is necessary to provide $R_0 = \frac{ab\sigma}{g\mu}$ smaller than 1. To do that, it is allowed to:

- increase μ using pesticides to reduce the number of snails;
- increase g by killing parasites inside hosts with drugs;
- decrease a by change the behavior of people who should avoid contact with dirty water.

In Figure 3.7, we show the value of equilibirum (x^*, y^*) for different values of μ. We notice that when $R_0 < 1$, the disease disappears.

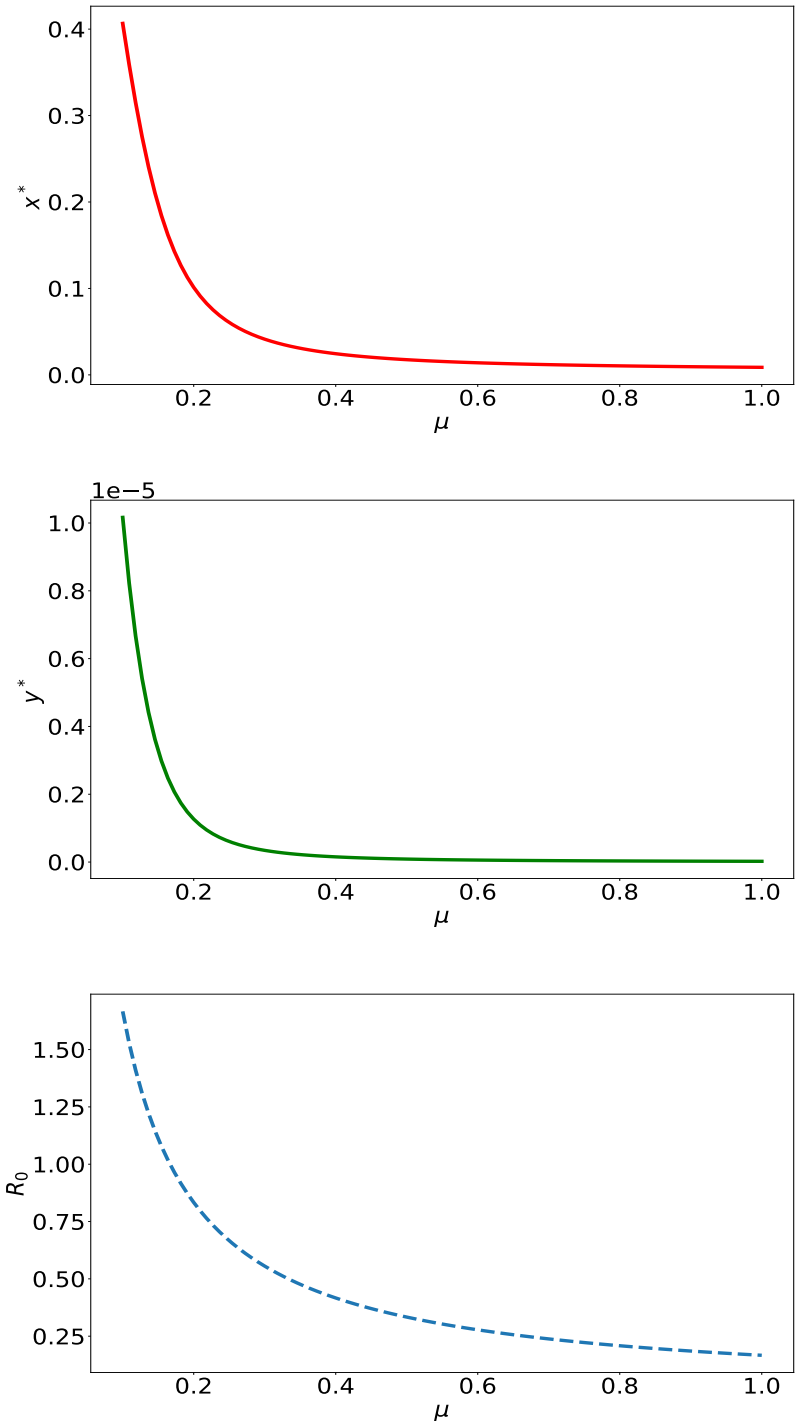


Figure 3.7: Bifuraction with respect to μ the mortality rate of snails.

3.3 A Human-Mammal Model

We propose a new mathematical model that describes here four definite mammalian host subpopulations and two intermediate snail host subpopulations. It shall be assumed here that infected snails and infected mammals do not recover from schistosomiasis as their life spans are short in comparison to that for humans. The dynamical quantities in the model are

Symbol	Description
H_s	susceptible (uninfected) human population density
H_i	infected human population density
S_s	susceptible snail host population density
S_i	infected snail host population density
M_s	susceptible mammal population density
M_i	infected mammal population density
t_H	disease transmission
r_H	recovery
t_M	disease transmission
m	death rate
a	growth rate
K	capacity
c	competition coefficient
θ	disease transmission
μ	death rate
α	growth rate
κ	capacity
χ	competition coefficient

Table 3.3: Parameters of the Human-Mammal Model.

Each population is split into susceptible and infected as follows:

1. Human with constant population

$$\begin{aligned} H_s'(t) &= -t_H H_s(t) S_i(t) + r_H H_i(t) && (3.10)\\ H_i'(t) &= t_H H_s(t) S_i(t) - r_H H_i(t); && (3.11) \end{aligned}$$

2. Mammals, *e.g.* dogs or pigs, with logistic growth

$$\begin{aligned} M_s'(t) &= a_s(K_s - M_s(t) - c_{si} M_i(t)) M_s(t) - m_s M_s(t) - t_M M_s(t) S_i(t) \\ M_i'(t) &= a_i(K_i - M_i(t) - c_{is} M_s(t)) M_i(t) - m_i M_i(t) + t_M M_s(t) S_i(t); \end{aligned} \quad (3.12)$$

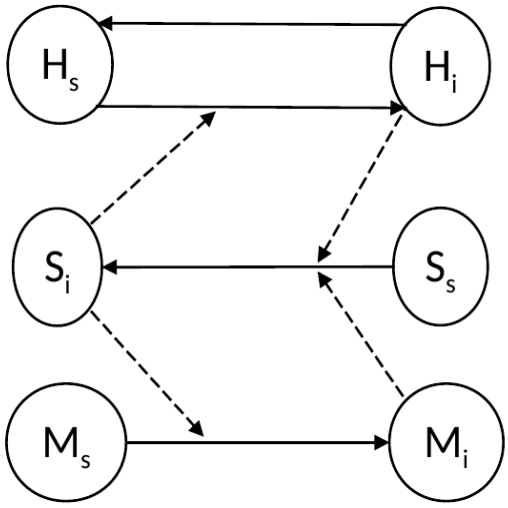


Figure 3.8: Compartimental representation of the human-mammal model.

3. Snails with logistic growth

$$\begin{aligned} S_s'(t) &= \alpha_s(\kappa_s - S_s(t) - \chi_{si}S_i(t))S_s(t) - \mu_s S_s(t) \\ &\quad - \theta_H H_i(t)S_s(t) - \theta_M M_i(t)S_s(t) \end{aligned} \tag{3.13}$$

$$\begin{aligned} S_i'(t) &= \alpha_i(\kappa_i - S_i(t) - \chi_{is}S_s(t))S_i(t) - \mu_i S_i(t) \\ &\quad + \theta_H H_i(t)S_s(t) + \theta_M M_i(t)S_s(t). \end{aligned} \tag{3.14}$$

3.3.1 Qualitative Study

Theorem 3.3.1 *Let $(H_s^0, H_i^0, M_s^0, M_i^0, S_s^0, S_i^0)$ be non negative. Then there exits $T > 0$ and a unique solution of the differential equation $(H_s, H_i, M_s, M_i, S_s, S_i) \in \mathcal{C}([0,T];\mathbb{R})^6$ associated to the initial datum $(H_s^0, H_i^0, M_s^0, M_i^0, S_s^0, S_i^0)$.*

Proof: We rewrite the equation with

$$u = \begin{pmatrix} u_1 \\ u_2 \\ u_3 \\ u_4 \\ u_5 \\ u_6 \end{pmatrix} = \begin{pmatrix} H_s \\ H_i \\ M_s \\ M_i \\ S_s \\ S_i \end{pmatrix}, f(t,u) = \begin{pmatrix} -t_H u_1 u_6 + r_H u_2 \\ t_H u_1 u_6 - r_H u_2 \\ a_s(K_s - u_3 - c_{si}u_4)u_3 - m_s u_3 - t_M u_3 u_6 \\ a_i(K_i - u_4 - c_{is}u_3)u_4 - m_i u_3 + t_M u_3 u_6 \\ \alpha_s(\kappa_s - u_5 - \chi_{si}u_6)u_5 - \mu_s u_5 - \theta_H u_2 u_5 - \theta_M u_4 u_5 \\ \alpha_i(\kappa_i - u_6 - \chi_{is}u_5)u_5 - \mu_i u_6 + \theta_H u_2 u_5 + \theta_M u_4 u_5 \end{pmatrix}.$$

The function f is $\mathcal{C}^\infty$ in particular f is locally Lipschitz with respect to u. The Cauchy-Lipschitz theorem B.1.3 allows to conclude. □

Corollary 3.3.2 *Let $(H_s^0, H_i^0, M_s^0, M_i^0, S_s^0, S_i^0) > 0$. Then the solution $(H_s, H_i, M_s, M_i, S_s, S_i)$ remains positive and bounded for all the time. In particular, the solution is global in time, i.e. $T = +\infty$.*

Proof: The proof bases on the phase portrait using that the function $(0,0,0,0,0,0)$ is solution and the uniqueness given by the previous theorem.
To describe the phase portrait of humans (Fig. 3.9), we denote $x = H_s, y = H_i$, thus

$$\begin{aligned} x' &= -t_H S_i x + r_H y > 0 \text{ if } y > \frac{t_H S_i}{r_H} x \\ y' &= t_H S_i x - r_H y > 0 \text{ if } y > \frac{t_H S_i}{r_H} x. \end{aligned}$$

Concerning mammals (Fig. 3.10), the phase portrait reads for $x = M_s, y = M_i$

$$\begin{aligned} x' &= a_s(K_s - x - c_{si}y)x - m_s x - t_M S_i x > 0 \text{ if } y < \frac{a_s(K_s - x) - m_s - t_M S_i}{c_{si} a_s} \\ y' &= a_i(K_i - y - c_{is}x)y - m_i y + t_M S_i x > 0 \text{ if } x > \frac{m_1 y - a_i(K_1 - y)}{t_M S_i - a_i c_{is} y}. \end{aligned}$$

Finally, the phase portrait for snail (Fig. 3.11) is given by, for $x = S_s, y = S_i$

$$\begin{aligned} x' &= \alpha_s(\kappa_s - x - \chi_{si}y)x - \mu_s x - \theta_H H_i x - \theta_M M_i x > 0 \\ &\quad \text{if } y > \frac{\alpha_s(\kappa_s - x) - \mu_s - \theta_H H_1 - \theta_M M_i}{\chi_{si}\alpha_{si}} \\ y' &= \alpha_i(\kappa_i - y - \chi_{is}x)y - \mu_i y + \theta_H H_i x + \theta_M M_1 x > 0 \\ &\quad \text{if } x > \frac{\mu_i y - \alpha(\kappa_i - y)}{\theta_H H_i + \theta_M M_i - \chi_{is}\alpha_i y}. \end{aligned}$$

□

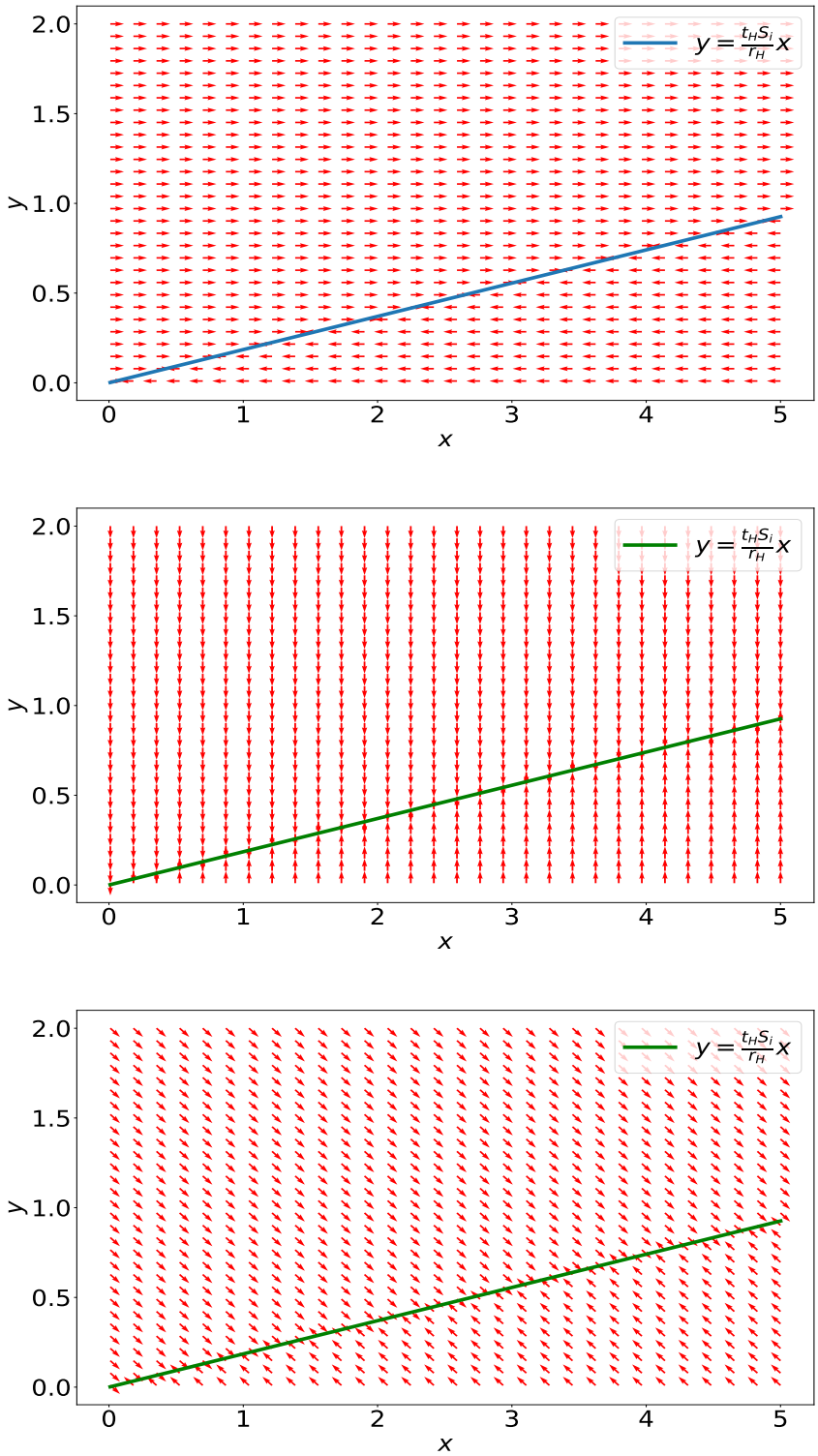


Figure 3.9: Phase portrait of Human dynamics.

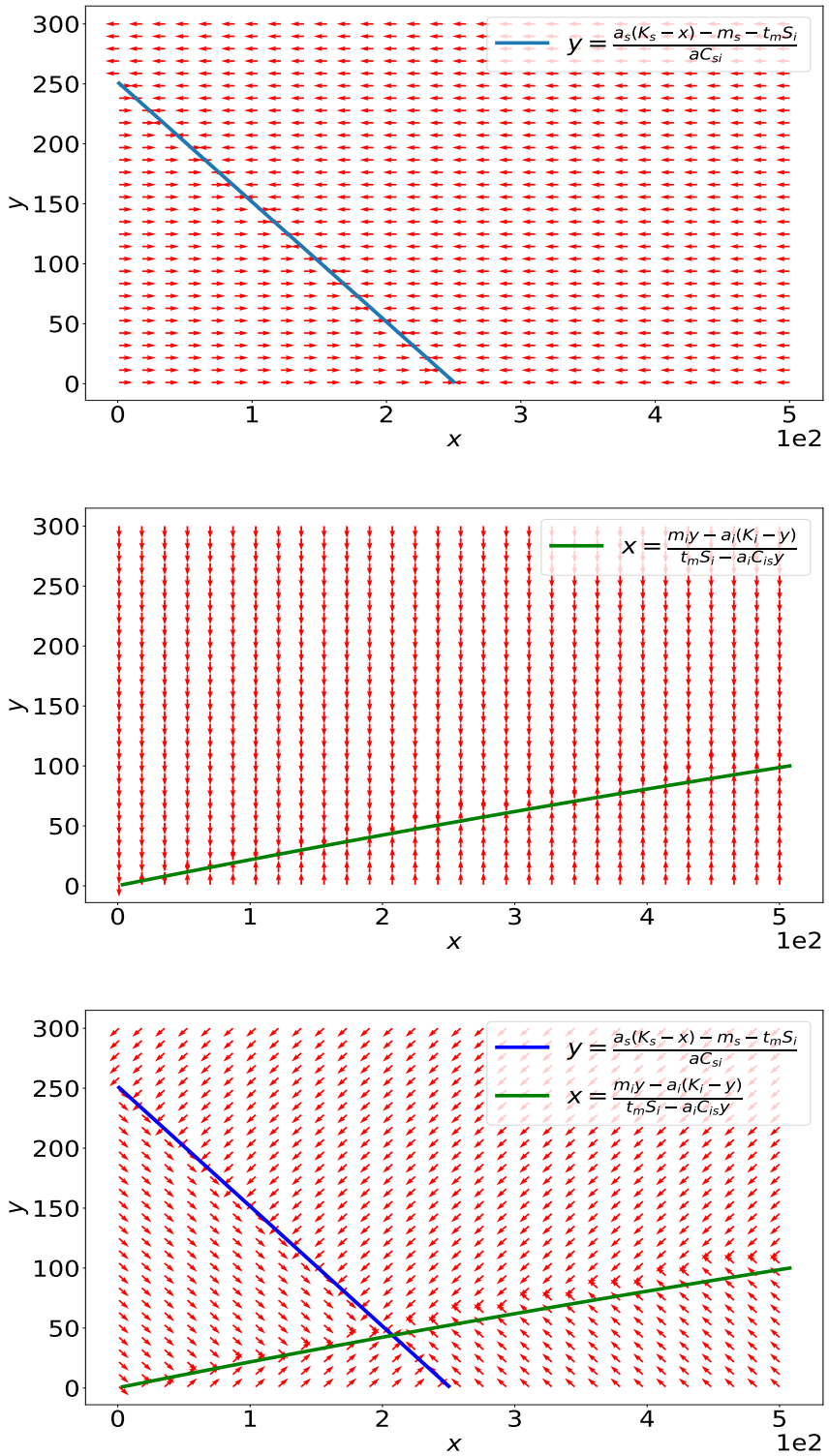


Figure 3.10: Phase portrait of Mammal dynamics.

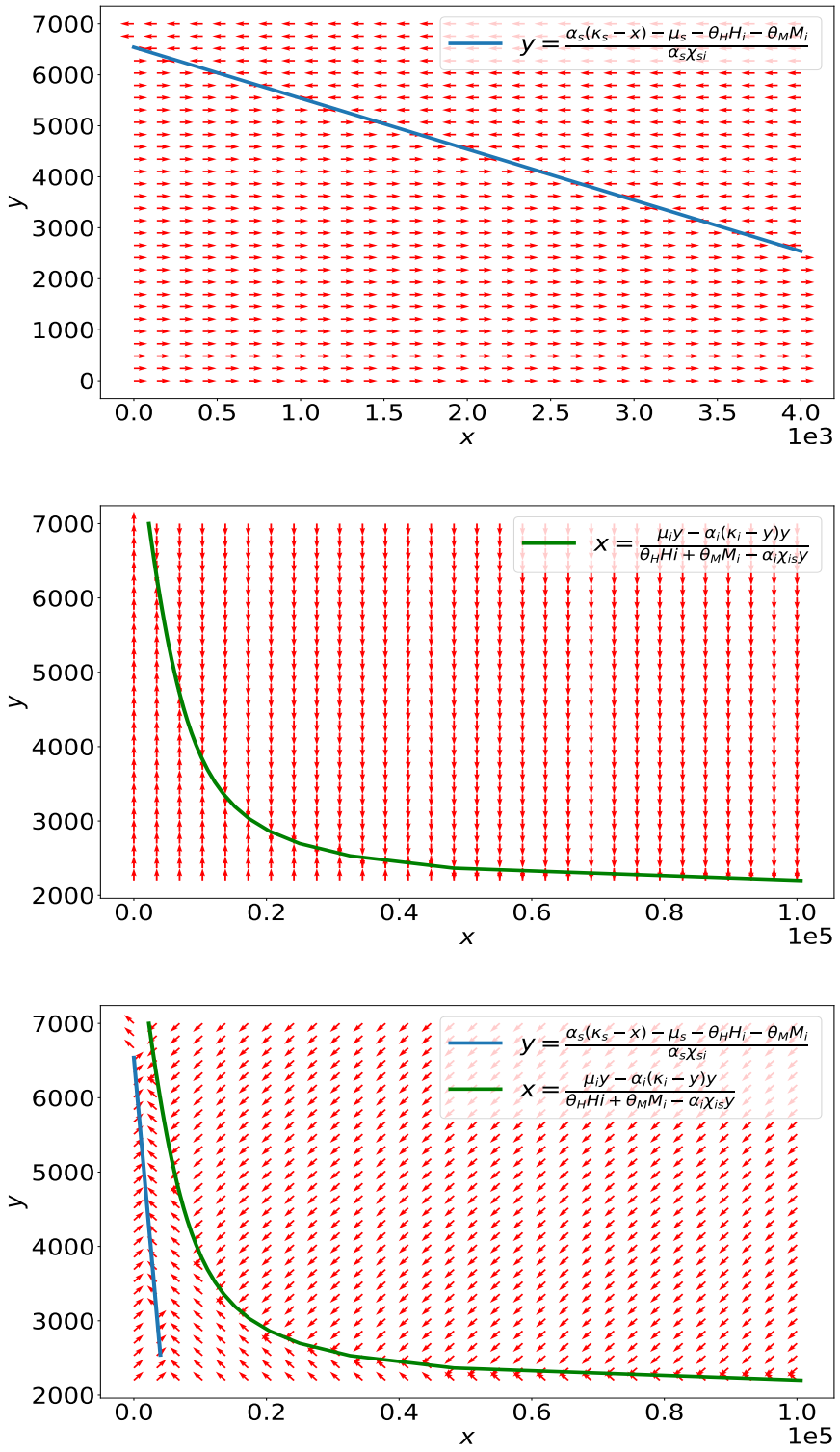


Figure 3.11: Phase portrait of Snail dynamics.

We content ourselves to the study of the Disease Free Equilibirum (DFE) $f = (H_s^*, H_i^0 * M_s^*, M_i^*, S_s^*, S$ $(H_s^*, 0, M_s^*, 0, S_s^*, 0)$. It is solution of the system

$$f\left(H_s^*, 0, M_s^*, 0, S_s^*, 0\right) = \begin{pmatrix} 0 \\ 0 \\ a_s\left(\kappa_s - M_s^*\right) M_s^* - m_s M_s^* \\ 0 \\ \alpha_s\left(\kappa_s - S_s^*\right) S_s^* - \mu_s S_s^* \\ 0 \end{pmatrix}.$$

We deduce

$$\left(a_s K_s - a_s M_s^* - m_s\right) M_s^* = 0.$$

Then

$$M_s^* = 0 \text{ and } M_s^* = \frac{a_s K_s - m_s}{a_s} \quad \text{(biologically relevent if } M_s^* \geq 0),$$

and

$$\left(\alpha_s \kappa_s - \alpha_s S_s^* - \mu_s\right) S_s^* = 0$$

which provides

$$S_s^* = 0 \text{ and } S_s^* = \frac{\alpha_s \kappa_s - \mu_s}{\alpha_s} \quad \text{(biologically relevent if } S_s^* \geq 0).$$

Finally the Disease Free Equilibrium are written

$$\begin{aligned} u_0^* &= (0,0,0,0,0,0) \\ u_1^* &= (H_s^*, 0,0,0,0,0) \\ u_2^* &= \left(H_s^*, 0, \frac{a_s K_s - m_s}{a_s}, 0, 0, 0\right) \\ u_3^* &= \left(H_s^*, 0, 0, 0, \frac{\alpha_s \kappa_s - \mu_s}{\alpha_s}, 0\right) \\ u_4^* &= \left(H_s^*, 0, \frac{a_s K_s - m_s}{a_s}, 0, \frac{\alpha_s \kappa_s - \mu_s}{\alpha_s}, 0\right). \end{aligned}$$

For $\left(u_0, u_1, u_2, u_3, u_4, u_5\right)'(t) = \begin{pmatrix} f(u_0,u_1,u_2,u_3,u_4,u_5) \\ g(u_0,u_1,u_2,u_3,u_4,u_5) \\ k(u_0,u_1,u_2,u_3,u_4,u_5) \\ l(u_0,u_1,u_2,u_3,u_4,u_5) \\ c(u_0,u_1,u_2,u_3,u_4,u_5) \end{pmatrix}$, the Jacobian is defined as

$$J(u_0^*, u_1^*, u_2^*, u_3^*, u_4^*, u_5^*) = \begin{pmatrix} \frac{\partial f}{\partial u_0} & \frac{\partial f}{\partial u_1} & \frac{\partial f}{\partial u_2} & \frac{\partial f}{\partial u_3} & \frac{\partial f}{\partial u_4} & \frac{\partial f}{\partial u_5} \\ \frac{\partial g}{\partial u_0} & \frac{\partial g}{\partial u_1} & \frac{\partial g}{\partial u_2} & \frac{\partial g}{\partial u_3} & \frac{\partial g}{\partial u_4} & \frac{\partial g}{\partial u_5} \\ \frac{\partial k}{\partial u_0} & \frac{\partial k}{\partial u_1} & \frac{\partial k}{\partial u_2} & \frac{\partial k}{\partial u_3} & \frac{\partial k}{\partial u_4} & \frac{\partial k}{\partial u_5} \\ \frac{\partial l}{\partial u_0} & \frac{\partial l}{\partial u_1} & \frac{\partial l}{\partial u_2} & \frac{\partial l}{\partial u_3} & \frac{\partial l}{\partial u_4} & \frac{\partial l}{\partial u_5} \\ \frac{\partial c}{\partial u_0} & \frac{\partial c}{\partial u_1} & \frac{\partial c}{\partial u_2} & \frac{\partial c}{\partial u_3} & \frac{\partial c}{\partial u_4} & \frac{\partial c}{\partial u_5} \end{pmatrix}.$$

Then the Jacobian is computed for the DFE $(H_s^*, 0, M_s^*, 0, S_s^*, 0)$ to give

$$J\left(H_s^*, 0, M_s^*, 0, S_s^*, 0\right) =$$

$$\begin{pmatrix} 0 & r_H & 0 & 0 & 0 & -t_H H_s^* \\ 0 & -r_H & 0 & 0 & 0 & t_H H_s^* \\ 0 & 0 & a_s K_s - 2a_s M_s^* - m_s & -a_s c_{si} M_s^* & 0 & -t_M M_s^* \\ 0 & 0 & 0 & a_i K_i - a_i c_{is} M_s^* - m_i & 0 & t_M M_s^* \\ 0 & -\theta_H S_s^* & 0 & -\theta_M S_s^* & \alpha_s \kappa_s - 2\alpha_s S_s^* - \mu_s & -\alpha_s \chi_{si} S_s^* \\ 0 & \theta_H S_s^* & 0 & \theta_M S_s^* & 0 & \alpha_i \kappa_i - \alpha_i \chi_{is} S_s^* - \mu_i \end{pmatrix}.$$

Starting with the DFE $(0, 0, 0, 0, 0, 0)$, the Jacobian reduces to
$J(0, 0, 0, 0, 0, 0) =$

$$\begin{pmatrix} 0 & r_H & 0 & 0 & 0 & 0 \\ 0 & -r_H & 0 & 0 & 0 & 0 \\ 0 & 0 & a_s K_s - m_s & 0 & 0 & 0 \\ 0 & 0 & 0 & a_i K_i - m_i & 0 & 0 \\ 0 & 0 & 0 & 0 & \alpha_s \kappa_s - \mu_s & 0 \\ 0 & 0 & 0 & 0 & 0 & \alpha_i \kappa_i - \mu_i \end{pmatrix}.$$

The eigenvalues are

$$\left(0, -r_H, a_s K_s - m_s, a_i K_i - m_i, \alpha_s \kappa_s - \mu_s, \alpha_i \kappa_i - \mu\right).$$

Then u_0^* is asymptotically stable if the real part of all eigenvalues is negative. The eigenvalues of $J(u_1^*)$ are the same.
We deduce

Theorem 3.3.3 *Assume that*

$$\begin{cases} a_s K_s < m_s \\ a_i K_i < m_i \\ \alpha_s \kappa_s < \mu_s \\ \alpha_i \kappa_i < \mu \end{cases}$$

then u_0^* and u_1^* are asymptotically stable.

Concerning u_2^*, the Jacobian reads

$$\begin{pmatrix} 0 & r_H & 0 & 0 & 0 & -t_H H_s^* \\ 0 & -r_H & 0 & 0 & 0 & t_H H_s^* \\ 0 & 0 & a_s K_s + m_s & -c_{si}(a_s K_s - m_s) & 0 & -\frac{t_M (a_s K_s - m_s)}{a_s} \\ 0 & 0 & 0 & a_i K_i - m_i & -\frac{a_i c_{is} (a_s K_s - m_s)}{a_s} & \frac{t_M (a_s K_s - m_s)}{a_s} \\ 0 & 0 & 0 & 0 & \alpha_s \kappa_s - \mu_s & 0 \\ 0 & 0 & 0 & 0 & 0 & \alpha_i \kappa_i - \mu_i \end{pmatrix},$$

and its eigenvalues are

$$\left(-r_H, -a_s K_s + m_s, \alpha_s \kappa_s - \mu_s, \alpha_i \kappa_i - \mu_i, \frac{a_i c_{is} m_s - a_s m_i - K_s a_i c_{is} + K_i a_i a_s}{a_s}\right).$$

We deduce

Theorem 3.3.4 *Assume that*

$$\begin{cases} -a_s K_s > m_s \\ \alpha_s \kappa_s < \mu_s \\ \alpha_i \kappa_i < \mu_i \\ a_i c_{is} m_s + K_i a_i a_s < a_s m_i + K_s a_i c_{is} \end{cases}$$

then u_2^* *is asymptotically stable.*

The eigenvalues of $J(u_3^*)$ are computed with Python which provides

$$0, a_s K_s - m_s,$$

$$-\frac{\alpha_i\alpha_s\chi_{is}\kappa_s - \alpha_i\alpha_s\kappa_i - \alpha_i\chi_{is}\mu_s + \alpha_s\mu_i + \alpha_s r_H}{2\alpha_s} - \frac{\sqrt{4H_s^*\alpha_s^2\kappa_s t_H\theta_H - 4H_s^*\alpha_s\mu_s t_H\theta_H + \alpha_i^2\alpha_s^2\chi_{is}^2\kappa_s^2}}{2\alpha_s}$$

$$\frac{-2\alpha_i^2\alpha_s^2\chi_{is}\kappa_i\kappa_s + \alpha_i^2\alpha_s^2\kappa_i^2 - 2\alpha_i^2\alpha_s\chi_{is}^2\kappa_s\mu_s + 2\alpha_i^2\chi_{is}\kappa_i\mu_s + \alpha_i^2\chi_{is}^2\mu_s^2 + 2\alpha_i\alpha_s^2\chi_{is}\kappa_s\mu_i - 2\alpha_i\alpha_s^2\chi_{is}\kappa_s r_H}{2\alpha_s}$$

$$\frac{-2\alpha_i\alpha_s^2\kappa_i\mu_i + 2\alpha_i\alpha_s^2\kappa_i r_H - 2\alpha_i\alpha_s\chi_{is}\mu_i\mu_s + 2\alpha_i\alpha_s\chi_{is}\mu_s r_H + \alpha_s^2\mu_i^2 - 2\alpha_s^2\mu_i r_H + \alpha_s^2 r_H^2}{2\alpha_s},$$

and

$$-\frac{\alpha_i\alpha_s\chi_{is}\kappa_s - \alpha_i\alpha_s\kappa_i - \alpha_i\chi_{is}\mu_s + \alpha_s\mu_i + \alpha_s r_H}{2\alpha_s} + \frac{\sqrt{4H_s^*\alpha_s^2\kappa_s t_H\theta_H - 4H_s^*\alpha_s\mu_s t_H\theta_H + \alpha_i^2\alpha_s^2\chi_{is}^2\kappa_s^2}}{2\alpha_s}$$

$$\frac{-2\alpha_i^2\alpha_s^2\chi_{is}\kappa_i\kappa_s + \alpha_i^2\alpha_s^2\kappa_i^2 - 2\alpha_i^2\alpha_s\chi_{is}^2\kappa_s\mu_s + 2\alpha_i^2\chi_{is}\kappa_i\mu_s + \alpha_i^2\chi_{is}^2\mu_s^2 + 2\alpha_i\alpha_s^2\chi_{is}\kappa_s\mu_i - 2\alpha_i\alpha_s^2\chi_{is}\kappa_s r_H}{2\alpha_s}$$

$$\frac{-2\alpha_i\alpha_s^2\kappa_i\mu_i + 2\alpha_i\alpha_s^2\kappa_i r_H - 2\alpha_i\alpha_s\chi_{is}\mu_i\mu_s + 2\alpha_i\alpha_s\chi_{is}\mu_s r_H + \alpha_s^2\mu_i^2 - 2\alpha_s^2\mu_i r_H + \alpha_s^2 r_H^2}{2\alpha_s}.$$

Again the eigenvalues of $J(u_4^*)$ can be computed with Python (see code in the appendix).

3.3.2 Numerical Simulations

The values of parameters are chosen from (Allen & Victory, 2003; Hisakane et al., 2008) and reflecting data from Ban Houadonhi village, in Champasak Province, Laos. Here the parameters for mammals are calibrated considering dogs. The initial population is 2750 http://www.fallingrain.com/world/LA/02/Ban_Houadonhi.html.

t_H	disease transmission	10^{-4}
r_H	recovery	5×10^{-4}
t_M	disease transmission	6.32×10^{-5}
m_s	death rate of susceptible mammals	2×10^{-4}
m_i	death rate of infected mammals	2×10^{-4}
a_s	growth rate of susceptible mammals	7×10^{-8}
a_i	growth rate of infected mammals	7×10^{-8}
K_s	capacity of susceptible mammals	750
K_i	capacity of infected mammals	750
C_{si}	competition coefficient between susceptible and infected mammals	0
C_{is}	competition coefficient between infected and susceptible mammals	0
μ_s	death rate of susceptible snails	7×10^{-3}
μ_i	death rate of infected snails	7×10^{-3}
α_s	growth rate of susceptible snails	5×10^{-6}
α_i	growth rate of infected snails	5×10^{-6}
κ_s	capacity of susceptible snails	10^4
κ_i	capacity of infected snails	10^4
χ_{si}	competition coefficient between susceptible and infected snails	0
χ_{is}	competition coefficient between infected and susceptible snails	0
θ_H	disease transmission from humans	5.15×10^{-6}
θ_M	disease transmission from mammals	5.15×10^{-6}

Simulations are made during 4 years with a time step equal to 1 day. Figures 3.12–3.13–3.14 represents the evolution with respect to day of humans, mammals and snails.

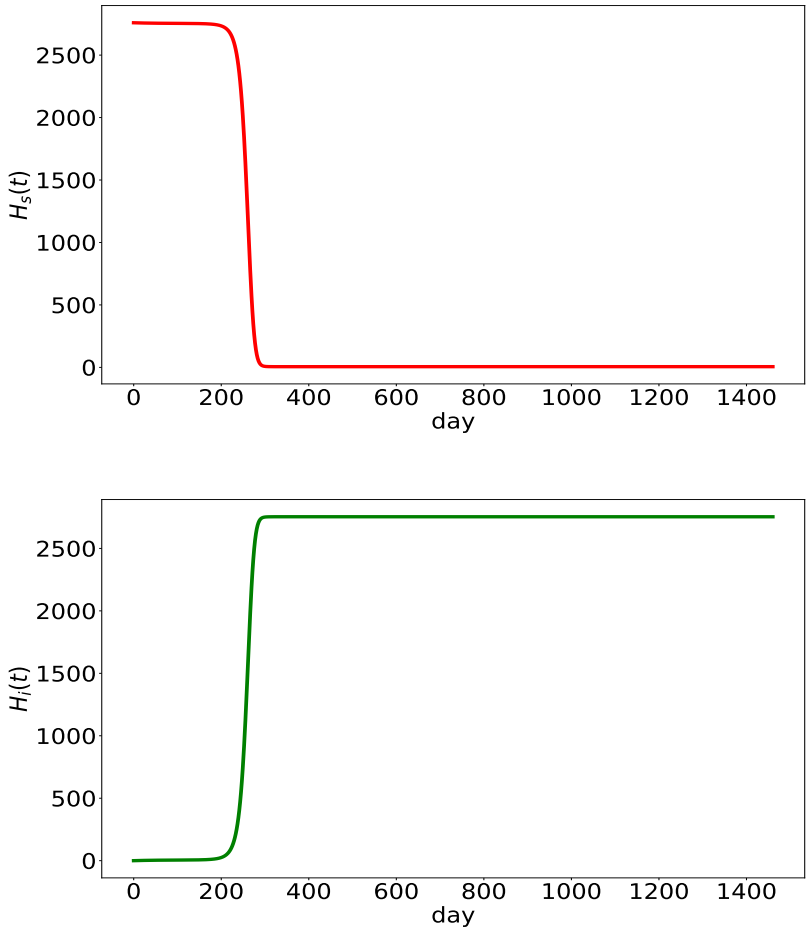


Figure 3.12: Evolution of incidence in human population with respect to day.

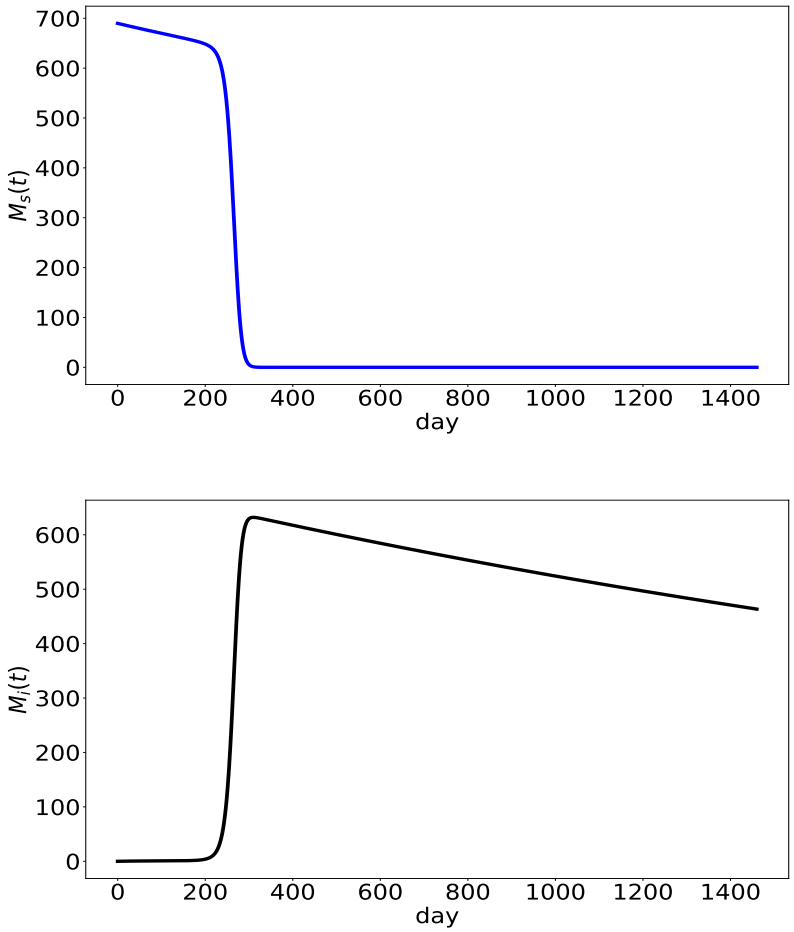


Figure 3.13: Evolution of incidence in mammal population with respect to day.

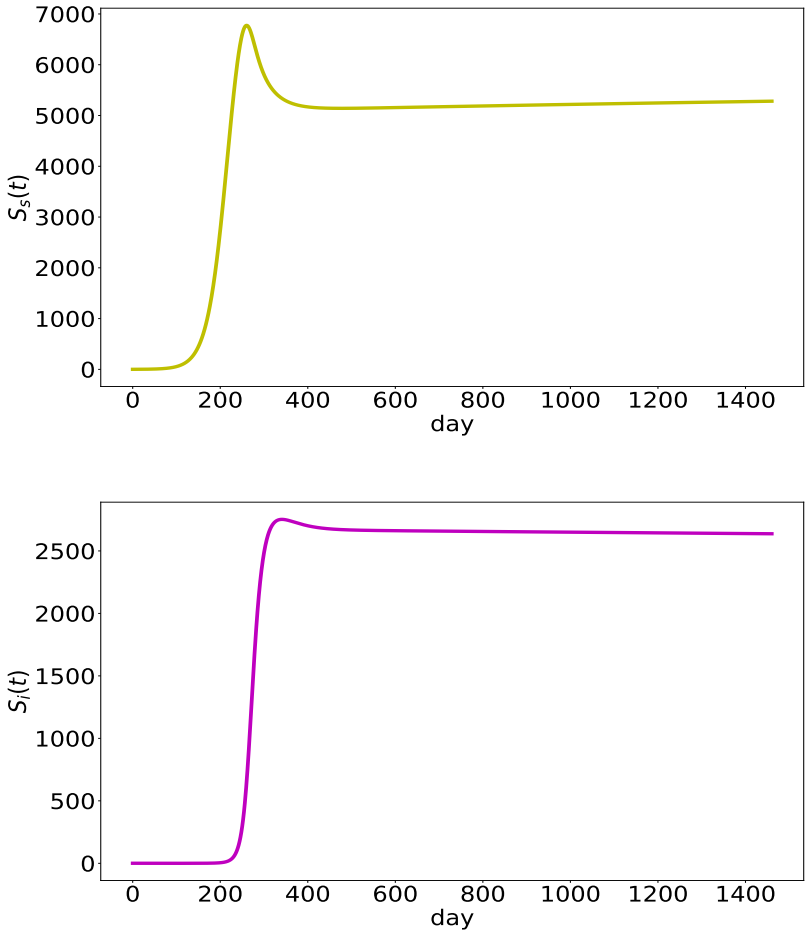


Figure 3.14: Evolution of incidence in snail population with respect to day.

Chapter 4

Study of Time Dependent Model with Spatial Invasion

We study the prevalence of infection in the population of humans as well as in the population of mammals, denoted by H and M respectively. Ross' model is applied to describe the evolution of the prevalence

$$H'(t) = a_H \delta S(t)(1 - H(t)) - g_H H(t) \tag{4.1}$$
$$M'(t) = a_M \delta S(t)(1 - M(t)) - g_M M(t). \tag{4.2}$$

Figure 4.1: Compartimental representation of the human-mammal-snail model. Snails are living inside the Mekong river.

We investigate the spatial propagation of the epidemics following snails prevalence (S). Snails are living inside the river and their movement is governed by the reaction-diffusion

equation

$$\frac{\partial S(t,x)}{\partial t} = \underbrace{\left(\frac{b_H \sigma_H H}{\delta} + \frac{b_M \sigma_M M}{\delta}\right) S(t,x)\,(1 - S(t,x))}_{\text{infection}} - \overbrace{\mu S(t,x)}^{\text{mortality}} + \underbrace{d\Delta S(t,x)}_{\text{spatial diffusion}} . \quad (4.3)$$

4.1 Progressive Waves for the Quasi-Steady State

The quasi-steady state consists in assuming that the recovery is faster for humans and mammals than for snails. It can be translated in equations (4.1)-(4.2) by

$$0 = a_H \delta S(1 - H) - g_H H \quad \Leftrightarrow \quad H = \frac{a_H \delta S}{a_H \delta S + g_H}$$
$$0 = a_M \delta S(1 - M) - g_M M \quad \Leftrightarrow \quad M = \frac{a_M \delta S}{a_M \delta S + g_M}.$$

The reaction-diffusion equation (4.3) becomes

$$\frac{\partial S(t,x)}{\partial t} = \left(\frac{a_H b_H \sigma_H}{a_H \delta S(t,x) + g_H} + \frac{a_M b_M \sigma_M}{a_M \delta S(t,x) + g_M}\right) S(t,x)\,(1 - S(t,x)) - \mu S(t,x) + d\Delta S(t,x). \quad (4.4)$$

Theorem 4.1.1 *Let $S_0 \in L^\infty(\mathbb{R})$. Then there exist $T > 0$ and a unique solution $S \in \mathcal{C}^\infty([0,T] \times \mathbb{R})$.*
Moreover, if S_0 is non-negative, then the solution remains non-negative for all time.

Proof: The nonlinear part

$$f(t,S) = \left(\frac{a_H b_H \sigma_H}{a_H \delta S + g_H} + \frac{a_M b_M \sigma_M}{a_M \delta S + g_M}\right) S\,(1 - S)$$

being locally Lipschitz with respect to S, we deduce from Corollary B.4.3 the existence of solution.
We note that

$$f(0) = f(1) = 0 \text{ and for } 0 < S < 1, f(S) \geq 0,$$

and thus apply corollary B.4.5. □

Progressive waves are solution of the form

$$S(t,x) = \Phi(x - ct)$$

which relates the unstable equilibrium to the stable equation. It represents waves moving in one direction (from left to right if $c > 0$ and from right to left if $c < 0$). Here c denotes the speed of the wave. If $z = x - ct$, we deduce that

$$\frac{\partial S(t,x)}{\partial t} = \frac{\partial \Phi}{\partial z}\frac{\partial z}{\partial t} = -c\Phi'(z), \quad \frac{\partial S(t,x)}{\partial x} = \frac{\partial \Phi}{\partial z}\frac{\partial z}{\partial x} = \Phi'(z)$$

and

$$\frac{\partial^2 S(t,x)}{\partial x^2} = \frac{\partial}{\partial x}\left(\frac{\partial S(t,x)}{\partial x}\right) = \frac{\partial \Phi'(z)}{\partial x} = \frac{\partial \Phi'}{\partial z}\frac{\partial z}{\partial t} = \Phi''(z).$$

The partial differential equation (4.4) turns to the second order ordinary differential equation

$$-c\Phi'(z) = \left(\frac{a_H b_H \sigma_H}{a_H \delta \Phi(z) + g_H} + \frac{a_M b_M \sigma_M}{a_M \delta \Phi(z) + g_M}\right) \Phi(z)\left(1 - \Phi(z)\right) - \mu S(t,x) + d\Phi''(z).$$

Let $x = \Phi, y = \Phi'$, we then obtain the system of first order ordinary differential equations

$$\begin{aligned} x' &= y & (4.5)\\ y' &= \frac{1}{d}\left(-cy - \left(\frac{a_H b_H \sigma_H}{a_H \delta x + g_H} + \frac{a_M b_M \sigma_M}{a_M \delta x + g_M}\right) x\left(1-x\right) + \mu x\right). & (4.6) \end{aligned}$$

4.2 Qualitative Study

Theorem 4.2.1 *Let (x_0, y_0) be non negative. Then there exits $T > 0$ and a unique solution of the differential equation $(x, y) \in \mathcal{C}([0,T];\mathbb{R}) \times \mathcal{C}([0,T];\mathbb{R})$ associated to the initial datum (x_0, y_0).*

Proof: We rewrite (4.5) and (4.6) as

$$u'(t) = f(t, u(t)),$$

where

$$u = \begin{pmatrix} x \\ y \end{pmatrix}, f(t,u) = \begin{pmatrix} y \\ \frac{1}{d}\left(-cy - \left(\frac{a_H b_H \sigma_H}{a_H \delta x + g_H} + \frac{a_M b_M \sigma_M}{a_M \delta x + g_M}\right) x\left(1-x\right) + \mu x\right) \end{pmatrix}.$$

The function f is $\mathcal{C}^\infty$ in particular f is locally Lipschitz with respect to u. The Cauchy-Lipschitz theorem B.1.3 allows to conclude. □

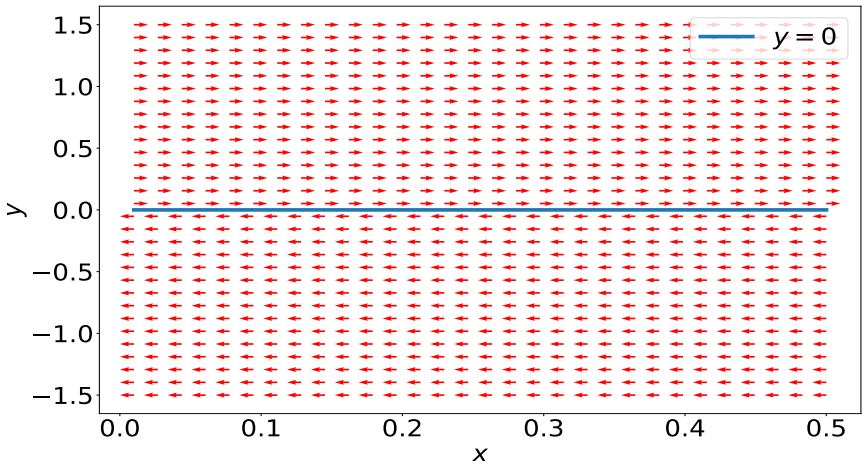
Corollary 4.2.2 *Let $(x_0, y_0) > 0$. Then the solution $(x(t), y(t))$ remains positive and bounded for all the time. In particular, the solution is global in time, i.e. $T = +\infty$.*

Proof: The proof reads in the phase portrait (Figure 4.2C) since $(0,0)$ is solution and

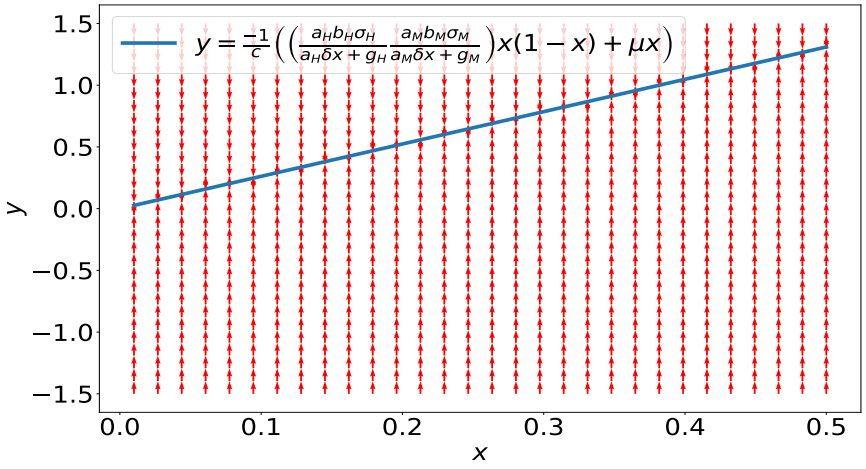
$$\begin{aligned} x' &= y > 0 \text{ when } y > 0\\ y' &= \frac{1}{d}\left(-cy - \left(\frac{a_H b_H \sigma_H}{a_H \delta x + g_H} + \frac{a_M b_M \sigma_M}{a_M \delta x + g_M}\right) x\left(1-x\right) + \mu x\right) > 0 \text{ (Fig. 4.2A)}\\ &\quad \text{when } y < \frac{-1}{c}\left(\left(\frac{a_H b_H \sigma_H}{a_H \delta x + g_H} + \frac{a_M b_M \sigma_M}{a_M \delta x + g_M}\right) x\left(1-x\right) + \mu x\right) \text{ (Fig. 4.2B).} \end{aligned}$$

□

A.



B.



C.

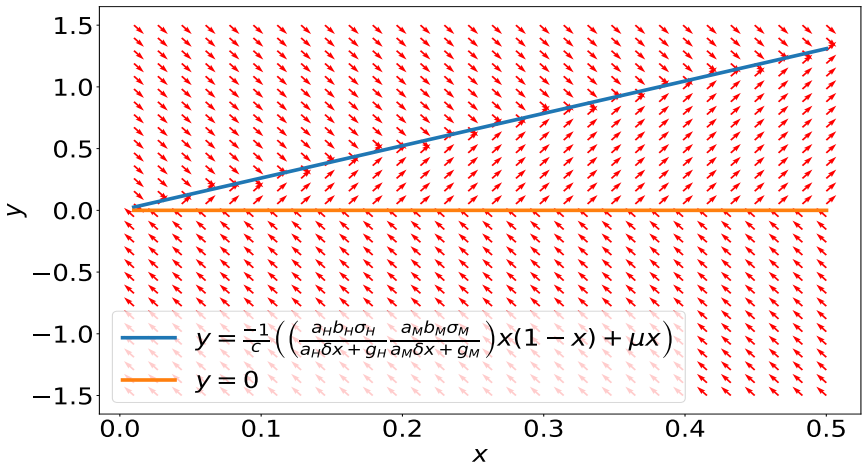


Figure 4.2: Phase portrait of the progressive waves system.

Equilibrium are given as the solution of

$$\begin{cases} y^* = 0 \\ -cy^* - \left(\frac{a_H b_H \sigma_H}{a_H \delta x + g_H} + \frac{a_M b_M \sigma_M}{a_M \delta x + g_M} \right) x^* (1 - x^*) + \mu x^* = 0. \end{cases}$$

Here the two equilibrium are

$$(0,0) \text{ and } (x^*, 0)$$

with $x^* > 0$.

We look for progressive waves moving from left to right that link the unstable equilibrium $(x^*, 0)$ to the stable equilibrium $(0,0)$. We compute the Jacobian for the equilibrium $(0,0)$

$$J(0,0) = \begin{pmatrix} 0 & 1 \\ -\frac{1}{d}\left(\frac{a_H b_H \sigma_H}{g_H} + \frac{a_M b_M \sigma_M}{g_M} \right) + \frac{\mu}{d} & -\frac{c}{d} \end{pmatrix} = \begin{pmatrix} 0 & 1 \\ \frac{\mu}{d}(1 - R_0) & -\frac{c}{d} \end{pmatrix},$$

where $R_0 := \frac{a_H b_H \sigma_H}{\mu g_H} + \frac{a_M b_M \sigma_M}{\mu g_M}$.

Finally, the eigenvalues are

$$\frac{-c - \sqrt{c^2 - 4(R_0 - 1)\mu d}}{2d} \text{ and } \frac{-c + \sqrt{c^2 - 4(R_0 - 1)\mu d}}{2d}.$$

Theorem 4.2.3 *The progressive waves that link the unstable equilibrium* $(x^*, 0)$ *to the stable equilibrium* $(0,0)$ *exist if*

$$c > 2\sqrt{(1 - R_0)\mu d} \text{ and } R_0 > 1.$$

Proof: The equilibrium $(0,0)$ is asymptotically stable if the eigenvalues are negative real values *i.e.*

$$c^2 - 4(R_0 - 1)\mu d > 0.$$

□

4.3 Numerical Simulations of the Progressive Waves

The values of parameters are chosen to obtain the progressive waves that link the unstable equilibrium $(x^*, 0)$ to the stable equilibrium $(0,0)$.

a_H	rate of incidence for one single human host	1
b_H	rate of snail infections to human	10^{-2}
σ_H	density of human hosts	10
g_H	recovery rate for human host infections	6×10^{-4}
a_M	rate of incidence for one single human host	1
b_M	rate of snail infections to human	10^{-2}
σ_M	density of human hosts	10
g_M	recovery rate for human host infections	6×10^{-4}
δ	density of snails	40
μ	death rate of the snails	10^2
d	diffusion coefficient	1
R_0	reproduction number	10/3
c	wave speed	$2.5\sqrt{(R_0 - 1)\mu d}$

Simulations are made during 10 days with a time step equal to 0.01 day. Figure 4.3 represents the evolution with respect to day of x and y.

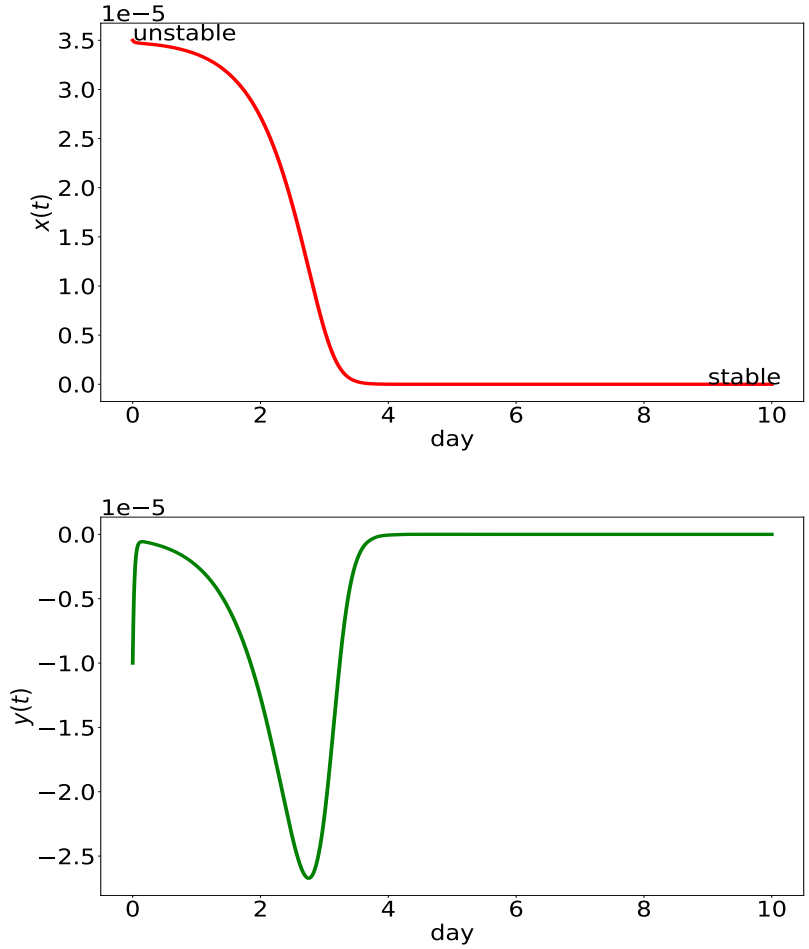


Figure 4.3: Evolution with respect to day of x and y.

4.4 Numerical Simulations of the Reaction-Diffusion System

We come back to the partial differential equation (4.4). Snails are spatially spreading inside the Mekong river. Here we focus on a part of Champasak border (Figure 4.4).

Figure 4.4: Maps of Champasak border river pictures from Google Maps and extracted river for the simulation.

Finite differences are used to solve the equation. The partial differential equation turns to the system of ordinary differential equations for $S_{i,j}$ the approximation of S at the point (x_i, y_j)

$$S'_{i,j}(t) = \left(\frac{a_H b_H \sigma_H}{a_H \delta S_{i,j}(t) + g_H} + \frac{a_M b_M \sigma_M}{a_M \delta S_{i,j}(t) + g_M} \right) S_{i,j}(t) \left(1 - S_{i,j}(t)\right) - \mu S_{i,j}(t) + d D S_{i,j}(t),$$

where D is the discretization operator associated with the Laplacian (see Appendix B.3) given by

$$D S_{i,j} = \frac{S_{i+1,j} - 2S_{i,j} + S_{i-1,j}}{\delta x^2} + \frac{S_{i,j+1} - 2S_{i,j} + S_{i,j-1}}{\delta y^2}.$$

The values of parameters are chosen to reflect the behavior around Champasak province, Laos.

a_H	rate of incidence for one single human host	1
b_H	rate of snail infections to human	10^{-4}
σ_H	density of human hosts	1
g_H	recovery rate for human host infections	6×10^{-4}
a_M	rate of incidence for one single human host	1
b_M	rate of snail infections to human	10^{-4}
σ_M	density of human hosts	1
g_M	recovery rate for human host infections	6×10^{-4}
δ	density of snails	40
μ	death rate of the snails	7×10^{-3}
d	diffusion coefficient	0.1

Simulations are made during 1 year with a time step equal to 0.01 day. Figure 4.5 represents the spatial propagation of the prevalence in the snail population.

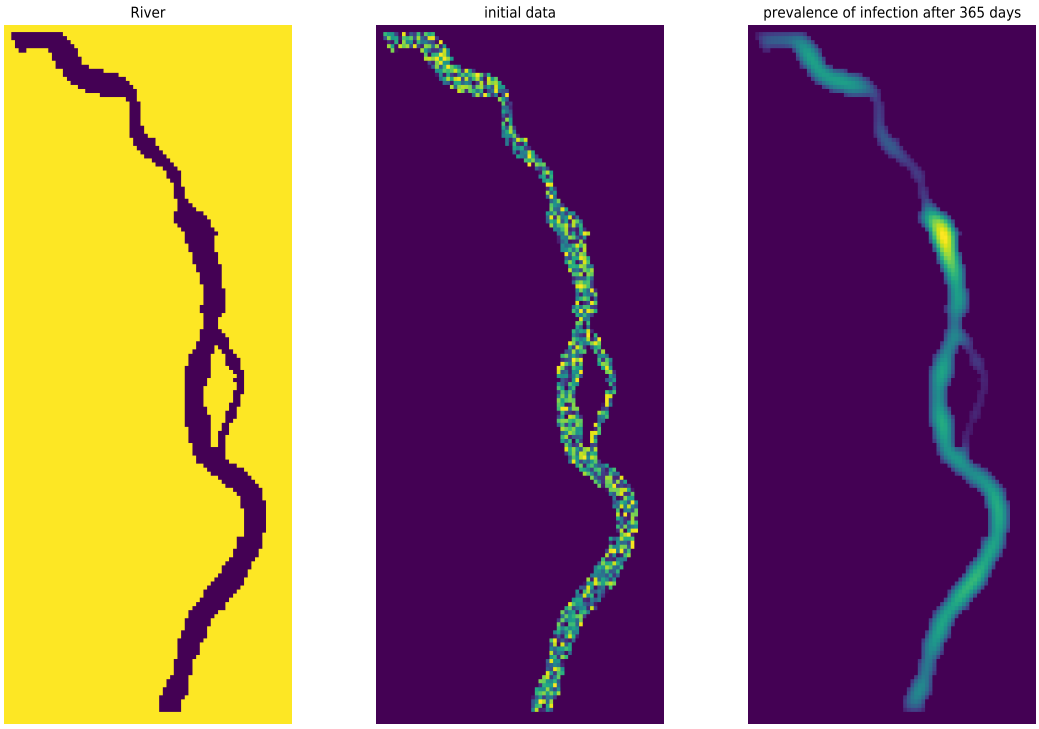


Figure 4.5: Evolution of the prevalence in the snail population.

Chapter 5

Conclusion

In this dissertation, we aim at better understanding water borne diseases especially, Shistosoma Mekongi and its trasmission in Laos. To do this, we start studying well-known the Macdonalds and Ross mathematical models. Macdonald first proposed a mathematical model for the transmission of schistosomiasis. Based on Ross' model, we then developed new system of differential equations accounting for human, mammal as four definite mammalian hosts and and snail as two intermediate hosts. A new time dependent model with spatial invasion was proposed to observe the prevalence of infection through the Mekong river in Champassak state.

Computational simulations, performed here with Python, can become as a planning instrument of Schistosomiasis control measures among the following strategies:

1. increase the death rate of the snails by using pesticides;
2. killing parasites inside hosts with drugs;
3. change the behavior of people to reduce contact with dirty water.

Values of parameters used in this dissertation were estimated from (Allen & Victory, 2003; Hisakane et al., 2008) and reflected data from Ban Houadonhi village, in Champasak state, Laos and the initial population is from http://www.fallingrain.com/world/LA/02/Ban_Houadonhi.html. It would be interesting to retrieve more specific data and to conduct an advanced biological study about Laos.

References

Allen, E., & Victory, J. H. (2003). Modelling and simulation of a schistosomiasis infection with biological control. *Acta Tropica*, *87*, 251–267.

Barbour, A. (1978). Macdonald's model and the transmission of bilharzia. *Trans R. Soc. Trop. Med. Hyg.*, *72*, 6–15.

Barbour, A. (1994). *Modelling the transmission of schistosomiasis: an introductory view.*

Chan, M. S., Guyatt, H. L., Bundy, D., Booth, M., Fulford, A., & Medley, G. (1995). The development of an age structured model for schistosomiasis transmission dynamics and control and its validation for schistosoma mansoni. *Epidemiol. Infect.*, *115*, 325–344.

Chitsulo, L., Engels, D., Montresor, A., & Savioli, L. (2000). The global status of schistosomiasis and its control. *Acta Tropica*, *77*, 41–51.

Cohen, J. (1977). Mathematical models of schistosomiasis. *Ann. Rev. Ecol. Syst.*, *8*, 209–233.

Evans, L. C. (2010). *Partial differential equations.* American Mathematical Society.

Fukuhara, K., Phompida, S., Insisiengmay, S., Kirinoki, M., Chigusa, Y., Nakamura, S., ... Ishikawa, H. (2011). Analysis of the effectiveness of control measures against schistosoma mekongi using an intra- and inter-village model in champasak province, lao pdr. *Parasitology International*, *60*(4), 452–445.

Garrett, L. (1994). *The coming plague: Newly emerging diseases in a world out of balance.* Penguin Books New York.

Ghiboda, M., Engels, D., & Berquist, N. (2000). Post-transmission schistosomiasis: a new agenda. *Acta Tropica*, *77*, 3–7.

Hairer, E., Norsett, P., & Wanner, G. (1993). *Solving ordinary differential equations i.* Springer-Verlag.

Henry, D. (1981). *Geometric theory of semilinear parabolic equations.* Springer-Verlag.

Hisakane, N., Kirinoki, M., Chigusa, Y., Sinuon, M., Sochea, D., Matsuda, H., & Ishikawa, H. (2008). he evaluation of control measures against schistosoma mekongi in cambodia by a mathematical model. *Parasitology International*, *57*(3), 379–385.

Ishikawa, H., Ohmae, H., Pangilinan, R., Redulla, A., & Matsuda, H. (2006). Modeling the dynamics and control of schistosoma japonicum transmission on bohol island, the philippines. *Parasitol Int.*, *23–29*, 325–344.

Leshem, E., Meltzer, E., Marva, E., & Schwartz, E. (2009). Travel-related schistosomiasis acquired in laos. *Emerging Infectious Diseases*, *15*(11).

Lewis, M., Petrovskii, S., & Potts, J. (2016). *The mathematics behind biological invasions*. Interdisciplinary Applied Mathematics, Springer.

Li, Y., Sleigh, A., Williams, G., Ross, A., Li, Y., Forsyth, S., ... McManus, D. (2000). easuring exposure to schistosoma japonicum in china. iii.activity diaries, snail and human infection, transmission ecology and options for control. *Acta Tropica*, *75*, 279–289.

Macdonald, G. (1965). The dynamics of helminth infections, with special reference to schistosomes. *Trans R. Soc. Trop. Med. Hyg.*, *59*, 489–506.

McNeill, W. (1977). *Plagues and peoples*. Doubleday New York.

Murray, J. (2010a). *Mathematical biology i: An introduction*. Springer-Verlag.

Murray, J. (2010b). *Mathematical biology ii: Spatial models and biomedical applications*. Springer-Verlag.

Okubo, A. (1980). *Diffusion and ecological problems: Mathematical models*. Springer-Verlag.

Organization, W. H. (1993). *The control of schistosomiasis. second report of the who expert committee* (Tech. Rep.). WHO Technical Report Series 830.

Quarteroni, A., Sacco, R., & Saleri, F. (2000). *Numerical mathematics*. Springer-Verlag.

Shigesada, N., & Kawasaki, K. (1997). *Biological invasions: theory and practice*. Oxford University Press.

Woolhouse, M. (1991). On the application of mathematical models of schistosome transmission dynamics. i. natural transmission. *Acta Tropica*, *49*, 241–270.

Woolhouse, M. (1992). On the application of mathematical models of schistosome transmission dynamics. ii. control. *Acta Tropica*, *50*, 189–204.

Wu, J., & Feng, Z. (2002). *Mathematical models for schistosomiasis with delays and multiple definite hosts*. In C. Castillo-Chavez, S. Blower, P. van der Driessche, D. Kirchner, A.-A. Yakubu (Eds.), Mathematical Approaches for Emerging and Reemerging Infectious Diseases: Models, Methods, and Theory. Springer, New York.

Appendix A

Source codes

The codes we developped are available below. They are written in Python using numpy, scipy and matplotlib libraries.

A.1 The Macdonald model

The first code allows to solve the system of differential equations.

```
#############################################################
"""
Created January 2017

Author: May

Macdonald's schistosomiasis model
"""

# import
from math import *
from numpy import *
from matplotlib.pylab import *

# import ode solver
from scipy.integrate import odeint

# Time
T = 25*365. # final time 25 years
dt = 1. # time step 1 day
Nt = int(T/dt) # iterations in time
t = linspace(0,T,Nt) # time interval

# Parameters
alpha = 1.
delta = 40.
gamma = 6.e-4
beta = 1e-4
sigma = 1.
mu = 7e-3
```

```
# basic reproduction number
R0 = alpha*beta*sigma/(mu*gamma)
print('the basic reproduction number is equal to ' + str(R0))
if R0 > 1:
    print('the disease is endemic.')
else:
    print('the disease disapears.')

# random initial condition
x0 = abs(randn(1))
y0 = abs(randn(1))
u0 = [x0[0], y0[0]]

# define the ODE
def funct(u,t):
    x = u[0]
    y = u[1]
    xprime = alpha*delta*y - gamma*x
    yprime = beta*sigma/delta*x*(1.-y) - mu*y
    return [xprime, yprime]

# Solve the ode
u = odeint(funct, u0, t)

# plot the solution
rcParams['font.size'] = 32
x = u[:,0]
y = u[:,1]
figure(1)
plot(t,x,'r', linewidth=5)
ylabel(r'$x(t)$')
xlabel('day')
figure(2)
plot(t,y,'g', linewidth=5)
ylabel(r'$y(t)$')
xlabel('day')

# display
show()
##############################################################
```

The second code is related with the phase portrait.

```
#############################################################
"""
Created February 2017

Author: May

Macdonald's schistosomiasis phase portrait
"""

# import
from math import *
from numpy import *
from matplotlib.pylab import *

# import ode solver
from scipy.integrate import odeint

# Time
T = 25*365 # final time 25 years
dt = 1 # time step 1 day
Nt = int(T/dt) # iterations in time
t = linspace(0,T,Nt) # time interval

# Parameters
alpha = 1.
delta = 40.
gamma = 6.e-4
beta = 1e-4
sigma = 1.
mu = 7e-3

# phase portrait
rcParams['font.size'] = 32
x = linspace(0.01, 8e4, 30); y = linspace(0.01, 2, 30)
[X,Y] = meshgrid(x, y) # generate a grid
Xprime = alpha*delta*Y - gamma*X
Yprime = beta*sigma/delta*X*(1.-Y) - mu*Y

figure(1)
quiver(X,Y,Xprime/sqrt(Xprime**2),zeros(Y.shape), color='r')
plot(x, gamma*x/(alpha*delta), linewidth=5, \
        label=r'$y=\frac{\gamma}{\alpha\delta}x$')
legend(loc=0)
xlabel('$x$')
ylabel('$y$')
ticklabel_format(style='sci', axis='x', scilimits=(0,0))

figure(2)
quiver(X,Y,zeros(X.shape),Yprime/sqrt(Yprime**2), color='r')
plot(x, x/(x+delta*mu/(beta*sigma)), 'g',linewidth=5, \
        label=r'$y=\frac{x}{x+\frac{\delta\mu}{\beta\sigma}}$')
legend(loc=0)
xlabel('$x$')
```

```
ylabel('$y$')
ticklabel_format(style='sci', axis='x', scilimits=(0,0))

figure(3)
quiver(X,Y,Xprime/sqrt(Xprime**2),Yprime/sqrt(Yprime**2), color='r')
plot(x, gamma*x/(alpha*delta), 'b',linewidth=5)
plot(x, x/(x+delta*mu/(beta*sigma)), 'g', linewidth=5)
legend((r'$y=\frac{\gamma}{\alpha\delta}x$' \
    ,r'$y=\frac{x}{x+\frac{\delta\mu}{\beta\sigma}}$'),loc=0)
xlabel('$x$')
ylabel('$y$')
ticklabel_format(style='sci', axis='x', scilimits=(0,0))

# display
show()
##############################################################
```

The third code explains how to handle bifurcations.

```
##############################################################
"""
Created February 2017

Author: May

Macdonald's schistosomiasis bifurcation
"""

# import
from math import *
from numpy import *
from matplotlib.pylab import *

# import ode solver
from scipy.integrate import odeint

# Time
T = 25*365 # final time 25 years
dt = 1. # time step 1 day
Nt = int(T/dt) # iterations in time
t = linspace(0,T,Nt) # time interval

# random initial condition
x0 = abs(randn(1))
y0 = abs(randn(1))
u0 = [x0[0], y0[0]]

# parameters initialization
alpha = 1; delta = 40.; gamma = 6.e-4; beta = 1e-4; sigma = 1.; mu = 7e-3

# define the ODE
def funct(u,t):
    x = u[0]
    y = u[1]
```

```
    xprime = alpha*delta*y - gamma*x
    yprime = beta*sigma/delta*x*(1.-y) - mu*y
    return [xprime, yprime]

# generate solutions wrt to the bifuraction parameter
i = 0; n = 100
xx = zeros(n); yy = zeros(n); R0 = zeros(n)
mm = linspace(1e-1, 1., n)
for mu in mm:

    # parameters
    alpha = 1.
    delta = 40.
    gamma = 6.e-4
    beta = 1e-4
    sigma = 1.

    # solve
    u = odeint(funct, u0, t)
    xx[i] = u[-1,0]
    yy[i] = u[-1,1]
    R0[i] = alpha*beta*sigma/(mu*gamma)
    i = i + 1

# plot the solution
rcParams['font.size'] = 32
figure(1)
plot(mm,xx,'r', linewidth=5)
xlabel('$\mu$')
ylabel('$x^*$')
figure(2)
plot(mm,yy,'g', linewidth=5)
xlabel('$\mu$')
ylabel('$y^*$')
figure(3)
plot(mm,R0,'--', linewidth=5)
xlabel('$\mu$')
ylabel('$R_0$')

# display
show()
#####################################################################
```

A.2 The Ross model

The first code allows to solve the system of differential equations.

```
#############################################################
"""
Created April 2017

Author: May

Ross' schistosomiasis model
"""

# import
from math import *
from numpy import *
from matplotlib.pylab import *

# import ode solver
from scipy.integrate import odeint

# Time
T = 25*365. # final time 25 years
dt = 1. # time step 1 day
Nt = int(T/dt) # iterations in time
t = linspace(0,T,Nt) # time interval

# Parameters
a = 1.
delta = 40.
g = 6.e-4
b = 1e-4
sigma = 1.
mu = 7e-3

# basic reproduction number
R0 = a*b*sigma/(mu*g)
print('the basic reproduction number is equal to ' + str(R0))
if R0 > 1:
    print('the disease is endemic.')
else:
    print('the disease disapears.')

# random initial condition
x0 = abs(randn(1))
y0 = abs(randn(1))
u0 = [x0[0], y0[0]]

# define the ODE
def funct(u,t):
    x = u[0]
    y = u[1]
    xprime = a*delta*y*(1.-x) - g*x
    yprime = b*sigma/delta*x*(1.-y) - mu*y
```

```
    return [xprime, yprime]

# Solve the ode
u = odeint(funct, u0, t)

# plot the solution
rcParams['font.size'] = 32
x = u[:,0]
y = u[:,1]
figure(1)
plot(t,x,'r', linewidth=5)
ylabel(r'$x(t)$')
xlabel('day')
figure(2)
plot(t,y,'g', linewidth=5)
ylabel(r'$y(t)$')
xlabel('day')

# display
show()
#########################################################################
```

The second code is related with the phase portrait.

```
#############################################################
"""
Created April 2017

Author: May

Ross' schistosomiasis phase portrait
"""

# import
from math import *
from numpy import *
from matplotlib.pylab import *

# import ode solver
from scipy.integrate import odeint

# Time
T = 25*365 # final time 25 years
dt = 1 # time step 1 day
Nt = int(T/dt) # iterations in time
t = linspace(0,T,Nt) # time interval

# Parameters
a = 1.; delta = 40.; g = 6.e-4; b = 1e-4; sigma = 1.; mu = 7e-3

# phase portrait
rcParams['font.size'] = 32
x = linspace(0.01, 8e4, 30); y = linspace(0.01, 2, 30)
[X,Y] = meshgrid(x, y) # generate a grid
Xprime = a*delta*Y*(1.-X) - g*X
Yprime = b*sigma/delta*X*(1.-Y) - mu*Y

figure(1)
plot(a*delta*y/(a*delta*y+g), y, linewidth=5, \
        label=r'$x=\frac{a\delta y}{a\delta y+g}$')
legend(loc=0)
quiver(X,Y,Xprime/sqrt(Xprime**2),zeros(Y.shape), color='r')
xlabel('$x$')
ylabel('$y$')
ticklabel_format(style='sci', axis='x', scilimits=(0,0))

figure(2)
quiver(X,Y,zeros(X.shape),Yprime/sqrt(Yprime**2), color='r')
plot(x, 1/(1+delta*mu/(b*sigma*x)), 'g',linewidth=5, \
        label=r'$y=\frac{1}{1+\frac{\delta\mu}{b\sigma x}}$')
legend(loc=0)
xlabel('$x$')
ylabel('$y$')
ticklabel_format(style='sci', axis='x', scilimits=(0,0))

figure(3)
quiver(X,Y,Xprime//sqrt(Xprime**2),Yprime/sqrt(Yprime**2), color='r')
```

```
plot(a*delta*y/(a*delta*y+g), y, 'b',linewidth=5)
plot(x, 1/(1+delta*mu/(b*sigma*x)), 'g', linewidth=5)
legend((r'$x=\frac{a\delta y}{a\delta y+g}$' \
    ,r'$y=\frac{1}{1+\frac{\delta\mu}{b\sigma x}}$'),loc=0)
xlabel('$x$')
ylabel('$y$')
ticklabel_format(style='sci', axis='x', scilimits=(0,0))

# display
show()
#####################################################################
```

The third code explains how to handle bifurcations.

```
#####################################################################
"""
Created April 2017

Author: May

Ross' schistosomiasis bifurcation
"""

# import
from math import *
from numpy import *
from matplotlib.pylab import *

# import ode solver
from scipy.integrate import odeint

# Time
T = 25*365 # final time 25 years
dt = 1. # time step 1 day
Nt = int(T/dt) # iterations in time
t = linspace(0,T,Nt) # time interval

# random initial condition
x0 = abs(randn(1))
y0 = abs(randn(1))
u0 = [x0[0], y0[0]]

# parameters initialization
a = 1.; delta = 40.; g = 6.e-4; b = 1e-4; sigma = 1.; mu = 7e-3

# define the ODE
def funct(u,t):
    x = u[0]; y = u[1]
    xprime = a*delta*y*(1.-x) - g*x
    yprime = b*sigma/delta*x*(1.-y) - mu*y
    return [xprime, yprime]

# generate solutions wrt to the bifuraction parameter
i = 0; n = 100
```

```
xx = zeros(n); yy = zeros(n); R0 = zeros(n)
mm = linspace(1e-1, 1., n)
for mu in mm:

    # parameters
    a = 1.; delta = 40.; g = 6.e-4; b = 1e-4; sigma = 1.

    # solve
    u = odeint(funct, u0, t)
    xx[i] = u[-1,0]
    yy[i] = u[-1,1]
    R0[i] = a*b*sigma/(mu*g)
    i = i + 1

# plot the solution
rcParams['font.size'] = 32
figure(1)
plot(mm,xx,'r', linewidth=5)
xlabel('$\mu$')
ylabel('$x^*$')
figure(2)
plot(mm,yy,'g', linewidth=5)
xlabel('$\mu$')
ylabel('$y^*$')
ticklabel_format(style='sci', axis='y', scilimits=(0,0))
figure(3)
plot(mm,R0,'--', linewidth=5)
xlabel('$\mu$')
ylabel('$R_0$')

# display
show()
##############################################################
```

A.3 Human-Mammal model

The first code allows to solve the system of 6 differential equations.

```
#############################################################
"""
Created April 2017

Author: May

Human–Mammal schistosomiasis model
"""

# import
from math import *
from numpy import *
from matplotlib.pylab import *

# import ode solver
from scipy.integrate import odeint

# Time
T = 4*365. # final time 4 years
dt = 1. # time step 1 day
Nt = int(T/dt) # iterations in time
t = linspace(0,T,Nt) # time interval

# Parameters
th = 1e-4 ; rh =  0.0038/7.
a = 7e-8; Ks = 3000./4.; Csi = 0.0; ms = 0.002/7.; tm = 6.32e-5
ai = 7e-8; Ki = 3000./4.; Cis = 0.0; mi = 0.002/7.
alpha = 5e-6; Kappas = 10000 ; Xsi = 0.0; mus = 7e-3; thetah = 5.15e-6 ; thetam = 5.15e-
alphai = 5e-6; Kappai = 10000; Xis = 0.0; mui = 7e-2

# initial condition from Ban Khatouay, Laos
Hs0 = 2750.; Hi0 = 0.
Ms0 = 2750./4.; Mi0 = 0.
Ss0 = abs(randn(1))[0]; Si0 = abs(randn(1))[0]
u0 = [Hs0,Hi0, Ms0,Mi0, Ss0, Si0]

# define the ODE
def funct(u,t):
    Hs = u[0] ; Hi = u[1]
    Ms = u[2] ; Mi = u[3]
    Ss = u[4] ; Si = u[5]

    Hsprime = -th*Hs*Si + rh*Hi
    Hiprime = th*Hs*Si - rh*Hi

    Msprime = a*(Ks - Ms - Csi*Mi)*Ms - ms*Ms - tm*Ms*Si
    Miprime = ai*(Ki -Mi - Cis*Ms)*Mi - mi*Mi + tm*Ms*Si

    Ssprime = alpha*(Kappas - Ss - Xsi*Si)*Ss - mus*Ss - thetah*Hi*Ss - thetam*Mi*Ss
    Siprime = alphai*(Kappai -Si - Xis*Ss)*Si - mui*Si + thetah*Hi*Ss + thetam*Mi*Ss
```

```
    return [Hsprime, Hiprime, Msprime, Miprime, Ssprime, Siprime]

# Solve the ode
u = odeint(funct, u0, t)

# plot the solution
rcParams['font.size'] = 32
Hs = u[:,0] ; Hi = u[:,1]
Ms = u[:,2] ; Mi = u[:,3]
Ss = u[:,4] ; Si = u[:,5]
figure(1)
plot(t,Hs,'r', linewidth=5)
ylabel(r'$H_s(t)$')
xlabel('day')
figure(2)
plot(t,Hi,'g', linewidth=5)
ylabel(r'$H_i(t)$')
xlabel('day')
figure(3)
plot(t,Ms,'b', linewidth=5)
ylabel(r'$M_s(t)$')
xlabel('day')
figure(4)
plot(t,Mi,'k', linewidth=5)
ylabel(r'$M_i(t)$')
xlabel('day')
figure(5)
plot(t,Ss,'y', linewidth=5)
ylabel(r'$S_s(t)$')
xlabel('day')
figure(6)
plot(t,Si,'m', linewidth=5)
ylabel(r'$S_i(t)$')
xlabel('day')


# display
show()
##################################################################
```

The second code is related with the phase portrait of human population.

```
#############################################################
"""
Created April 2017

Author: May

Human phase portrait
"""

# import
from math import *
from numpy import *
from matplotlib.pylab import *

# import ode solver
from scipy.integrate import odeint

# Time
T = 4*365. # final time 4 years
dt = 1. # time step 1 day
Nt = int(T/dt) # iterations in time
t = linspace(0,T,Nt) # time interval

# Parameters
th = 1e-4 ; rh =  0.00054
Si = 1.

# phase portrait
rcParams['font.size'] = 32
x = linspace(0.01, 5, 30); y = linspace(0.01, 2, 30)
[X,Y] = meshgrid(x, y) # generate a grid
Xprime = -th*X*Si + rh*Y
Yprime = th*X*Si - rh*Y

figure(1)
plot(x,th/rh*Si*x, linewidth=5, \
        label=r'$y= \frac{t_H S_i}{r_H}x$')
legend(loc=0)
quiver(X,Y,Xprime/sqrt(Xprime**2),zeros(Y.shape), color='r')
xlabel('$x$')
ylabel('$y$')

figure(2)
quiver(X,Y,zeros(X.shape),Yprime/sqrt(Yprime**2), color='r')
plot(x,th/rh*Si*x, 'g',linewidth=5, \
        label=r'$y= \frac{t_H S_i}{r_H}x$')
legend(loc=0)
xlabel('$x$')
ylabel('$y$')

figure(3)
quiver(X,Y,Xprime//sqrt(Xprime**2),Yprime/sqrt(Yprime**2), color='r')
plot(x,th/rh*Si*x, 'g',linewidth=5, \
```

```
            label=r'$y=\frac{t_H S_i}{r_H}x$')
legend(loc=0)
xlabel('$x$')
ylabel('$y$')

# display
show()
##################################################################
```

The third code computed eigevalues.

```
from sympy import *

# parameters
H, M, S = symbols("H M S")
tH, rH = symbols("tH rH")
a, Ks, csi, ms, tM, ai, Ki, cis, mi = symbols("a_s K_s c_si m_s t_M a_i K_i c_is m_i")
als, Kas, Qsi, mus, teH, teM, ali, Kai, Qis, mui = symbols("alpha_s kappa_s chi_si mu_s

# Jacobian of U1
JU1 = Matrix([[0, rH,  0, 0, 0, -tH*H], \
        [0, -rH,  0, 0, 0, tH*H], \
        [0, 0,  a*Ks-ms, 0, 0, 0], \
        [0, 0,  0, ai*Ki-mi, 0, 0], \
        [0, 0,  0, 0, als*Kas-mus, 0], \
        [0, 0,  0, 0, 0, ali*Kai-mui] ])
# eigenvalues of JU1
eU1 = JU1.eigenvals()
print 'the eigenvalues of J(U1) are ', eU1

# Jacobian of U2
JU2 = Matrix([[0, rH,  0, 0, 0, -tH*H], \
        [0, -rH,  0, 0, 0, tH*H], \
        [0, 0,  -a*Ks+ms, -csi*(a*Ks-ms), 0, -tM*(a*Ks-ms)/a], \
        [0, 0,  0, ai*Ki-mi, -ai*cis*(a*Ks-ms)/a, tM*(a*Ks-ms)/a], \
        [0, 0,  0, 0, als*Kas-mus, 0], \
        [0, 0,  0, 0, 0, ali*Kai-mui] ])
# eigenvalues of JU2
eU2 = JU2.eigenvals()
print 'the eigenvalues of J(U2) are ', eU2

# Jacobian of U3
JU3 = Matrix([[0, rH,  0, 0, 0, -tH*H], \
        [0, -rH,  0, 0, 0, tH*H], \
        [0, 0,  a*Ks-ms, 0, 0, 0], \
        [0, 0,  0, ai*Ki-mi, 0, 0], \
        [0,-teH*(als*Kas-mus)/als,0,-teM*(als*Kas-mus)/als,-als*Kas+mus,-als*Qsi*(als*Ka
        [0,teH*(als*Kas-mus)/als,0,teM*(als*Kas-mus)/als,0,ali*Kai-ali*Qis*(als*Kas-mus)
# eigenvalues of JU3
eU3 = JU3.eigenvals()
print 'the eigenvalues of J(U3) are ', eU3

# Jacobian of U4
JU4 = Matrix([[0, rH,  0, 0, 0, -tH*H], \
        [0, -rH,  0, 0, 0, tH*H], \
        [0, 0,  -a*Ks+ms, -csi*(a*Ks-ms), 0, -tM*(a*Ks-ms)/a], \
        [0, 0,  0, ai*Ki-mi -ai*cis*(a*Ks-ms)/a, 0, tM*(a*Ks-ms)/a], \
        [0,-teH*(als*Kas-mus)/als,0,-teM*(als*Kas-mus)/als,-als*Kas+mus,-als*Qsi*(als*Ka
        [0,teH*(als*Kas-mus)/als,0,teM*(als*Kas-mus)/als,0,ali*Kai-ali*Qis*(als*Kas-mus)
# eigenvalues of JU4
eU4 = JU4.eigenvals()
print 'the eigenvalues of J(U4) are ', eU4
```

A.4 Progressive waves

The first code allows to solve the system of differential equations.

```
#############################################################
"""
Created May 2017

Author: May

Progressive waves
"""

# import
from math import *
from numpy import *
from matplotlib.pylab import *

# import ode solver
from scipy.integrate import odeint
from scipy.optimize import newton

# Time
T = 10. # final time
dt = .01 # time step
Nt = int(T/dt) # iterations in time
t = linspace(0,T,Nt) # time interval

# Parameters
aH = 1.; bH = .01; sH = 10.; gH = 6.e-4
aM = 1.; bM = .01; sM = 10.; gM = 6.e-4
delta = 40.
mu = 100.
d = 1.
R0 = aH*bH*sH/(mu*gH) +  aM*bM*sM/(mu*gM)
c = 2.5*sqrt((R0-1)*mu*d)

# equilibrium
def f(x):
    return (aH*bH*sH*(aM*delta*x+gM) + aM*bM*sM*(aH*delta*x+gH))*(1.-x) - mu*(aH*delta*x
xs = newton(f, 1.0)
ys = 0.
u0 = [xs,ys-1e-5]

# define the ODE
def funct(u,t):
    x = u[0]
    y = u[1]
    xprime = y
    yprime = 1./d*(-c*y -(aH*bH*sH/(aH*delta*x+gH) + aM*bM*sM/(aM*delta*x+gM))*x*(1.-x)
    return [xprime, yprime]

# Solve the ode
u = odeint(funct, u0, t)
```

```
# plot the solution
rcParams['font.size'] = 32
x = u[:,0]
y = u[:,1]
figure(1)
plot(t,x,'r', linewidth=5)
ylabel(r'$x(t)$')
xlabel('day')
text(0,xs,'unstable')
text(9,0,'stable')
ticklabel_format(style='sci', axis='y', scilimits=(0,0))

figure(2)
plot(t,y,'g', linewidth=5)
ylabel(r'$y(t)$')
xlabel('day')
ticklabel_format(style='sci', axis='y', scilimits=(0,0))

# display
show()
##################################################################
```

The second code is related with the phase portrait.

```
#############################################################
"""
Created May 2017

Author: May

Progressive waves phase portrait
"""

# import
from math import *
from numpy import *
from matplotlib.pylab import *

# import ode solver
from scipy.integrate import odeint

# Time
T = 10. # final time
dt = .01 # time step 1 day
Nt = int(T/dt) # iterations in time
t = linspace(0,T,Nt) # time interval

# Parameters
aH = 1.; bH = .01; sH = 10.; gH = 6.e-4
aM = 1.; bM = .01; sM = 10.; gM = 6.e-4
delta = 40.
mu = 100.
d = 1.
R0 = aH*bH*sH/(mu*gH) +  aM*bM*sM/(mu*gM)
c = 2.5*sqrt(abs(R0-1)*mu*d)


# phase portrait
rcParams['font.size'] = 32
x = linspace(0.01, .5, 30); y = linspace(-1.5, 1.5, 30)
[X,Y] = meshgrid(x, y) # generate a grid
Xprime = Y
Yprime = 1./d*(-c*Y -(aH*bH*sH/(aH*delta*X+gH) + aM*bM*sM/(aM*delta*X+gM))*X*(1.-X) + mu

figure(1)
quiver(X,Y,Xprime/sqrt(Xprime**2),zeros(Y.shape), color='r')
plot(x, zeros(len(x)), linewidth=5, \
        label=r'$y=0$')
legend(loc=0)
xlabel('$x$')
ylabel('$y$')

figure(2)
quiver(X,Y,zeros(X.shape),Yprime/sqrt(Yprime**2), color='r')
plot(x, -1./c*((aH*bH*sH/(aH*delta*x+gH) + aM*bM*sM/(aM*delta*x+gM))*x*(1.-x) - mu*x), li
        label=r'$y=\frac{-1}{c}\left(\left(\frac{a_Hb_H\sigma_H}{a_H\delta x+g_H}\
legend(loc=0)
```

```
xlabel('$x$')
ylabel('$y$')

figure(3)
quiver(X,Y,Xprime//sqrt(Xprime**2),Yprime/sqrt(Yprime**2), color='r')
plot(x, -1./c*((aH*bH*sH/(aH*delta*x+gH) + aM*bM*sM/(aM*delta*x+gM))*x*(1.-x) - mu*x), li
        label=r'$y=\frac{-1}{c}\left(\left(\frac{a_Hb_H\sigma_H}{a_H\delta x+g_H}\
plot(x, zeros(len(x)), linewidth=5, \
        label=r'$y=0$')
legend(loc=0)
xlabel('$x$')
ylabel('$y$')

# display
show()
############################################################
```

A.5 Reaction-diffusion

This code show how to solve the partial differential equation within an image.

```
############################################################
"""
Created May 2017

Author: May

Spatial schistosomiasis model
"""

from numpy import *
import matplotlib.pyplot as plt
from diffusion import *

# image processing
from scipy import misc

# Time
T = 365 # final time

# Parameters
aH = 1.; bH = 1e-4; sH = 1.; gH = 6.e-4
aM = 1.; bM = 1e-4; sM = 1.; gM = 6.e-4
delta = 40.
mu = 7e-3
d = .1

# Read image
image = misc.imread('mekong.png',flatten=True)
imn = image/image.max() # nomalized
nx, ny = image.shape

# Initial data
u0 = np.random.rand(nx,ny)
u0 = u0*(1-imn)

# Solve the pde
u = diffusion(image, u0, d, T)

# Display solution
plt.subplot(1,3,1)
plt.imshow(image)
plt.title('River')
plt.axis("off")
plt.subplot(1,3,2)
plt.imshow(u0)
plt.title('initial_data')
plt.axis("off")
plt.subplot(1,3,3)
plt.imshow(u)
plt.title('prevalence_of_infection_after_' + str(T) + '_days')
```

```
plt.axis("off")
plt.show()
#####################################################################
```

Appendix B

Mathematical tools

This part contains some useful tools for the study of ordinary and parabolic differential equations. The content is based on Professor Mammeri's lecture notes during the SEAMS and CIMPA schools that held in NUOL in December 2016 and January 2017.

B.1 Existence and uniqueness of ODE

We consider the ODE of order 1

$$u'(t) = f(t, u(t)). \tag{B.1}$$

Lemma B.1.1 *The function $u : I \to \mathbb{R}^n$ is solution of (B.1) with initial datum $u(t_0) = u_0$ of class $\mathcal{C}^1$ if and only if*

1. $\forall t \in I, (t, u(t)) \in I \times U$,
2. $u(t) = u_0 + \int_{t_0}^{t} f(s, u(s))ds$.

Proof: It is enough to write

$$u(t) = u(t_0) + \int_{t_0}^{t} u'(s)ds.$$

□

Definition B.1.2 *A function $f : I \times U \to \mathbb{R}^n$ is said locally Lipschitz with respect to u if $\forall (t_0, u_0) \in I \times U$, there exists a neighborhood $\mathcal{V} = \mathcal{V}(t_0, u_0)$ and $k > 0$ such that $\forall (t, u_1), (t, u_2) \in \mathcal{V}$, we have*

$$||f(t, u_1) - f(t, u_2)|| \leq k||u_1 - u_2||.$$

Theorem B.1.3 *(Cauchy-Lipschitz, Picard-Lindelöf) Let $f : I \times \mathbb{R}^n$ a continuous function and locally Lipschitz with respect to the second variable. Then there exists $T > 0$ and a unique solution, without extension u of class $\mathcal{C}^1$ on $]-T + t_0, t_0 + T[$.*
Moreover if $f \in \mathcal{C}^k$ then $u \in \mathcal{C}^{k+1}$.

Proof: We define the operator

$$\phi u(t) = u_0 + \int_{t_0}^{t} f(s, u(s))ds,$$

and we prove that there exists a unique fixed point $u = \phi u$ in the closed ball

$$B = \left\{ u \in \mathcal{C}^1(]-T+t_0, t_0+T); \sup_{t\in]-T+t_0,t_0+T} ||u(t) - u_0|| \leq R \right\}.$$

Let us prove that ϕ is a contraction: we have for u and v in B

$$\begin{aligned} ||\phi u(t) - \phi v(t)|| &= || \int_{t_0}^{t} f(s, u(s)) - f(s, v(s))ds|| \\ &\leq k \sup_{t\in]-T+t_0,t_0+T} ||u(t) - v(t)||\,|t - t_0| \\ &\leq kT \sup_{t\in]-T+t_0,t_0+T} ||u(t) - v(t)||, \end{aligned}$$

and it is enough to choose $0 < T < \frac{1}{k}$.
Similarly

$$\begin{aligned} ||\phi u(t) - u_0|| &= ||\phi u(t) - \phi u(t_0)|| \\ &\leq kTR \end{aligned}$$

and $\phi B \subset B$ if $\sup_{t\in]-T+t_0,t_0+T} ||\phi u(t)|| \leq R$ *i.e.* $T \leq 1/(2k)$. □

Corollary B.1.4 *Under the same assumptions, if u_1 and $u_2 : I \to \mathbb{R}^n$ are two solutions of (B.1) which coincide in one point then $u_1 \equiv u_2$ in all I.*

Proof: It is a direct consequence of the uniqueness given by the previous theorem. □

Theorem B.1.5 *Let u be the solution defined in the maximal interval $]a, b[$. Then either*

$$b = +\infty \text{ or } \lim_{t\to b^-} ||u(t)|| = +\infty,$$

and either

$$a = -\infty \text{ or } \lim_{t\to a^+} ||u(t)|| = +\infty.$$

Proof: The solution does not has any extension. □

Corollary B.1.6 *1. If there exists a continuous function $k : I \to \mathbb{R}_+$ such that $\forall t \in I$ the map $u \to f(t, u)$ is $k(t)-$Lipschitz,*

2. or if there exist two continuous functions $c, k : I \to \mathbb{R}_+$ such that

$$||f(t,u)|| \leq c(t) + k(t)||u||,$$

then the solution is global.

Remark B.1.7 (1) $\Rightarrow$ (2) *with* $c(t) = ||f(t,0)||$.

Proof: We only prove (2). Since

$$u(t) = u_0 + \int_{t_0}^{t} f(s,u(s))ds,$$

we have

$$||u(t)|| \leq ||u_0|| + \int_{t_0}^{t} ||f(s,u(s))||ds =: \psi(t).$$

Then

$$\psi'(t) \leq c(t) + k(t)||u(t)|| \leq C + K\psi,$$

where $C = \sup_t c(t), K = \sup_t k(t)$. In onther words,

$$\begin{aligned} \frac{d}{dt}\left(\psi \mathrm{e}^{-K(t-t_0)}\right) = (\psi' - k\psi)\mathrm{e}^{-K(t-t_0)} &\leq C\mathrm{e}^{-K(t-t_0)} \\ \psi(t)\mathrm{e}^{-K(t-t_0)} - \psi(t_0) &\leq \frac{C}{K}\left(1 - \psi\mathrm{e}^{-K(t-t_0)}\right), \end{aligned}$$

i.e.

$$\sup_t ||x(t)|| \leq \sup_t \psi(t) \leq \frac{C}{K}\left(1 - \psi\mathrm{e}^{-K(t-t_0)}\right) + ||u_0||,$$

and $T = +\infty$. □

B.2 Stability of equilibrium

We consider the autonomous ordinary differential equation

$$\begin{cases} u'(t) = f(u(t)) \\ u(t_0) = u_0, \end{cases} \tag{B.2}$$

with $f : U \to \mathbb{R}^n$.

Definition B.2.1 *The point $u^* \in U$ is an equilibrium (or fixed point, or stationnary point) of (B.2) if $f(u^*) = 0$.*
The equilibrium u^* is said stable if $\forall \varepsilon > 0$, $\exists \delta > 0$ such that if $||u_0 - u^*|| \leq \delta$ then $\forall t \in I$, $||u(t) - u^*|| \leq \varepsilon$.
If the limit $\lim_{t\to+\infty} ||u(t) - u^*|| = 0$, the equilibrium is asymptotically stable. If furthermore, $||u_0 - u^*|| \leq \delta$, the equilibrium is said locally asymptotically stable.

Theorem B.2.2 *(Routh-Hurwitz) Let u^* an equilibrium of (B.2).*

1. *If $\forall \lambda \in \sigma(Jf(u^*)),\ \mathrm{Re}(\lambda) < 0$, then u^* is asymptotically stable;*
2. *If $\exists \lambda \in \sigma(Jf(u^*)),\ \mathrm{Re}(\lambda) > 0$, then u^* is unstable.*

Proof: From Taylor's expansion, we have in dimension 1

$$f(u(t)) = f(u^*) + (u(t) - u^*)f'(u^*) + o(u(t) - u^*).$$

Let $v(t) = u(t) - u^*$. The stability is reduced to the one of the linearized ODE

$$v'(t) = f'(u^*)v(t).$$

In higher dimension, the Taylor expansion can be written

$$f(u(t)) = f(u^*) + Jf(u^*)(u(t) - u^*) + o(u(t) - u^*),$$

where Jf is the jacobian matrix of f. □

Remark B.2.3 *If $u = (u_1, \dots, u_n)$ and $f = (f_1, \dots, f_m)$, the jacobian matrix is*

$$Jf(u) = \left(\frac{\partial f_i}{\partial u_j}\right)_{1 \le i \le n, 1 \le j \le m} = \begin{pmatrix} \frac{\partial f_1}{\partial u_1} & \cdots & \frac{\partial f_1}{\partial u_n} \\ \frac{\partial f_2}{\partial u_1} & \cdots & \frac{\partial f_2}{\partial u_n} \\ \vdots & \ddots & \vdots \\ \frac{\partial f_m}{\partial u_1} & \cdots & \frac{\partial f_m}{\partial u_n} \end{pmatrix} = \begin{pmatrix} \nabla f_1 \\ \nabla f_2 \\ \vdots \\ \nabla f_m \end{pmatrix}.$$

In dimension 2, the study of the stability of an equilibrium is reduced to

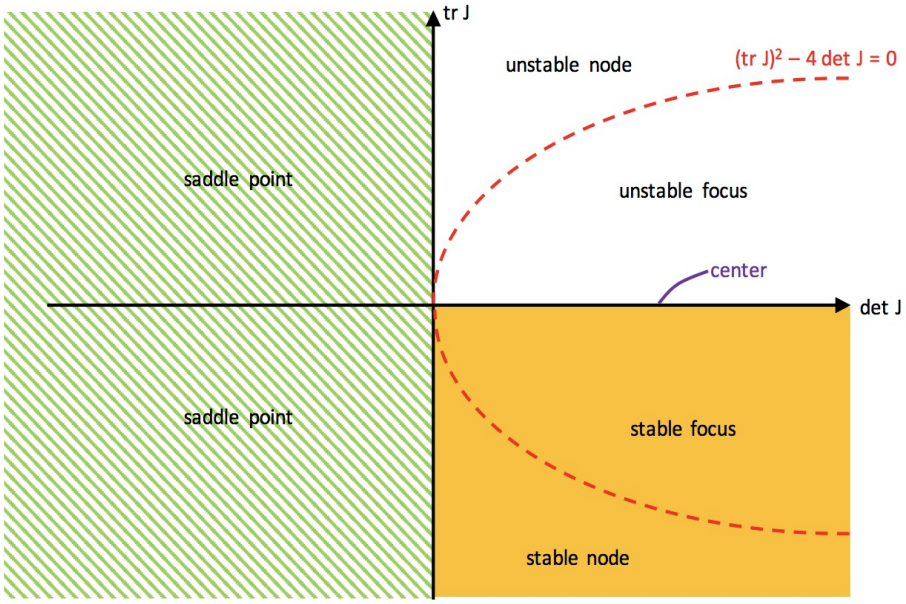


Figure B.1: Stability of equilibrium.

Theorem B.2.4 *(Lyapunov) Let u^* an equilibrium of (B.2). Assume that there exists a function $L : U \to \mathbb{R}$ of class $\mathcal{C}^1$ such that*

1. *$L(u^*) = 0$,*
2. *$L(u) > 0$ for all $u \in U - \{u^*\}$,*
3. *$L'(u) \leq 0$ along all trajectories in U.*

Then u^* is stable. The function L is called a Lyapunov function.
If furthermore,

4. *$L'(u) < 0$, $\forall u \neq u^*$, then u^* is locally asymptotically stable.*

Proof: Let $\varepsilon > 0$ such that the ball $B(u^*, \varepsilon) \subset U$ and $M = \inf_{||u-u^*||=\varepsilon} L(u)$ and $U_\varepsilon = \{u \in B(u^*, \varepsilon); L(u) < M\}$ is a neighborhood of u^* in U. Then if $u_0 \in U_\varepsilon$ and since $t \to L(u(t))$ is decreasing, we deduce that

$$L(u(t)) \leq L(u_0) < M, \ \forall t > 0$$

and $u(t)$ remains in the neighborhood of u^*. □

B.3 Finite differences

To numerically solve an ordinary differential equation, for $t \in [0, T]$

$$u'(t) = f(t, u(t)), \tag{B.3}$$

we choose a subdivision $0 = t_0 < t_1 < t_2 \ldots < t_N = T$ and we try to find a "good" approximation u_i of $u(t_i)$.
The idea of finite differences consists of approximating $u'(t_i)$ thanks to Taylor's formulas: let $u \in \mathcal{C}^{k+1}(I)$, then for t and $t + h \in U$, we have

$$u(t+h) = u(t) + hu'(t) + \frac{h^2}{2!}h''(t) + \ldots + \frac{h^k}{k!}h^{(k)}(t) + R_k(t),$$

Taylor-Young: $R_k(t) = o(h^k)$, *i.e.* $\lim_{h\to 0} \dfrac{R_k(t)}{h^k} = 0$

Taylor-Lagrange: $R_k(t) = \mathcal{O}(h^{k+1})$, *i.e.* $||R_k(t)|| \leq Ch^{k+1}$

Taylor with integral remainder: $R_k(t) = \dfrac{h^{k+1}}{(k+1)!} \displaystyle\int_0^1 (1-\tau)^k u^{(k+1)}(t + \tau h)dt.$

We consider one-step methods written as

$$\begin{cases} u_{i+1} = u_i + h\phi(t_i, u_i, h) \\ u_{0,h} = u_0, \end{cases}$$

where ϕ is a continuous function on $[0, T] \times \mathbb{R}^n \times [0, H]$.

Definition B.3.1 *The quantity*

$$\mathcal{E}_h = \sum_{i=0}^{n-1} |u(t_{i+1} - u(t_i) - h\phi(t_i, u_i, h)|$$

is the consistency error.
The method is said consitent with the ODE (B.3) if, for $u(t)$ solution of (B.3), $\mathcal{E}_h \to_{h\to 0} 0$.

Definition B.3.2 *A one-step method is said stable if there exists $C > 0$ such that if the sequence $(\widetilde{u}_i)_i$ defined by*

$$\begin{cases} \widetilde{u}_{i+1} = \widetilde{u}_i + h\phi(t_i, \widetilde{u}_i, h) + \varepsilon_i \\ \widetilde{u}_0 = \widetilde{u}_{0,h}. \end{cases}$$

Then

$$\max_{0\le i\le n} |u_i - \widetilde{u}_i| \le C \left(|u_{0,h} - \widetilde{u}_{0,h}| + \sum_{i=0}^{n-1} |\varepsilon_i| \right).$$

Definition B.3.3 *The method is convergent if $\max_{O\le i\le n} |u(t_i) - u_i| \to_{h\to 0} 0$.*

Theorem B.3.4 *(Lax) A method stable and consitent is convergent as soon as $u_{0,h} \to_{h\to 0} u_0$.*

Proof: Let us choose $\widetilde{u}_i = u(t_i)$. Then

$$\begin{cases} \widetilde{u}_{i+1} = \widetilde{u}_i + h\phi(t_i, \widetilde{u}_i, h) + \mathcal{E}_i \\ \widetilde{u}_0 = u_0. \end{cases}$$

By stability, we have

$$\max_{0\le i\le n} |u_i - \widetilde{u}_i| \le C \left(|u_{0,h} - \widetilde{u}_{0,h}| + \sum_{i=0}^{n-1} |\mathcal{E}_i| \right).$$

and thanks to the consistence, the error converges to zero when $h \to 0$. □

Proposition B.3.5 *A one-step method is consistent if $\phi(t, u, 0) = f(t, u)$, for all $t \in [0, T], u \in \mathbb{R}^n$.*

Proof: We write

$$\begin{aligned} \mathcal{E}_i &= u(t_{i+1}) - u(t_i) - h\phi(t_i, u(t_i), h) \\ &= \int_{t_i}^{t_{i+1}} (f(s, u(s)) - \phi(t_i, u(t_i), h))ds. \end{aligned}$$

However for $s \in [t_i, t_{i+1}]$, we have

$$\begin{aligned} |f(s, u(s)) - \phi(t_i, u(t_i), h)| \le\ & |f(s, u(s)) - f(t_i, u(t_i))| + |f(t_i, u(t_i)) - \phi(t_i, u(t_i), 0)| \\ & + |\phi(t_i, u(t_i), 0) - \phi(t_i, u(t_i), h)|. \end{aligned}$$

□

Proposition B.3.6 *A one-step method is stable if the function $\phi(t,u,h)$ is Lipschitz with respect to u with a constant independent of t and u.*

Proof: Let $\theta_i = |u_i - \widetilde{u}_i|$. We have

$$\begin{aligned}\theta_{i+1} &= |u_{i+1} - \widetilde{u}_{i+1}| \\ &= |u_i + h\phi(t_i,u_i,h) - \widetilde{u}_i - \phi(t_i,\widetilde{u}_i,h) - \varepsilon_i| \\ &\leq \theta_i + h|\phi(t_i,u_i,h) - \phi(t_i,\widetilde{u}_i,h)| + |\varepsilon_i| \\ &\leq (1+Lh)\theta_i + |\varepsilon_i|.\end{aligned}$$

The discrete Gronwall lemma implies

$$\theta_i \leq \exp(Lt_i)\theta_0 + \sum_{j=0}^{i-1}\exp(Lt_{i-j})|\varepsilon_j|$$

$$\exp(LT)\left(\theta_0 + \sum_{j=0}^{i-1}|\varepsilon_j|\right).$$

□

B.4 Reaction-diffusion equations

Assume that $D > 0$ is the diffusion coefficient, we define

$$K(x,t) = \lim_{\delta x,\delta t\to 0}\frac{p\left(\frac{x}{\delta x},\frac{t}{\delta t}\right)}{2\delta x} = \left(\frac{1}{4\pi Dt}\right)^{1/2}\mathrm{e}^{-\frac{x^2}{4Dt}}.$$

Theorem B.4.1 *The function $K : (x,t) \in \mathbb{R}^d \times \mathbb{R}_+^* \to K(t,x)$ is the fundamental solution of the heat equation*

$$\begin{aligned}\frac{\partial K}{\partial t} &= D\Delta K \\ K(x,0) &= 0,\end{aligned}$$

with

$$\int_{\mathbb{R}^d} K(x,t)dx = 1.$$

Corollary B.4.2 *Let $u_0 \in L^\infty(\mathbb{R})$.*
1. The function

$$u(x,t) = \int_{\mathbb{R}^d} K(x-y,t)u_0(y)dy = K \star u_0(x)$$

is solution of the initial value problem

$$\begin{aligned}\frac{\partial u}{\partial t} - D\Delta u &= 0 \\ u(x,0) &= u_0(x).\end{aligned}$$

The solution $u(x,t) \in \mathcal{C}^\infty$ in time and space. Moreover,

$$\begin{aligned} ||u(t,x)|| &\leq \frac{C}{|t|^{1/2}}||u_0|| \\ \left|\left|\frac{\partial u(x,t)}{\partial x}\right|\right| &\leq \frac{C}{|t|}||u_0||. \end{aligned}$$

Proof: The first part is deduced from the Fubini theorem.
We note that

$$\frac{\partial u}{\partial x} = \frac{\partial K}{\partial x} \star u,$$

and

$$\frac{x}{t^{1/2}} \mathrm{e}^{\frac{x^2}{4t}} \leq C.$$

□

Corollary B.4.3 *The function*

$$u(x,t) = \int_{\mathbb{R}^d} K(x-y,t)u_0(y)dy + \int_0^t \int_{\mathbb{R}^d} K(x-y,s)f(s)dyds$$

is solution of the reaction-diffusion problem

$$\begin{aligned} \frac{\partial u}{\partial t} - D\Delta u &= f \\ u(x,0) &= u_0(x). \end{aligned}$$

In particular, if $f = f(t,u)$ is Lipschitz with respect to u, there exists a unique strong solution.

Proof: It is enough to use the Duhamel formula. □

Proposition B.4.4 *Assume v, w, f be continuous with $f > 0, \phi \geq 0$ and $u_0 > M$. Then the solution for $x \in \Omega \subset \mathbb{R}^d, t > 0$*

$$\begin{aligned} \frac{\partial u}{\partial t} - D\frac{\partial^2 u}{\partial x^2} &= v\frac{\partial u}{\partial x} + wu + f \\ u(x,0) &= u_0(x) \\ u(x,t)_{|x\in\partial\Omega} &= \phi \end{aligned}$$

verifies $u(x,t) > M$ for all $x \in \Omega$ and $t \geq 0$.

Proof: Suppose first $w > 0$ and $f > 0$. Assume that there exist $x_* \in \Omega$ and $t^* > 0$ such that

$$u(x^*, t^*) = M \text{ is the minimum.}$$

Then

$$\frac{\partial u}{\partial t} = 0,\ \frac{\partial u}{\partial x} = 0,\ \frac{\partial^2 u}{\partial x^2} \geq 0$$

and

$$\begin{aligned} v\frac{\partial u}{\partial x} + wu = wu + f &\geq 0 \\ = \frac{\partial u}{\partial t} - D\frac{\partial^2 u}{\partial x^2} &\leq 0. \end{aligned}$$

For any w, we take $\widetilde{u} = u\mathrm{e}^{-kt}$ which satisfies

$$\frac{\partial \widetilde{u}}{\partial t} - D\frac{\partial^2 \widetilde{u}}{\partial x^2} = v\frac{\partial \widetilde{u}}{\partial x} + (w+k)\widetilde{u} + f.$$

□

Corollary B.4.5 *Suppose v, w, f continuous such that $f \geq 0, \phi \geq 0$ and $u_0 \geq M$. Then the solution of*

$$\begin{aligned} \frac{\partial u}{\partial t} - D\frac{\partial^2 u}{\partial x^2} &= v\frac{\partial u}{\partial x} + wu + f \\ u(x,0) &= u_0(x) \\ u(x,t)_{|x\in\partial\Omega} &= \phi \end{aligned}$$

verifies $u(x,t) \geq M$ for all $x \in \Omega$ and $t \geq 0$.