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Modélisation en dynamique des populations

Impacts des changements climatiques sur les populations de tiques

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ABSTRACT. Epidemiology had an important development these last years allowing the resolution of a large number of problems and had good prediction on disease evolution. However, the transmission of several vector-borne diseases is closely connected to environmental protagonists, specially in the parasite-host interaction. Moreover, understanding the disease transmission is related to studying the ecology of all protagonists. These two levels of complexity (epidemiology and ecology) cannot be separated and have to be studied as a whole in a systematic way. Our goal is to understand the interaction of climate change on the evolution of a disease when the vector has ecological niche that depends on physiological state of development. We are particularly interested in tick vector diseases which are serious health problem affecting humans as well as domestic animals in many parts of the world. These infections are transmitted through a bite of an infected tick, and it appears that most of these infections are widely present in some wildlife species.

RÉSUMÉ. L'épidémiologie a connu un développement important ces dernières années. Cette discipline a permis une meilleure compréhension de l'évolution de maladies. Cependant, plusieurs maladies à transmission vectorielle sont étroitement liées aux protagonistes environnementaux. Ce constat est particulièrement vrai dans le contexte des interactions du parasite avec son hôte. De plus, comprendre la transmission de maladie est lié à l'étude de l'écologie de tous les protagonistes. Notre objectif est de comprendre l'influence du changement climatique sur l'évolution des maladies lorsque la niche écologique du vecteur dépend de l'état de développement physiologique de son hôte. Nous sommes particulièrement intéressés par les maladies vectorielles à tiques qui constituent un grave problème de santé touchant l'être humain et les animaux domestiques dans de nombreuses régions du monde. Ces infections sont généralement transmises par la piqûre d'une tique infectée et il apparaît que la plupart de ces infections sont largement présentées dans certaines espèces fauniques.

KEYWORDS : Epidémiologie, McKendrick-Von Foerster equation, Partial differential equation (PDE), Transport equation

MOTS-CLÉS : Epidémiologie, Equation de McKendrick-Von Foerster, Equations aux dérivées partielles (EDP), Equation de transport



1. Introduction

Tick-borne diseases (theileriosis, rickettsiosis, Lyme disease, Ehrlichiosis, relapsing fever, TBE(tick-borne encephalitis)) are serious health problem affecting humans as well as domestic animals in many parts of the world. These infections are generally transmitted through a bite of an infected tick, and it appears that most of these infections are widely present in some wildlife species; hence, an understanding of tick population dynamics and its interaction with hosts is essential to understand and control such diseases [6]. For example, the vector of tropical theileriosis in North Africa, the tick *Hyalomma detritum*, has seasonal activity, while *Hyalomma anatolicum* is active throughout the year in several parts of Africa and Asia leading to animals being challenged with infection all over the year, this provides a solid immunity during the year contrasting with a very high infection leading to possible endemic stability.

The object of the present work is to develop a tick-borne biology model specific to *Hyalomma detritum* species in Tunisia. The model will be fitted to field data that have been previously gathered from several Tunisian farms [1].

Our ultimate goal in this paper is to construct models in order to study :

- Epidemiology: The effect of climate change on the evolution of tick-borne diseases particularly Theileriosis.

- Ecological question: What is the most important fact of tick life cycle regulation: Seasonality vs food.

- Control result: The effect of different control actions on tick population.

In order to achieve our goal, we need to solve the two following steps:

- 1) Modeling the tick life cycle, taking account of temperature fluctuation and seasonality: In this part our objective is to model tick life cycle in order to study the effect of temperature and seasonality on density of the ticks. The model used here will be a partial differentiable equation. The model will be tested using the data from [12] that have been previously gathered from several Tunisian farms [1]. This model will be the foundation of the late epidemiological model.

- 2) Integration the preceding model of tick life cycle into an epidemiological model:

- Tick: SI model and host: SIR model.

Our work is organized as follows: in the next section, we describe the biology of tick population and present the epidemiological interactions between ticks and their hosts. In section three, we describe both the tick life cycle and its mathematical models; introduce the model which represents the host-parasite epidemiological interaction. Section four is devoted to the conclusion and recommendation.

2. Biological Model

Several field observations on tick biology show a huge polymorphism in their biology (prolificity, mortality, phenology). This polymorphism is enhanced during the parasitic stages of the tick (during feeding stages) because of the interaction between the tick and the host (immunity of the host, surface of exposure, biology of the host). This degree of interaction is again more complicated when the tick-borne infections are considered. Describing this biology of the tick is possible by monitoring infested animals and questing instars and presenting the observations as descriptive results. Nevertheless, understanding

and predicting the mechanisms leading to a determined phenology is quite impossible. Moreover, the prediction of the impact of different control actions is difficult. Modeling represents a powerful tool offering the opportunity to counter account these difficulties. It is possible to model in silico both tick dynamic and the impact of different control options before implementing them, offering then a dramatic decrease of the control costs.

Mathematical modeling represents a powerful tool offering the opportunity to avoid these difficulties. Indeed, it is possible to model in silico both tick-host and epidemiological interactions in order to investigate and understand climate change on disease evolution. Moreover, modeling offer tools to test impact of different control options before implementing them, offering then a dramatic decrease of the control costs.

2.1. Effect of vector life cycle on disease transmission

The tick life cycle includes three post-embryonic developmental stages: larva, nymph and adult. Each stage can be subdivided in turn according to the activity phases: 'questing', in which the unfed tick seeks a host and 'feeding', in which the attached tick feeds, becomes engorged and drops off. After dropping off their hosts, *the cattle*, ticks go through a period of development, after which they emerge as questing ticks at the next stage (or eggs hatch, if the feeding ticks are adult females). The transition from one stage to an other depends closely on the successful questing period that depends on host density. Moreover, the physiological development depends on temperature fluctuations . These two phenomenons are strictly connected to climate change. Indeed, on one hand, it is evident that temperature fluctuation depends on the climate change and on the other hand cattle populations are strictly connected to the agricultural habit which depends on environment.

A variety of approaches have been used to model the tick population with various degrees of complexity. Models often describe in a discrete way the various stages of tick development from egg-larvae-nymph-adult, whether the ticks are attached to hosts, and if disease is part of the model, whether the ticks themselves are infected [15], [16].

Therefore, we propose in this paper two kind of models. The first model is a system of ordinary differential equations with delay where physiological structure is described in a discrete form. This time delay cannot be ignored because the development of the ticks between stages takes time. Moreover, the time delay depends on the weather and climate situation. For this first model our aim is to model tick life cycle in order to study the effect of temperature and seasonality on ticks density. For the second model, the transition from one physiological stage to an other is considered as a continuous process. In this case, we propose to build a PDE model where tick population density satisfies the McKendrick-Von Foerster model with or without blood meal as a limiting factor. All models constructed will be tested using the data from [12], data that have been previously gathered from several Tunisian farms [1] and several data from laboratory colonies. These models will be the foundation of the previous epidemiological model.

2.2. Host - Tick epidemiological interaction

The infection transmission is incorporated into models by adding more states to record the infected status of the ticks and hosts. Typically a mass action law assumption is adopted by the rate of new infections which is directly proportional to the product of susceptible hosts and infectious ticks. However, if larval and nymphs bites are statistically independent, then such clustering would tend to reduce tick and host infection prevalence. In this sense, as positive co-variance of larval and nymphal bites would tend to increase

infection prevalence, as larval bites would be clustered on the host individuals most likely to be infected and infective. An alternative approach to explicitly modeling the host and tick populations was provided by [4] who instead consider the life cycle of the *Theileria parva* parasite as it progresses through the vertebrate and tick hosts and estimates the time in days (from infection) of disease characteristics in cattle considering challenges from different numbers of infective ticks. It is often assumed that infected ticks behave in the same way as uninfected ones with the mortality of ticks being independent of their infection status. Although as has been seen a pathogen may have a negative impact on the tick in the same manner as a host. Generally models do not consider non-systemic infection (see above) although in a study by [16] this possibility was introduced. However trans-ovarian infection is usually excluded due to the lack of evidence for this in the literature. Reservoir decay or host turnover might enhance positive feedback of infection transmission, for example an increasing prevalence of infected nymphs would increase the frequency at which hosts are re-infected, keeping hosts in a state of high specific infective with a greater probability of infecting the next generation of ticks.

Infection is a one-way through the tick vectors, larvae/nymphae can transmit (trans-stadially) to the hosts of the adults they become, and adults can transmit (trans-ovally) to hosts of the larvae/nymphae that they become. There are two basic frameworks: those who treat the tick density as a parameter, and those who include the processes determining the density of ticks.

3. Implementation of models

3.1. Tick life cycle models

A structured population model is a summary of rules specifying how the number and distribution of individuals within a population changes over time [17]. Most structured population models fall into one of three categories: matrix models, ordinary differential equation (ODE) models, and partial differential equation (PDE) models. In this classification, model type is determined by whether time is discrete (matrix) or continuous (ODE, PDE), and whether the individual-level state is treated as a discrete (matrix, ODE) or a continuous (PDE) variable.

Matrix projection models are popular, because they have relatively simple structure and provide useful information. The eigenvalues and eigenvectors of the projection matrix provide estimates of the population growth rate, the stable age or stage distribution, reproductive value, and the sensitivities of population growth rate to changes in life history parameters [2]. However, whenever a matrix projection or ODE model is applied to population characterized by a continuous state variable (e.g., age, mass, or physiological stage), individuals must be divided into a discrete set of classes.

In partial differential equation models, the individual-level state variables are continuous, and individuals are not lumped into categories. Like the matrix models, PDE models can incorporate a variety of biological situations, including density dependence, and stage- or age-structured populations [7], that's why the basic model structure is the same in all cases. Furthermore, tick population dynamics can be expressed by the McKendrick-Von Foerster equation which is based on partial differential equations (PDE).

As we announced previously, our first objective is to construct a physiological stage dependent PDE model for the tick population dynamics. This model will be in order to fit

to field data from Tunisia that have been previously gathered from several Tunisian farms and several data from laboratory colonies.

As a second step we will investigate the effects of climate on geographic range and seasonality of the tick and compare our results with the ones in [9].

3.2. Parameter definition

We denote by s the tick physiological parameter and t the time parameter and suppose that host populations are fixed at given densities H . To understand the relationship between our PDE model and classical ODE model: we use a physiological parameters s and interstadal development rate, g and let us define s_{egg}^{max} , s_{larvae}^{max} , s_{nymph}^{max} , s_{adult}^{max} , the maximum length in the eggs, larvae, nymph and adult class.

To properly model the tick population the rates of tick mortality, reproduction rate (egg-laying) K , and interstadal development rate, g , must be obtained, while to prevent the tick population exponentially increasing issues regarding density dependence should be addressed.

3.3. Mathematical Models

We describe here the mathematical models that we propose to study.

3.3.1. Model 1

The functional equation considered in this model is derived from a physiological-structured model for a population divided into several stages in which individuals change their stage when a certain magnitude reaches a predetermined threshold value. This means that the physiological parameter s of passing from one stage to the next is time-dependent, giving rise to a moving boundary. More details can be found in [10].

To illustrate the ideas underlying the model, consider a population divided into two stages, larvae (l) and adults (L), each one being structured by the age in the stage.

Denote by $l(s, t)$ the density of larvae, $n(s, t)$ the density of nymph and $a(s, t)$ the density of adult at time t and in physiological state s . Capitals, L , N and A , denote the total population of larvae, nymph and adult respectively at time t .

3.3.1.1. Transition from larvae to nymph stage

Let us describe the passage through the larvae stage. We assume that the larvae turn adult when some variable reaches a prescribed value. For example, in [10] the passage to (n) is described in terms of a blood meal which can be measured by *weight function of larvae* $w_l(s, t)$ representing the quantity of blood eaten until time t by an individual until reaches stage s . Larvae turn nymph when the food index reaches a prescribed value $Q_l > 0$. We also assume that there is a finite maximum age $s_{larvae}^{max} > 0$ for individuals in the larval stage: individuals which have not acquired the amount Q of food past $s_{larvae}^{max} > 0$ will die or never reach the nymph stage.

In the model considered in [10], the weight function of larvae depends on the total population of larvae, so that:

$$w_l(s, t) := \int_{t-a}^t \frac{K_l}{L(\sigma) + J_l} d\sigma; \quad L(t) := \int_0^{s_{larvae}^{max}} l(s, t) ds \quad (1)$$

which means that the quantity of food available is shared in equal parts by all the individuals occupying the same space at time t . $K_l > 0$ is the quantity of food entering the species habitat per unit of volume and per unit of time, which for simplicity is considered

to be constant. The constant $J > 0$ represents the food (converted into a number of individuals) taken per unit of volume by consumers other than larvae.

Then, the age of passage to the (l) stage, denoted by $s_l^*(t)$, is defined by the *threshold condition*:

$$w_l(s, t) = Q \quad (2)$$

so that

$$s_l^*(t) = \begin{cases} s(t) & \text{solution to (2), if it exists and satisfies } 0 \leq s(t) \leq s_{larvae}^{max}, \\ s_{larvae}^{max} & \text{otherwise.} \end{cases}$$

Bearing in mind the above considerations, the density of larvae $l(s, t)$ satisfies the following model:

$$\begin{cases} \frac{\partial l}{\partial t}(s, t) + \frac{\partial}{\partial s}(g_l(s, t)l(s, t)) = -\mu_l(s)l(s, t), & 0 < s < s_l^*(t), t > 0, \\ l(s, t) = 0, & s_l^*(t) \leq s \leq s_{larvae}^{max}, t > 0, \\ l(s, 0) = 0, & 0 \leq s \leq s_{larvae}^{max}, \\ l(0, t) = B(t), & t > 0, \end{cases}$$

where $\mu_l(s)$ is the age-dependent mortality rate of larvae, the initial condition expresses the fact that at time $t = 0$ no individuals are in the (l) stage and $B(t)$ is the recruitment of larvae at time t . We will assume that μ_l is a nonnegative continuous function on $[0, s_{larvae}^{max})$ such that

- 1) $l(s, t)$ is the density of larvae that have absorbed a quantity of blood s at time t .
- 2) $n(s, t)$ is the density of nymphs that have absorbed a quantity of blood s at time t .

- 3) $a(s, t)$ is the density of adults that have absorbed a quantity of blood s at time t .

The tick population dynamic is given by the following system which is composed by three PDE:

Equation of larvae:

$$\begin{cases} \frac{\partial l(s, t)}{\partial t} + \frac{\partial}{\partial s}(g_l(s, t)l(s, t)) = -\mu_l(s)l(s, t), \\ l(0, t) = \lambda \int_0^{s_l^*(t)} B(\sigma)a(\sigma, t)d\sigma, \\ l(s, 0) = \psi_l(s). \end{cases} \quad (3)$$

Equation of nymphs

$$\begin{cases} \frac{\partial n(s, t)}{\partial t} + \frac{\partial}{\partial s}(g_n(s, t)n(s, t)) = -\mu_n(s)n(s, t), \\ n(0, t) = \delta \int_{t-\bar{s}_n}^t l(s_n^*(\sigma), \sigma)d\sigma, \\ n(s, 0) = \psi_n(s), \end{cases} \quad (4)$$

with $\bar{s}_n = \sup_{[0, t]} s_n^*(t)$.

Dynamic equation of adults:

$$\begin{cases} \frac{\partial a(s, t)}{\partial t} + \frac{\partial}{\partial s} (g_a(s, t)a(s, t)) = -\mu_a(s)a(s, t), \\ a(0, t) = \gamma \int_{t-\bar{s}_a}^t n(s_a^*(\sigma), \sigma) d\sigma, \\ a(s, 0) = \psi_a(s), \end{cases} \quad (5)$$

with $\bar{s}_a = \sup_{[0, t]} s_a^*(t)$.

- The functions g_l , g_n and g_a are the growth of blood's quantity which have absorbed by ticks at stages l , n and a respectively.

3.3.2. Model 2

The tick population density varies satisfying the following model for all $t \in [0, \mathbb{T}]$ and $s \in [s_{min}, s_{max}]$ given by

$$\begin{cases} \frac{\partial n(s, t)}{\partial t} + \frac{\partial}{\partial s} (g(s, t)n(s, t)) = -\mu(n(s, t))n(s, t), \\ n(s_{min}, t) = \int_{s_{min}}^{s_{max}} K(n(s, t))n(s, t) ds, \\ n(s, 0) = n_0(s), \end{cases}$$

with s_{min} and s_{max} the min and the max physiological stage of the tick life cycle and \mathbb{T} the maximum study time.

We are going to work on a set of differentiable C^1 periodic functions on t , and C^1 non-negative functions on s such that $n(s_{max}, t) = 0$ for all times t .

On this basis, since we are dealing with C^1 non-negative functions on s , we may consider that $a(s)$ and $b(s)$, functions appearing in the somatic growth rate $g(s, t)$ as non-negative functions of s so that $g(T) \leq a(s)$ for all $s \in [s_{min}, s_{max}]$ and $t \in [0, \mathbb{T}]$. Moreover, we may suppose that $a(s)$ is a bounded function i.e there exists a constant $\mathcal{C} > 0$ such that

$$a(s) \leq \mathcal{C}, \quad \forall s \in [s_{min}, s_{max}].$$

Thus,

$$g(T) \leq \mathcal{C}, \quad \forall s \in [s_{min}, s_{max}], \quad \forall t \in [0, \mathbb{T}].$$

Also let \mathcal{N} be the maximum tick population density so that

$$n(s, t) \leq \mathcal{N}, \quad \forall s \in [s_{min}, s_{max}], \quad \forall t \in [0, \mathbb{T}].$$

3.3.3. Model 3

The following model aims to analyze the impact of climate change on life cycle tick and especially on hibernation period. Let $x_1(t)$ be the density of larvae at time t , $x_2(t)$ the density of nymphs after hibernation at time t and $x_3(t)$ the density of adults at time t .

We suppose that $T(t)$ the temperature at time t , $\rho(T)$ the fertility rate of adult females at time t and $\mu(t, T)$ the mortality rate. Thus, the system equations are written in the following way:

$$\begin{cases} \frac{dx_1(t)}{dt} = \int_{t-\tau}^t \rho(T(\sigma))x_3(\sigma) d\sigma - \mu_1(t, T(t))x_1(t) - f_1(t, T, H, x_1), \\ \frac{dx_2(t)}{dt} = \lambda_1 \alpha_1(t, T, H, x_1(t - r(t, T(t))))x_1(t - r(t, T(t))) - \mu_2(t, T(t))x_2(t) - f_2(t, T, H, x_2(t)), \\ \frac{dx_3(t)}{dt} = \lambda_2 \alpha_2(t, T, H, x_2(t))x_2(t) - \mu_3(t, T(t))x_3(t). \end{cases}$$

With

$$\begin{aligned} - f_1(t, T, H, x_1) &= \alpha_1(t, T, H, x_1(t))x_1(t). \\ - f_2(t, T, H, x_1) &= \alpha_2(t, T, H, x_2(t))x_2(t). \end{aligned}$$

3.4. Physiological SIS for ticks and SIR ODE for host Model

We consider that the number of tick is governed by the equation of section 3.2 and that the tick are subdivided in two class Susceptible and Infected. Let $n_T^s(t)$ and $n_T^i(t)$ be respectively the frequencies of susceptible and infected tick parasites, i.e.,

$$n_T^s(t) + n_T^i(t) = P(t).$$

But

$$P(t) = \int_{a_{min}}^{a_{max}} (l(a, t) + n(a, t) + a(a, t))da, \quad \forall a \in [a_{min}, a_{max}],$$

where $P(t)$ is total population of tick parasites, a_{min} and a_{max} are the min and the max physiological age of the tick life cycle.

And that the host population number is constant, let $n_H^s(t)$, $n_H^i(t)$ and $n_H^r(t)$ be respectively the frequencies of susceptible, infected and removed host population, i.e. $n_H^s(t) + n_H^i(t) + n_H^r(t) = 1$.

Consider the following assumptions:

- Let $\phi(n)$ be the factor representing the influence of ticks on the host. Thus the model representing the host-parasite epidemiological interaction is given by the following SIR-SIS model:

$$\frac{dn_H^s(t)}{dt} = -K_1 n_H^s(t) n_H^i(t) \quad (6)$$

$$\frac{dn_H^i(t)}{dt} = K_1 n_H^s(t) n_H^i(t) - K_2 n_T^i(t) n_H^i(t) \quad (7)$$

$$\frac{dn_H^r(t)}{dt} = K_2 n_T^i(t) n_H^i(t) \quad (8)$$

$$\frac{dn_T^i(t)}{dt} = K_1 n_H^s(t) n_H^i(t) - \phi(n) K_2 n_T^i(t) n_H^i(t) + n_T^s(t) \quad (9)$$

$$n_T^s(t) = 1 - n_T^i(t) \quad (10)$$

4. Conclusion and Recommendation

In this paper, we present the various stages of tick population dynamics which is composed by three partial differential equations.

Our aim in the future is to adapt the numerical method developed in subsection 3.2 in order to solve the correlated EDO-EDP equations. This method will be used to test impact of climate change on transmission of Tick disease, for that the model will be fitted to field data that have been previously gathered from several Tunisian farms [1] and several data from laboratory colonies (Darghouth, unpublished data) and with data from Tunisian National Institute of Meteorology. Furthermore, our goal is to develop new numerical methods in order to approximate solutions of the previous type of equations in subsection 3.3.2.

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