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Identifiablility of parameters in an epidemiologic model

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ABSTRACT : *In the last years, several epidemics have been reported in particular the chikungunya epidemic on the Réunion Island. For predicting its possible evolution, new models describing the transmission of the chikungunya to the human population have been proposed and studied in the literature. In such models, some parameters are not directely accessible from experiments and for estimating them, iterative algorithms can be used. However, before searching for their values, it is essential to verify the identifiability of models parameters to assess whether the set of unknown parameters can be uniquely determined from the data. Thus, identifiability is particularly important in modeling, indeed, if the model is not identifiable, numerical procedures can fail and in that case, some supplementary data have to be added or the set of admissible data has to be reduced. Thus, this paper proposes to study the identifiability of the proposed models by (Moulay, Aziz-Alaoui & Cadivel 2011).*

KEY WORDS : *Identifiability; Nonlinear models; Epidemiologic model; Chikungunya virus.*

1 Introduction

The *chikungunya* virus is a vector-borne disease transmitted by mosquitoes of *Aedes* genus. Several epidemics of this tropical disease have been reported these last 50 years. Recently an unprecedented epidemic has been observed in the Réunion island (a French island in the Indian Ocean) in 2005-2006 where one third of the total population has been infected. A pic of 40 000 infected per week has been reached in february 2006. Another *chikungunya* epidemic has been reported in Italy in 2007. It was the first time that such disease was observed in a non tropical region. The responsible vector of these two epidemics is identified: the *Aedes Albopictus* mosquito (Reiter, Fontenille & Paupy 2006). Contrary to *Aedes Aegypti*, the main vector of Dengue, which also transmits the chikungunya virus, *Aedes Albopictus* has developed capabilities to adapt to non tropical region. Chikungunya is now a major health problem. European health authorities are now strongly engaged in the control of this disease. Since there is no vaccine nor specific treatment, efforts are mostly directed towards prevention measures and the control of mosquito proliferation. Since these events, several works and models are proposed to try to understand their emergence or re-emergence. Various fields of research are concerned, such as epidemiology, biology, medicine or mathematics. For instance, Dengue, a vector borne disease mainly transmitted by *Aedes Aegypti* mosquitoes was the subject of several studies (Esteva & Vargas 1999, Esteva & Vargas 1998).

Models for the chikungunya virus have been recently proposed (Dumont, Chiroleu & Domerg 2008), (Moulay, Aziz-Alaoui & Cadivel 2011).... Since the models are recent, the not well-known parameters have not yet been studied. In this paper, we propose to take again the models proposed by (Moulay, Aziz-Alaoui & Cadivel 2011) and to do an identifiability study. For this, let us consider ordinary controlled or uncontrolled dynamical systems described in a general state-space form:

$$\Gamma^\theta = \begin{cases} \dot{x}(t,\theta) = f(x(t,\theta),\theta) + u(t)g(x(t,\theta),\theta), \\ y(t,\theta) = h(x(t,\theta),\theta). \end{cases} \tag{1}$$

Here $x(t,\theta) \in \mathbb{R}^n$ and $y(t,\theta) \in \mathbb{R}^m$ denote the state variables and the measured outputs, respectively and $\theta \in \mathcal{U}_p$ the unknown parameters vector ($\mathcal{U}_p$ is an open subset in $\mathbb{R}^p$). The functions $f(.,\theta)$, $g(.,\theta)$ and $h(.,\theta)$ are real, rational and analytic for every $\theta \in \mathcal{U}_p$ on M (a connected open subset of $\mathbb{R}^n$ such that $x(t,\theta) \in M$ for every $\theta \in \mathcal{U}_p$ and every $t \in [0,T]$). In the case of uncontrolled system u is equal to 0.

Since the initial conditions are not considered, the solution of Γ^θ may be nonunique and some solutions might be of a degenerate character. Thus, the set of nondegenerate solutions will be denoted by $\bar{x}(t,\theta)$, the set of corresponding outputs by $\bar{y}(t,\theta)$. The defi-

nition introduced by (Ljung & Glad 1994) is adopted here. For uncontrolled systems, one gets:

Definition 1.1. *The model Γ^θ is globally identifiable at $\theta \in \mathcal{U}_p$ if for any $\bar{\theta} \in \mathcal{U}_p$, $\bar{\theta} \neq \theta$, $\bar{y}(\theta) \neq \emptyset$ and $\bar{y}(\theta) \cap \bar{y}(\bar{\theta}) = \emptyset$.*

The identifiability definition of the controlled model Γ^θ is the following:

Definition 1.2. *The model Γ^θ is globally identifiable at $\theta \in \mathcal{U}_p$ if for any $\bar{\theta} \in \mathcal{U}_p$, $\bar{\theta} \neq \theta$, there exists an input u, such that $\bar{y}(\theta, u) \neq \emptyset$ and $\bar{y}(\theta, u) \cap \bar{y}(\bar{\theta}, u) = \emptyset$.*

The identifiability of models has been extensively studied (Ljung & Glad 1994), (Vajda, Godfrey & Rabitz 1989), (Verdière, Denis-Vidal, Joly-Blanchard & Domurado 2005) and different approaches have been proposed for studying the global identifiability of nonlinear systems. We can mention for example, the Taylor Series approach of (Pohjanpalo 1978). He proposed a method based on the analysis of a power series expansion of the output which gives rise to an algebraic system constituted of an infinite number of equations. A second method is based on the local state isomorphism theorem ((Walter & Lecourtier 1982), (Chappell & Godfrey 1992), (Denis-Vidal, Joly-Blanchard & Noiret 2001), (Chapman, Godfrey, Chappell & Evans 2003)). It leads to study the solution of a specific set of partial differential equations. A third one is a method based on differential algebra that was introduced by (M. Fliess 1993), (Ljung & Glad 1994) and (Ollivier 1997). It allows one to obtain relations linking the observations, the inputs and the unknown parameters of the system. These relations can be used to obtain a first estimation of the unknown parameters without *a priori* any knowledge of them (Verdière et al. 2005). It is the latter method which will be used in this paper for studying the parameters identifiability.

The paper is organized as follows. In the second section, models describing the transmission of the chikungunya virus to human population are presented. Some results obtained in (Moulay, Aziz-Alaoui & Cadivel 2011) will be recalled since they will give us first, the framework of our study then, the steps to study the models identifiability. In the third section, the identifiability results are given.

2 Presentation of the models

In (Bacaër 2007) the author formulate several methods to compute the basic reproduction number for epidemiological models. One of the first models describing the *chikungunya* transmission virus using SI-SIR type models is proposed (these classical models consist in the subdivision of a population depending on its epidemiological state : Susceptible, Infective or Removed). Moreover, some biological parameter values are given. Another approach is described in (Dumont et al. 2008), where a global aquatic stage for the mosquito dynamics supplements a classical transmission model. In (Dumont & Chiroleu 2010), authors formulate an ordinary differential equation system to study control of *chikungunya* virus using mechanical and chemical tools. In (Moulay, Aziz-Alaoui & Kwon 2011), control efforts are taken into account through the formulation of an optimal control problem, where the objective is to control the mosquito proliferation and limit the number of human and mosquito infections. This papers deal with the Réunion Island epidemic.

The model given in (Moulay, Aziz-Alaoui & Cadivel 2011, Moulay, Aziz-Alaoui & Kwon 2011) takes into account the mosquito biological life cycle and describes the virus transmission to human population. For the reader convenience, we briefly recall the modeling steps. The mosquito biological life cycle consists in four stages: eggs, larvae, pupae and adults. We use a stage structured model to describe the following stages: eggs number (E), larvae and pupae number (L), two stages biologically close and female adults number (A), only females can transmit the virus stages. The density variation of each stage is described by the following scheme:

$$density\ variation = entering - (leaving + death)$$

The egg density variation is then described by the number of eggs laid by females b, by eggs becoming larvae with a transfer rate s and by eggs death with a natural mortality rate d. We assume that the number of eggs is proportional to the number of females $b(t)A(t)$, and regulated by a carrying capacity K_E since mosquitoes are able to detect the best breeding site ensuring the egg development, then $b(t) = bA(t)(1 - E(t)/K_E)$. Other stages, are described in the same way. The input in the larvae stage, given with a transfer s is also assumed to be regulated by a carrying capacity K_L which characterizes the availability of nutrients and space. The number of new larvae entering the L stage is then given by $s(t) = sE(t)(1-L(t)/K_L)$. These larvae become adult females with a transfer rate s_L. Natural deaths occur with a rate d_L, d_m for larvae and adults respectively.

This model is then included in a classical SI-SIR epidemiological model to describe the virus transmission to human population. To this aim, the adult stage A is divided into two epidemiological states: susceptible S_m and infective I_m, since mosquitoes carry

the infection along their life. The human population N_H (for which we assume an exponential growth,*i.e.* $\frac{dN_H}{dt}(t) = (b_H - d_H)N_H(t)$ where b_H and d_H are , respectively, the human birth and natural death rates) is subdivided into three stages: susceptible S_H, infected I_H and recovered (or immune) R_H. We assume that there is no vertical transmission for both humans and mosquitos. This means that human birth, with a rate b_H from susceptible, infected and removed are susceptible and eggs laid by susceptible or infected mosquitoes are susceptible. The vector infection of susceptible mosquitoes ($\bar{S}_m$) occurs during the blood meal (necessary to the female egg laying) from infectious humans ($\bar{I}_H$). The force of infection (or per-capita incidence rate among mosquitoes) given by $\beta_m \bar{I}_H/N_H$ depends on the fraction of infectious individuals $\bar{I}_H/N_H$ and the number of bites that would result in an infection β_m. Conversely, the *chikungunya* infection among humans occurs when susceptible humans ($\bar{S}_H$) are bitten by infectious mosquitoes ($\bar{I}_m$) during blood meal. The force of infection given by ($\beta_H \bar{I}_m/A(t)$) depends on the fraction of infectious mosquitoes ($\bar{I}_m/A(t)$) and the number of bites that would result in an infection β_H. Infected humans are infectious during $1/\gamma$ days, called the viremic period, and then become immune.

All previous assumptions are summed up in Fig. 1.

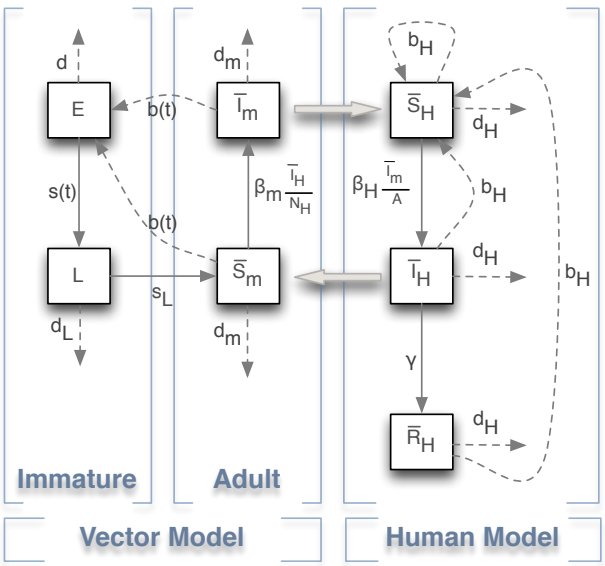

Figure 1: Compartmental model for the dynamics of *Aedes albopictus* mosquitoes and the virus transmission to human population. Stages E, L correspond to the immature stages, eggs and larvae/pupae respectively. The female adult stage A is described by an SI model where $\bar{S}_m$ and $\bar{I}_m$ designed the susceptible and infected mosquito stages, respectively.

Based on our model description (see Fig.1) and assumptions, we establish the following equations:

$$\begin{cases} E'(t) &= bA(t)\left(1 - \dfrac{E(t)}{K_E}\right) - (s+d)E(t) \\ L'(t) &= sE(t)\left(1 - \dfrac{L(t)}{K_L}\right) - (s_L + d_L)L(t) \\ A'(t) &= s_L L(t) - d_m A(t) \\ \bar{S}'_m(t) &= s_L L(t) - d_m \bar{S}_m(t) - \beta_m \dfrac{\bar{I}_H(t)}{N_H(t)} \bar{S}_m(t) \\ \bar{I}'_m(t) &= \beta_m \dfrac{\bar{I}_H(t)}{N_H(t)} \bar{S}_m(t) - d_m \bar{I}_m(t) \\ \bar{S}'_H(t) &= -\beta_H \dfrac{\bar{I}_m(t)}{A(t)} \bar{S}_H(t) - d_H \bar{S}_H(t) \\ & \quad + b_H(\bar{S}_H(t) + \bar{I}_H(t) + \bar{R}_H(t)) \\ \bar{I}'_H(t) &= \beta_H \dfrac{\bar{I}_m(t)}{A(t)} \bar{S}_H(t) - \gamma \bar{I}_H(t) - d_H \bar{I}_H(t) \\ \bar{R}'_H(t) &= \gamma \bar{I}_H(t) - d_H \bar{R}_H(t) \end{cases} \tag{2}$$

Let us consider the following variable changes $S_m = \bar{S}_m/A$, $I_m = \bar{I}_m/A$, $S_H = \bar{S}_H/N_H$, $I_H = \bar{I}_H/N_H$ and $R_H = \bar{R}_H/N_H$ and the fact that then $S_m = 1 - I_m$ et $R_H = 1 - S_H - I_H$, we have :

$$\begin{aligned} S'_H &= (1/N_H^2)\left(\bar{S}'_H N_H - \bar{S}_H N'_H\right) \\ &= (1/N_H^2)\Big((-\beta_H \frac{\bar{I}_m}{A}\bar{S}_H - d_H \bar{S}_H + b_H N_H)N_H \\ &\quad - \bar{S}_H(b_H - d_H)N_H\Big) \\ &= \left(-\beta_H \frac{\bar{I}_m}{A}\frac{\bar{S}_H}{N_H} - d_H \frac{\bar{S}_H}{N_H} + b_H\right) - \frac{\bar{S}_H}{N_H}(b_H - d_H) \\ &= (-\beta_H I_m S_H - d_H S_H + b_H) - S_H(b_H - d_H) \\ &= -\beta_H I_m S_H - b_H S_H + b_H \end{aligned}$$

With the same computation for the other variables, system (2) reads as:

$$\begin{cases} \begin{cases} E'(t) = bA(t)\left(1 - \dfrac{E(t)}{K_E}\right) - (s+d)E(t) \\ L'(t) = sE(t)\left(1 - \dfrac{L(t)}{K_L}\right) - (s_L + d_L)L(t) \\ A'(t) = s_L L(t) - d_m A(t) \end{cases} & (a) \\ \begin{cases} S'_H(t) = -\left(b_H + \beta_H I_m(t)\right) S_H(t) + b_H \\ I'_H(t) = \beta_H I_m(t) S_H(t) - (\gamma + b_H) I_H(t) \\ I'_m(t) = -\left(s_L \dfrac{L(t)}{A(t)} + \beta_m I_H(t)\right) I_m(t) + \beta_m I_H(t) \end{cases} & (b) \end{cases} \tag{3}$$

and it is defined on $\Delta \times \Omega$ where

$$\Delta = \left\{ (E, L, A) \in (\mathbb{R}^+)^3 \;\middle|\; \begin{array}{l} 0 \le E \le K_E \\ 0 \le L \le K_L \\ 0 \le A \le \dfrac{s_L}{d_m} K_L \end{array} \right\} \tag{4}$$

and

$$\Omega = \left\{ (S_H, I_H, I_m) \in (\mathbb{R}^+)^3 \mid \begin{array}{l} 0 \leq S_H + I_H \leq 1 \\ 0 \leq I_m \leq 1 \end{array} \right\}. \tag{5}$$

The stability analysis of the model is detailed in (Moulay, Aziz-Alaoui & Cadivel 2011). We briefly recall some results about this model. The study was conducted in two steps and they will be taken again for the identifiability study. First, we analyze the mosquito dynamics in the absence of virus, which corresponds to the subsystem (3a). The mosquito dynamics is governed by the following threshold:

$$r = \left(\frac{b}{s+d}\right)\left(\frac{s}{s_L + d_L}\right)\left(\frac{s_L}{d_m}\right) \tag{6}$$

obtained from computation of the equilibrium.

Theorem 2.1.

- *System (3a) always has the mosquito-free equilibrium* $(0,0,0)$*, which is globally asymptotically stable (GAS) if* $r \leq 1$ *and unstable otherwise*
- *If* $r > 1$ *system (3a) has an endemic equilibrium* (E^*, L^*, A^*) *wich is GAS, where*

$$\begin{pmatrix} E^* \\ L^* \\ A^* \end{pmatrix} = \left(1 - \frac{1}{r}\right) \begin{pmatrix} \dfrac{K_E}{\gamma_E} \\ \dfrac{K_L}{\gamma_L} \\ \dfrac{s_L}{d_m}\dfrac{K_L}{\gamma_L} \end{pmatrix}$$

$$\gamma_E = 1 + \frac{(s+d)d_m K_E}{b s_L K_L} \quad \text{and} \quad \gamma_L = 1 + \frac{(s_L + d_L)K_L}{s K_E}$$

In both cases, the global stability is obtained by using Lyapunov function theory.

Now we assume $r > 1$, the biological interesting case, in order to ensure the persistence of mosquito population and we consider the subsystem (3b).

The stability of equilibrium of the transmission dynamics model is described thanks to the basic reproduction number (Van Den Driessche & Watmough 2002, Diekmann & Heesterbeek 2000), computed in the case $r > 1$ which is the biologically interesting case:

$$R_0 = \frac{\beta_m \beta_H}{d_m(\gamma + b_H)} \tag{7}$$

We show the following result

Theorem 2.2. *Assume* $r > 1$ *and let us denote* (E^*, L^*, A^*) *the endemic equilibrium of (3a).*

- *System (3b) always has the disease-free equilibrium* $(1,0,0)$*, which is GAS if* $R_0 \leq 1$ *and unstable otherwise.*
- *If* $R_0 > 1$ *system (3b) has an endemic equilibrium* (S_H^*, I_H^*, S_m^*) *which is GAS and where*

$$\begin{pmatrix} S_H^* \\ I_H^* \\ I_m^* \end{pmatrix} = \begin{pmatrix} \dfrac{b_H}{\beta_H + b_H} + \dfrac{\beta_H}{(\beta_H + b_H)R_0} \\ \dfrac{d_m b_H}{\beta_m(\beta_H + b_H)}(R_0 - 1) \\ \dfrac{b_H}{\beta_H + b_H R_0}(R_0 - 1) \end{pmatrix}$$

The first part of the theorem is obtained using Lypunov function theory. The case of the endemic equilibrium needs more study. The idea here is that the mosquito dynamic system drives the transmission dynamics. It may be assimilated to master-slave system. The coupling term is $s_L \dfrac{L(t)}{A(t)}$.

In order to study the equilibrium stability we use the result of (Vidyasagar 1980) for triangular systems :

Theorem 2.3. *Consider the following* $\mathcal{C}^1$ *system*

$$\begin{cases} \dfrac{dx}{dt} = f(x) \\ \dfrac{dy}{dt} = g(x,y), \end{cases} \tag{8}$$

with $(x,y) \in \mathbb{R}^n \times \mathbb{R}^m$*. Let* (x^*, y^*) *be an equilibrium point. If* x^* *is GAS in* $\mathbb{R}^n$ *for the system* $\frac{dx}{dt} = f(x)$ *and if* y^* *is GAS in* $\mathbb{R}^m$ *for the system* $\dfrac{dy}{dt} = g(x^*, y)$*, then* (x^*, y^*) *is (locally) asymptotically stable for system* (8)*. Moreover, if all trajectories of* (8) *are forward bounded, then* (x^*, y^*) *is GAS for* (8)*.*

The GAS of the endemic equilibrium (S_H^*, I_H^*, S_m^*) of system (3b) where $s_L \dfrac{L(t)}{A(t)}$ is replaced by $s_L \dfrac{L^*}{A^*}$ is then shown using the theory of competitive systems (Hirsch & Smale 1974), (Hirsch 1990), (Smith 1995) and the Poincaré-Bendixson property (Thieme 1992).

3 Identifiability Analysis

Recall that the parameters identifiability study consists in assessing whether the set of unknown parameters can be uniquely determined from the data. Thus, it is essential to determine what are the state variables that can be considered as observable. In the case of the *chikungunya* Réunion Island epidemic, authorities have registered the average number of eggs in each cottage. Thus, (E) can be considered as an observable variable. Furthermore, they estimate the number of new infections week by week. More generally, it seems to be realistic to assume that data about human population may

be obtained. For instance, we know that the entire Réunion island before the epidemic was susceptible. Data indicating week per week new cases of the disease may be provided by the INVS (French Institute for Health Care). We know that the epidemic was declared over by April 2006. In the end, the INVS counted 265,733 cases of chikungunya from March 2005 to April 2006 which represents more than 35% of the total population of the Island. That is why it seems reasonable to assume that susceptible (S_H) and infected human (I_H) are observable.

The parameters whose values are not directly accessible from the field are: s, s_L, K_E, K_L for the system (3a) and β_H, β_m for the system (3b). Let us recall the main results in differential algebra for proving the parameters identifiability.

3.1 Differential Algebra

This method consists in eliminating unobservable state variables in order to get relations between outputs and parameters. Let us recall the methodology. The system Γ^θ is rewritten as a differential polynomial system completed with $\dot{\theta}_i = 0$, $i = 1, \ldots, p$, thus the following system composed of polynomial equations and inequalities is obtained:

$$\Gamma \begin{cases} p(\dot{x}, x, u, \theta) = 0, \\ q(x, y, \theta) = 0, \\ r(x, y, \theta) \neq 0, \\ \dot{\theta}_i = 0,\ i = 1, \ldots, p. \end{cases} \tag{9}$$

Let us introduce some notations:

- $\mathcal{I}$ is the radical of the differential ideal generated by (9). $\mathcal{I}$, endowed with the following ranking which eliminates the state variables:

$$[\theta] \prec [y, u] \prec [x] \tag{10}$$

  is assumed to admit a characteristic presentation $\mathcal{C}$ (i.e., a canonical representant of the ideal) which has the following form:

$$\Big\{\dot{\theta}_1, \ldots \dot{\theta}_p, P_1(y, u, \theta), \ldots, P_m(y, u, \theta), Q_1(y, u, \theta, x), \ldots, Q_n(y, u, \theta, x)\Big\} \tag{11}$$

  $\mathcal{C}(\theta)$ will denote the particular characteristic presentation $\mathcal{C}$ evaluated in θ.

- $\mathcal{I}_\theta$ is the radical of the differential ideal generated by (9) for the particular value of parameter θ and $\mathcal{C}_\theta$ is the characteristic presentation associated with the ranking $[y, u] \prec [x]$.

- Finally, $\mathcal{I}_\theta^{i_0}$ is the ideal obtained after eliminating state variables and the set $\mathcal{C}_\theta^{i_0} = \mathcal{C}_\theta \cap \mathbb{Q}(\theta)\{U, Y\}$ is a characteristic presentation of this ideal.

The following proposition gives a necessary and sufficient condition for having the global identifiability.

Proposition 3.1. *If the system Γ does not admit non generic solution then the model is globally identifiable if and only if for all $\bar{\theta} \in \mathcal{U}_p$,*

$$\mathcal{C}_\theta^{i_0} = \mathcal{C}_{\bar{\theta}}^{i_0} \Rightarrow \theta = \bar{\theta}.$$

This proposition is difficult to verify since the initial system woud have to be evaluated in every parameter value as the associated caracteristic presentation $\mathcal{C}_\theta^{i_0}$. The authors in (Denis-Vidal, Joly-Blanchard, Noiret & Petitot 2001) have given some technical conditions for having the equality $\mathcal{C}_\theta = \mathcal{C}(\theta)$. Under these assumptions, the characteristic presentation $\mathcal{C}_\theta$, that is, $\mathcal{C}_\theta^{i_0}$ of $\mathcal{I}_\theta^{i_0}$ is proved to contain the differential polynomials $P_1(y, u, \theta), \ldots, P_m(y, u, \theta)$ which can be expressed as

$$P_i(y, u, \theta) = \gamma_0^i(y, u) + \sum_{k=1}^{n_i} \gamma_k^i(\theta) m_{k,i}(y, u) \tag{12}$$

where $(\gamma_k^i)_{1 \leq k \leq n_i}$ are rational in θ, $\gamma_u^i \neq \gamma_v^i$ $(u \neq v)$, $(m_{k,i})_{1 \leq k \leq n_i}$ are differential polynomials with respect to y and u and $\gamma_0^i \neq 0$.

The list $\{\gamma_1^i(\theta), \ldots, \gamma_{n_i}^i(\theta)\}$ is called the exhaustive summary of P_i. The size of the system is the number of observations. The identifiability analysis is based on the following proposition (Denis-Vidal, Joly-Blanchard, Noiret & Petitot 2001).

Proposition 3.2. *If for $i = 1, \ldots, m$, $\triangle P_i(y, u, \theta) = \det(m_{k,i}(y, u), k = 1, \ldots, n_i)$ is not in the ideal $\mathcal{I}_\theta^{i_0}$, then Γ^θ is globally identifiable at θ if and only if for every $\bar{\theta} \in \mathcal{U}_p$ $(\bar{\theta} \neq p)$, the characteristic presentations $\mathcal{C}_\theta^{i_0}$ and $\mathcal{C}_{\bar{\theta}}^{i_0}$ are distinct.*

The function *belongs_to* allows us to verify that the functional determinant does not vanish on the zeros of the radical differential ideal generated by Γ. Under this assumption, for proving that the model is globally identifiable, it is sufficient to verify for $i = 1, \ldots, m$ and $k = 1, \ldots, n_i$:

$$\gamma_k^i(\theta) = \gamma_k^i(\bar{\theta}) \Rightarrow \theta = \bar{\theta}.$$

This work will be done in using the Rosenfeld-Groebner algorithm in the package Diffalg of Maple. For studying the identifiability of the parameters s, s_L, K_E, K_L, β_L, β_m in (3a) and (3b), the two coupled systems can be considered as a unique system in which E, S_H and I_H are supposed to be observed.

However, we will take again the procedure done in (Moulay, Aziz-Alaoui & Kwon 2011). Indeed, for studying the parameters of the second system it is essential to know those of the first one. Besides, our aim is to propose an identifiability study which can be used for a numerical procedure. Indeed, recall that the use of differential algebra (Verdière et al. 2005) gives output polynomials usable for estimating the unknown parameters.

3.2 Application to the Vector population

Since E is supposed to be observed, the equation $y = E$ is added to the sytem (3a). In using the elimination order $[y] \prec [E, L, A]$, the package diffalg of Maple gives the caracteristic presentation constituted of the three following polynomials (13):

$$
\begin{aligned}
P_1 &= (-bK_E + by)A + \dot{y}K_E + K_E sy + K_E dy \\
P_2 &= (bK_E^2 s_L - 2K_E bys_L + by^2 s_L)L - K_E^2 d\dot{y} \\
&-K_E^2 s\dot{y} - K_E^2 \ddot{y} + K_E \ddot{y}y - K_E^2 d_m \dot{y} - K_E^2 d_m sy \\
&-K_E^2 d_m dy - K_E \dot{y}^2 + d_m K_E \dot{y}y + d_m K_E sy^2 \\
&+d_m K_E dy^2 \\
P_3 &= (K_E^3 s_L K_L d_m d + K_E^3 K_L d_L d_m s \\
&+K_E^3 K_L d_L d_m d + K_E^3 s_L K_L d_m s - bK_E^3 s_L s K_L)y \\
&+(K_E^3 K_L d_L s + K_E^3 K_L d_m d + K_E^3 K_L d_L d_m \\
&+K_E^3 s_L K_L d + K_E^3 s_L K_L s + K_E^3 s_L K_L d_m \\
&+K_E^3 K_L d_L d + K_E^3 K_L d_m s)\dot{y} + (K_E^3 K_L d_L \\
&+K_E^3 K_L d + K_E^3 K_L d_m + K_E^3 K_L s + K_E^3 s_L K_L)\ddot{y} \\
&+K_L K_E^3 \dddot{y} + (3K_E^2 bs_L s K_L - 2K_E^2 s_L K_L d_m d \\
&+K_E^3 sd_m d - 2K_E^2 K_L d_L d_m s - 2K_E^2 K_L d_L d_m d \\
&+K_E^3 s^2 d_m - 2K_E^2 s_L K_L d_m s)y^2 \\
&+(-2K_E^2 K_L d_L d_m + K_E^3 sd_m - K_E^2 K_L d_L s \\
&-K_E^2 K_L d_L d + K_E^3 sd - K_L d_m K_E^2 d - K_E^2 s_L K_L s \\
&-K_E^2 s_L K_L d - 2K_E^2 s_L K_L d_m - K_L d_m K_E^2 s \\
&+K_E^3 s^2)\dot{y}y + (K_E^2 K_L d_L + K_L d_m K_E^2 + 2K_E^2 K_L s \\
&+2K_E^2 K_L d + K_E^2 s_L K_L)\dot{y}^2 + (-2K_E^2 K_L d_L \\
&-2K_L d_m K_E^2 - K_E^2 K_L s - 2K_E^2 s_L K_L - K_E^2 K_L d \\
&+K_E^3 s)\ddot{y}y + 3K_L K_E^2 \ddot{y}\dot{y} - 2K_L K_E^2 \dddot{y}y \\
&+(s_L K_L d_m K_E s - 2K_E^2 s^2 d_m - 3K_E bs_L s K_L \\
&+K_L d_L d_m K_E s + s_L K_L d_m K_E d - 2K_E^2 sd_m d \\
&+K_L d_L d_m K_E d)y^3 + (-K_E^2 s^2 - 2K_E^2 sd_m \\
&-K_E^2 sd + s_L K_L d_m K_E + K_L d_L d_m K_E)\dot{y}y^2 \\
&+(-K_E K_L d_L + K_E^2 s - K_E s_L K_L - K_L d_m K_E)\dot{y}^2 y \\
&+2K_L K_E \dot{y}^3 + (-2K_E^2 s + K_L d_m K_E + K_E K_L d_L \\
&+K_E s_L K_L)\ddot{y}y^2 - 3K_L K_E \ddot{y}\dot{y}y + K_L K_E \dddot{y}y^2 \\
&+(s^2 d_m K_E + sd_m K_E d + bs_L s K_L)y^4 \\
&+sd_m K_E \dot{y}y^3 - sK_E \dot{y}^2 y^2 + sK_E \ddot{y}y^3.
\end{aligned}
\tag{13}
$$

The polynomials P_1 and P_2 permit to express L and A in function of y and the parameters of the model. The third one, P_3, links the output with the parameters: it is the output polynomial. With the function *belong_to*, we verify that the functional determinant $\triangle P_3$ is not in the ideal $\mathcal{I}_\theta^{i_0}$. The exhaustive summary is constituted of 21 expressions. In using the Rosenfeld-Groebner algorithm, we obtain the identifiability of the parameters s, s_L, K_E, K_L. Thus, from the observation of E, the unknown parameters can be estimated.

3.3 Application to the population Model

The third equation of (3b) links the human population to the vector population with the term $L(t)/A(t)$. According to the previous section, they can be explicitely determined from $E(t)$. Thus the ratio $L(t)/A(t)$ can be considered as a known input u. As previously, in adding $y_1 = I_H$, $y_2 = S_H$ to (3b) and in considering the elimination order $[y_1, y_2, u] \prec [I_H, S_H, I_m]$, one gets for the two following output polynomials:

$$
\begin{aligned}
P_4 &= y_2\ddot{y}_2 - \dot{y}_2^2 + (\beta_H\beta_m + \beta_m b_H)y_1 y_2^2 \\
&+s_L u y_2 \dot{y}_2 + s_L b_H u y_2^2 - s_L b_H u y_2 + b_H \dot{y}_2 \\
&+\beta_m y_2 y_1 \dot{y}_2 - \beta_m b_H y_2 y_1 \\
P_5 &= \dot{y}_2 + \dot{y}_1 - b_H + b_H y_2 + (b_H + \gamma)y_1.
\end{aligned}
\tag{14}
$$

Only the polynomial P_4 contains the parameters β_H and β_m and is used for studying their identifiability. The functional determinant $\triangle P_4$ is proved not to be in the ideal $\mathcal{I}_\theta^{i_0}$. In studying the exhaustive summary of P_4, we conclude that the parameters β_H and β_m are identifiable.

4 Conclusion

In this paper, the identifiability of models describing the transmission of the chikungunya virus to human population has been studied. According to the reemergence of this virus, the chikungunya becomes a major health problem especially since the main vector has developed capabilities to adapt to non tropical regions. The identifiability is an important step in the modeling. Indeed, the identifiability study enables one to know if a model is well-posed and if the unknown parameters can be assessed from some observations done in the field. For the chikungunya virus models, the identifiability of the unknown parameters has been established and the following step will be the parameters estimation of this epidemiologic model.

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