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Inverse problem for a coupling model of reaction-diffusion and ordinary differential equations systems. Application to an epidemiological model.

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Abstract

This paper investigates an identifiability method for a class of systems of reaction diffusion equations in the L^2 framework. This class is composed of a master system of ordinary differential equations coupled with a slave system of diffusion equations. It can model two populations, the second one being diffusive contrary to the first one. The identifiability method is based on an elimination procedure providing relations called *input-output polynomials* and linking the unknown parameters, the inputs and the outputs of the model. These polynomials can also be used to estimate the parameters as shown in this article. To our best knowledge, such an identifiability method and a parameter estimation procedure have not yet been explored for such a system in the L^2 framework. This work is applied on an epidemiological model describing the propagation of the chikungunya in a local population.

Keywords: Identifiability; PDEs and ODEs systems; Parameter estimation; Epidemiological models

1. Introduction

Many biological or physical processes are modeled using ordinary differential equations (ODE) or partial differential equations (PDE) to describe the (spatial) evolution over the time of quantities of interest. However, they depend on

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many parameters that need to be estimated from the measurements of the system to make the mathematical model useful. This kind of problem, called inverse problem, necessitates, in general, an identifiability study. An identifiability study ensures that the parameters of interest can be uniquely inferred from given measurements. Consequently, it is a necessary prerequisite before putting in place parameter identification procedures, otherwise, the latter can fail or give not realistic parameter values. This theoretical work is done in the 'best-case' that is from noise-free data.

Identifiability study for ODEs systems is well known and several methods exist in the literature for linear or nonlinear systems (see for example [11, 14, 16, 18, 26, 30, 31, 33] and the references therein). In the case of PDEs systems (or equations), most of the work on inverse problems concerns a source problem (see [2, 7, 10, 13, 23, 36]) or a Calderòn's problem (see the original paper [5] and the review on the subject [29]). This kind of inverse problems consists in identifying a source term, or to determine a space variable parameter, from boundary measurements.

The inverse problem studied in this paper for PDEs systems is of different type to the one handled in the previous references. Indeed, the difference comes from the knowledge of one (or more) of its solutions (on all the domain or just a part of it). Even if this assumption seems to be less considered, some works can be found in this direction. An identifiability study has been proposed in [34] (see also reference [6] for a more recent reference) for a SIS (Susceptible - Infectious - Susceptible) epidemic reaction-diffusion model using an optimal control method. In [24], using input-output relationships, identifiability of a system of nonlinear integro-partial differential equations of transport type was proposed. An approach based on semigroup theory to identify the mortality rate in an age-structured population dynamics model have been proposed in [25]. In the case of coupled ODEs and PDEs systems, a study of identifiability have been done in [15] by means of Carleman-type estimate, and in [28] using the differential algebra approach where the PDE model is an age-since-infection-structured population dynamics model.

In this paper, we propose an identifiability method, using the differential algebra approach, for some coupled nonlinear ODEs and reaction-diffusion systems composed of rational functions. This assumption is not so restrictive since by change of variables, lots of systems can be rewritten as rational ones. From the elimination theory developed in the case of ODEs systems, some input-output (IO) polynomials are obtained. The method that we propose is based on these specific relations permitting in the same way to propose a numerical procedure giving a first estimate of the parameters by direct measurements without any *a*

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priori knowledge. To our best knowledge, such an identifiability method has not yet been studied for a coupled nonlinear ODEs and reaction-diffusion systems in the L^2 framework.

For the application of the method, we propose to consider the model given in [20] and describing the transmission of the chikungunya to the human population by the mosquito vector, the Aedes Albopictus. This disease is still current since this vector has developed capabilities to adapt to non tropical regions and a genetic mutation has reduced the delay between the contamination of the host and its propagation to humans. In 2014, several cases have been reported in the South of America, the Caraïbes and central America. In August 2017, it is the France and Italy that have been concerned. In [20], the virus transmission to the human population has been modeled by a SI-SIR (Susceptible - Infectious and Susceptible - Infectious - Recovered) model taking into account the mosquito biological life cycle. An identifiability study of this model has been done in [27]. But this ODEs system does not consider an important factor favoring the re-emergence of diseases, that is the spatial mobility of humans. In order to consider this spatial mobility, a metapopulation model has been proposed in [21]. This spatio-temporal model can be seen as a discrete model in space. In this paper, we model human mobility by a diffusion term in the same way as [22] or [1, 17]. In [37], an identifiability study was proposed on this model in the continuous framework, that is with continuous initial datum. In this paper, we revisit this work with less assumptions on the regularity of the solutions. More precisely, we work in the L^2 framework.

The paper is structured as follows. In section 2, we present the coupling model which is considered in the sequel. Section 3 is devoted to general identifiability results based on the elimination theory and their applications on the coupling model. In section 4, the theoretical part is applied on a chikungunya epidemiological model and a parameter estimation method based on the input-output polynomials is proposed in section 5 to estimate two of the model parameters. Section 6 concludes the paper.

2. Coupling model

2.1. Notations

The notations are the following:

- Ω is a bounded domain of $\mathbb{R}^n$ with C^2-boundary.

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- $C_l([0, \infty); C(\overline{\Omega}))$ denotes the space of piecewise continuous functions from $[0, \infty)$ to $C(\overline{\Omega})$ and $C_l^1([0, \infty); C(\overline{\Omega}))$ the space of piecewise differentiable functions from $[0, \infty)$ to $C(\overline{\Omega})$.

- Given a local Lebesgue-integrable function F, T_F defines its regular distribution.

- $H_N^2(\Omega) := \{v \in H^2(\Omega) \mid \frac{\partial v}{\partial \nu} = 0 \text{ on } \partial\Omega\}$, where ν is the outward unit normal of $\partial\Omega$.

- For any function $f \in L^1(\Omega)$, we set $\langle f \rangle := \dfrac{1}{\mid \Omega \mid} \displaystyle\int_\Omega f(x)dx$.

2.2. Coupling model

The model we investigate in this paper is a master-slave model of two species where the slave one diffuses, contrary to the master one. The master model is a system of classical ordinary differential equations defined on the space $C(\overline{\Omega})$ given by:

$$\begin{cases} \partial_t \zeta &= F(t, \zeta), \quad \text{in } (0, \infty), \\ \zeta(0) &= \zeta_0. \end{cases} \tag{1}$$

where $\zeta_0 \in C(\overline{\Omega})$ and $F : \mathbb{R} \times \mathbb{R}^p \to \mathbb{R}^p$ is piecewise continuous with respect to the first component and uniformly Lipschitz continuous with respect to the second component. Then, from the Cauchy-Lipschitz theorem, there exists a unique piecewise differentiable solution ζ from any time interval of existence to $C(\overline{\Omega})$, *i.e.* $\zeta \in C_l^1\left([0, \infty); C(\overline{\Omega})\right)$.

The slave model is a system of reaction-diffusion equations defined on the Banach space $X := C(\Omega; \mathbb{R}^{q_0}) \times L^2(\Omega; \mathbb{R}^{q_1})$ and which depends on the solution ζ of the master model:

$$\begin{cases} \partial_t U + BU &= G(t, \zeta, U), \quad \text{in } (0, \infty), \\ U(0) &= U_0, \end{cases} \tag{2}$$

where $U_0 \in X$ and the diagonal operator $B := \text{diag}(B_i)$ on X satisfies

- for all $i \in \{1, \ldots, q_0\}$, $B_i := I$,

- for all $i \in \{q_0 + 1, \ldots, q\}$ (where $q := q_0 + q_1$), $B_i := d_i A + b_i$ with $d_i, b_i > 0$ and A is the realization of the Laplacian in $L^2(\Omega)$ with Neumann homogeneous boundary condition on $\partial\Omega$.

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In other words, (2) is composed of q_0 ODEs and q_1 PDEs which are all together coupled.

Moreover, $G(t, \zeta, \cdot)$ is a non-linear operator from $D(B^\eta)$ into X (see (24)), where $0 < \eta < 1$, which satisfies the following Lipschitz type condition: there exists an increasing function ϕ such that, for any compact time interval I where ζ is differentiable and for all $(t, U), (s, V) \in I \times D(B^\eta)$, we have

$$\|G(t, \zeta, U) - G(s, \zeta, V)\|_X \leq \phi(\|U\|_X + \|V\|_X)$$

$$\times \Big[\|B^\eta(U - V)\|_X + (\|B^\eta U\|_X + \|B^\eta V\|_X + 1)(|t - s| + \|U - V\|_X) \Big], \tag{3}$$

where $\| \cdot \|_X$ denotes the norm of X.

Then, a simple adaptation of Theorem 4.4 of [35] (p. 188, and p. 199 for the non autonomous case) implies that there exists $T_{U_0} > 0$ such that (2) admits a unique local solution

$$U \in C_l([0, T_{U_0}]; D(B)) \cap C_l^1((0, T_{U_0}]; X).$$

Note that U is piecewise continuous and piecewise differentiable due to the dependence with respect to ζ.

Moreover, if there exists $C_{U_0} > 0$ such that the local solution U satisfies:

$$\forall\, t \in I, \quad \|U(t)\|_2 \leq C_{U_0}, \tag{4}$$

for any compact time interval I where U is continuous with respect to the time variable, then U is a global solution:

$$U \in C_l([0, \infty); D(B)) \cap C_l^1((0, \infty); X).$$

Such systems depend on parameters not always directly accessible from measurements or by mean of a costly and experimental scheme. However, they must be estimated to make the model usable. Several numerical procedures, based on measurements, can be found in the literature. They carried out by optimizing some criterion function over the parameter space. However, an identifiability study should be done since it is a pre-condition for safely running a parameter estimation algorithm. Indeed, it will ensure that the algorithm will not converge towards an unrealistic solution.

More precisely, we introduce a parameter vector function $\theta := (\theta_a, \theta_b) \in L^\infty(\Omega; \mathcal{U}_p)$, where $\mathcal{U}_p$ is an open subset of $\mathbb{R}^p$, and some corresponding model outputs $y(t, \theta) := (y_a(t, \theta_a), y_b(t, \theta_b))$. Thus, we rewrite models (1) and (2) in the following form:

$$(\Gamma_a) \begin{cases} \partial_t \zeta(t, \theta_a) & = & f(t, \zeta, \theta_a), & t \in [0, \infty), \\ y_a(t, \theta_a) & = & h_a(\zeta), & t \in [0, \infty), \end{cases} \tag{5}$$

completed with $\zeta(t = 0, \theta_a) = \zeta_0$, and

$$(\Gamma_b) \begin{cases} \partial_t U(t, \theta_b) + B(\theta_b) U(t, \theta_b) & = & g(\zeta, U, \theta_b), & t \in [0, \infty), \\ y_b(t, \theta_b) & = & h_b(\zeta, U), & t \in [0, \infty), \end{cases} \tag{6}$$

completed with $U(t = 0, \theta_b) = U_0$. The notations are the following:

- $f := (f_1, \ldots, f_p)$ where f_i, $1 \le i \le p$, is a rational function with respect to ζ and θ_a,

- $g := (g_1, \ldots, g_q)$ where g_i, $1 \le i \le q$, is a rational function with respect to ζ, U and θ_b,

- $h_a := (h_{a,1}, \ldots, h_{a,m_a})$ (resp. $h_b := (h_{b,1}, \ldots, h_{b,m_b})$) where $h_{a,i}$, $1 \le i \le m_a$ (resp. $h_{b,i}$, $1 \le i \le m_b$), are rational functions with respect to ζ (resp. ζ and U).

Afterwards, (Γ_θ) will design either system (Γ_a) or (Γ_b).

3. Identifiability

3.1. General Case

The identifiability definition considered in this paper is the following:

Definition 3.1. *We say that the model (Γ_θ) is identifiable with respect to θ if there exists a time $t_1 > 0$ and a subset $\bar{\Omega}$ of Ω such that, for all $\theta, \tilde{\theta} \in L^\infty(\Omega; \mathcal{U}_p)$, we have*
$$\forall (t, \mathbf{x}) \in [0, t_1] \times \bar{\Omega}, \quad y(t, \theta)(\mathbf{x}) = y(t, \tilde{\theta})(\mathbf{x}) \implies \theta = \tilde{\theta}.$$

Definition 3.1 states that there exists a time interval and a space domain such that two distinct parameters will not generate identical model outputs. This definition can be easily extended to piecewise continuous outputs by considering the model's identifiability on each subinterval on which the outputs are defined.

We propose to extend an identifiability method based on the differential algebra theory applied to ODEs with constant parameters [3, 4, 8, 9]. This method is

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based on some differential polynomials obtained owing to an elimination procedure. The latter consists in eliminating unobservable variables for the benefit of the outputs and the parameters of the model.

Differential algebra theory provides an automatic elimination tool for performing specific relations depending only on the inputs, the outputs and the parameters of the system. These relations are considered as polynomials whose indeterminates are the inputs and the outputs of the model and are also called *input-ouptut* polynomials. In certain cases, the elimination procedure can be done by hand, however, dedicated packages are available, for example `DifferentialAlgebra` implemented in Maple [3, 4]. This method necessitates most of the times derivation operations and, in the case of the use of a dedicated software, the elimination is done in a formal way, that is, without any consideration of the solution space. The relations can also not be defined with respect to the solution regularity of the model. Nevertheless, new well-defined relations can be obtained in considering the previous relations in the distribution sense or from the mean value, so that an identifiability result can be deduced on the studied system.

Suppose that, from an elimination procedure considering only the derivation with respect to the time, the differential polynomials $P_i(y_\theta, \theta, u)$ depending on θ, y_θ and the input function u of the model have been obtained. The number of these polynomials is the number of model outputs according to [8]. To simplify the notations, we consider afterwards that we have only one output, that is one differential relation $P(y_\theta, \theta, u)$ (which correspond to the case of the application of section 4). This differential polynomial can be expressed as (see [8]):

$$P(y_\theta, \theta, u) = m_0(y_\theta, u) + \sum_{k=1}^{n} \gamma_k(\theta)\, m_k(y_\theta, u) \quad \text{and} \quad P(y_\theta, \theta, u) = 0, \quad (7)$$

where $(\gamma_k(\theta))_{1 \leq k \leq n}$ ($\gamma_\alpha \neq \gamma_\beta$ if $\alpha \neq \beta$ and $\alpha, \beta \in \{1, \ldots, n\}$) are rational in θ, $(m_k(y_\theta, u))_{0 \leq k \leq n}$ are differential polynomials with respect to y_θ and u, and $m_0 \neq 0$.

Remark 3.1.

1. *In the present case, a differential polynomial with respect to y_θ means a multivariate polynomial of the variables $y_\theta, \partial_t y_\theta, \partial_t^2 y_\theta, \ldots$.*
2. *The denominators of $\gamma_k(\theta)$ are supposed not to vanish.*
3. *For system (Γ_b), the function ζ can be considered as an input function.*

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4. *By using Rosenfeld-Groebner algorithm, one can obtain a relation of the form (7) such that the $m_k(y_\theta, u)$ for $k = 1, \ldots, n$ are linearly independent (see [12]).*

The family $\{\gamma_1(\theta), \ldots, \gamma_n(\theta)\}$ is called the *exhaustive summary* of P and the differential polynomial P is called an *input-output polynomial*.

Example 3.1. *We illustrate the notion of input-output polynomial on a simple problem. Consider an ODEs system given by*

$$\begin{cases} \dot{x}_1 & = & u, \\ \dot{x}_2 & = & x_1 + k\,u, \end{cases}$$

where $k \in \mathbb{R}$ is a parameter to identify ($\theta = k$) and u is an input function.

Suppose u is C^1 and assume that $y := x_2$ is observable. Then, y is C^2 and we have

$$\ddot{y} = \dot{x}_1 + k\,\dot{u} = u + k\,\dot{u}. \tag{8}$$

Thus, we deduce that we have an input-output polynomial P such that $P(y, k, u) = 0$ which is given by

$$P(y, k, u) := \ddot{y} - u - k\dot{u}.$$

Moreover, the exhaustive summary is simply $\{k\}$.

Note that we assumed that u is C^1. We will see below how we can handle a more general case of an input function with less regularity.

Suppose that the elimination process respected the regularity of the solutions of the ODEs or the PDEs system. Then the following proposition gives a necessary condition to obtain the identifiability of the model from the differential polynomial (7).

Proposition 3.1. *Assumed that the family $(m_k(y_\theta, u))_{1 \leq k \leq n}$ given by (7) is linearly independent. If, for all $(\theta, \tilde{\theta}) \in L^\infty(\Omega, \mathcal{U}_p)^2$, we have*

$$\forall\, k \in \{1, \ldots, n\}, \quad \gamma_k(\theta) = \gamma_k(\tilde{\theta}) \implies \theta = \tilde{\theta},$$

then the model is identifiable with respect to θ.

Proof 3.1. *Let $(\theta, \tilde{\theta}) \in L^\infty(\Omega, \mathcal{U}_p)^2$ be such that $y_\theta(t, \theta) = y_\theta(t, \tilde{\theta})$. From (7), one gets:*

$$\sum_{k=1}^{n} (\gamma_k(\theta) - \gamma_k(\tilde{\theta})) m_k(y_\theta, u) = 0. \tag{9}$$

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According to the linear independence of the family $(m_k(y_\theta, u))_{1 \le k \le n}$, relation (9) implies

$$\forall \, k \in \{1, \ldots, n\}, \quad \gamma_k(\theta) = \gamma_k(\tilde{\theta}).$$

Thus, by assumption, $\theta = \tilde{\theta}$.

By using dedicated software programs, relation (7) is obtained in a formal way by differentiation with respect to the time and combination of the equations of the initial system. Its derivative degrees may be too high with respect to the solution regularity.

Assume that, in (7), the $m_k(y_\theta, u)$, $k = 0, \ldots, n$, are well defined almost everywhere and are locally Lebesgue integrable. Then, one can replace the not well defined $m_k(y_\theta, u)$ by their distributions $T_{m_k(y_\theta, u)}$. Thus, we obtain a new relation of the form

$$T_{m_0(y_\theta, u)} + \sum_{k=1}^{n} \gamma_k(\theta) T_{m_k(y_\theta, u)} = 0. \tag{10}$$

In this case, similarly to Proposition 3.1, we have the following result in the distribution sense.

Proposition 3.2. *Assumed that the family of distributions $(T_{m_k(y_\theta, u)})_{1 \le k \le n}$ given by (10) is linearly independent. If, for all $(\theta, \tilde{\theta}) \in L^\infty(\Omega, \mathcal{U}_p)^2$, we have*

$$\forall \, k \in \{1, \ldots, n\}, \quad \gamma_k(\theta) = \gamma_k(\tilde{\theta}) \implies \theta = \tilde{\theta},$$

then the model considered in the distribution sense is identifiable with respect to θ.

Proof 3.2. *The proof is similar to the proof of Proposition 3.1.*

Remark 3.2. *It is easy to show that if the $(m_k(y_\theta, u))_{k=1,\ldots,n}$ are linearly independent then the $(T_{m_k(y_\theta, u)})_{1 \le k \le n}$ are linearly independent too. In the application of section 4, the linear independence assumption of Proposition 3.2 is substituted by the linear independence of the $(m_k(y_\theta, u))_{k=1,\ldots,n}$.*

3.2. Identifiability result for (Γ_a) when $\theta_a \in L^\infty$

The solution ζ of system (Γ_a) being piecewise differentiable in time, the output y_a is, in general, piecewise differentiable (or just continuous) in time. Using this property, one can obtain a more informative input-output relation taking account the discontinuous points of y_a (recall that only derivation with respect to the

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time variable is considered). These new relations can lead to a positive identifiability result.

Let s be the time derivative of highest order of y_a appearing in (7). If the function $y_a^{(s)}$ can be expressed formally in (7) as a term of the form $d(y_a, y_a', \ldots, y_a^{s-1}) y_a^{(s)}$ where d is a differential polynomial with respect to y_a and does not cancel, then (7) can be rewritten as follows:

$$y_a^{(s)} = \tilde{m}_0(y_a) + \sum_{k=1}^{n} \gamma_k(\theta_a) \tilde{m}_k(y_a), \tag{11}$$

where, for all $k = 0, \ldots, n$, $\tilde{m}_k(y_a)$ is a rational function assumed to be locally Lebesgue-integrable in time. Note that we omit the dependence on the input function u to simplify the notation, we will keep this notation in the sequel.

Assume that y_a is s times piecewise continuously differentiable in time and let $(t_\nu)_\nu$ be the corresponding finite increasing family of discontinuities points. Due to the discontinuities points, the relation (11) should be considered in the distribution sense:

$$T_{y_a^{(s)}} = T_{\tilde{m}_0(y_a)} + \sum_{k=1}^{n} \gamma_k(\theta_a) T_{\tilde{m}_k(y_a)}. \tag{12}$$

Now, for any $j = 0, \ldots, s$, denote the jump at t_ν of $y_a^{(j)}$ by

$$\sigma_{y_a,\nu}^{j}(\theta_a) := y_a^{(j)}(t_\nu^+) - y_a^{(j)}(t_\nu^-).$$

Note that the jump depends upon θ_a since y_a itself depends on θ_a. Then, jump formula yields

$$T_{y_a^{(s)}} = T_{y_a^{(s)}} + \sum_{\nu} \sum_{j=0}^{s-1} \sigma_{y_a,\nu}^{j} \delta_{t_\nu}^{(s-1-j)},$$

where δ_{t_ν} denotes the Dirac distribution at point t_ν. Thus, equation (12) can be rewritten

$$T_{y_a^{(s)}} = T_{\tilde{m}_0(y_a)} - \sum_{\nu} \sum_{j=0}^{s-1} \sigma_{y_a,\nu}^{j}(\theta_a) \delta_{t_\nu}^{(s-1-j)} + \sum_{k=1}^{n} \gamma_k(\theta_a) T_{\tilde{m}_k(y_a)}. \tag{13}$$

Remark 3.3.

1. *These relations are more informative than (11) since new constraints on the discontinuity points linking the parameters are added to the study of identifiability.*
2. *This operation can permit to obtain relations well-defined with respect to the solution regularity.*

The following proposition gives also a sufficient condition to obtain the identifiability of the parameters.

Proposition 3.3. *Assume that the family of distributions $(T_{\tilde{m}_k(y_a)})_{1 \leq k \leq n}$ is linearly independent. If, for all $(\theta_a, \tilde{\theta}_a) \in L^\infty(\Omega, \mathcal{U}_p)^2$, we have*

$$
\begin{cases}
\gamma_k(\theta_a) = \gamma_k(\tilde{\theta}_a) \\
\forall \nu, \quad \displaystyle\sum_{j=0}^{s-1} \sigma_{y_a,\nu}^j(\theta_a) = \sum_{j=0}^{s-1} \sigma_{y_a,\nu}^j(\tilde{\theta}_a)
\end{cases}
\implies \theta_a = \tilde{\theta}_a,
$$

then the model is identifiable with respect to θ_a.

Proof 3.3. *The proof is similar to the proof of Proposition 3.1 and follows from the linear independence of the families $(\delta_{t_\nu}^{(j)})_{j=0,\ldots,s}$ and $(\tilde{T}_{m_k(y_\theta)})_{k=1,\ldots,n}$.*

All these input-output polynomials (7), (10), (13) can be used to obtain a first estimate of the identifiable parameters. This will be illustrated at section 5.

Example 3.2. *Consider again Example 3.1 but now assume that u is a piecewise constant function given by*

$$
u(t) := \begin{cases} u_1 & \text{if} \quad t \in (0, t_1) \\ u_2 & \text{if} \quad t \in (t_1, T), \end{cases}
$$

where $u_1, u_2 \in \mathbb{R}$, $u_1 \neq u_2$. Then, equation (8) written in distribution sense yields

$$
T_y'' = T_u + k(u_2 - u_1)\delta_{t_1}.
$$

So, in this way, we obtained a new relation that could permit to identifiate k.

3.3. Identifiability result on (Γ_b) when θ_b is a constant parameter vector

In this part, we focus on the identifiability of system (Γ_b). We are interested in the identifiability of the parameter $\theta_b := (\theta_c, \theta_d)$ where $\theta_c \in \mathbb{R}^{q_0}$ and $\theta_d := (d_i)_{i \in I}$ with $I \subset \{q_0 + 1, \ldots, q\}$. Let $U := (U_i)_{i=1,\ldots,q}$ be the solution of (Γ_b) and y_b be given by (6).

Lemma 3.1. *Let y_b be given by $y_b := (y_c, y_d)$ where*

$$y_d := (U_i)_{i \in I}.$$

Assume there exists $\nu \in \mathbb{N}$ such that, for all $t \in (t_\nu, t_{\nu+1})$,

1. *there exists a family of positive reals $(\lambda_i)_{i \in I}$ such that*

$$\sum_{i \in I} \lambda_i (g_i(\zeta(t), U(t), \theta_d) - \partial_t U_i)$$

   is independent of θ_d,
2. *the family $(U_i(t, \cdot))_{i \in I}$ is linearly independent up to an additive constant in Ω,*
3. *the b_i defined in $B_i = d_i A + b_i$ are supposed to be known.*

Then, (Γ_b) is identifiable with respect to θ_d.

Remark 3.4. *In other words, Lemma 3.1 gives a sufficient condition for the identifiability of diffusion coefficients $(d_i)_{i \in I}$ when the associated solutions $(U_i)_{i \in I}$ are known.*

Proof 3.4. *Let $\theta_d, \tilde{\theta}_d$ be such that*

$$\forall (t, x) \in (t_\nu, t_{\nu+1}) \times \Omega, \quad y_b(t, x, \theta_d) = y_b(t, x, \tilde{\theta}_d).$$

Then, using assumption (1), we have

$$\begin{aligned}
\sum_{i \in I} \lambda_i B_i(\theta_d) U_i \ &= \sum_{i \in I} \lambda_i (g_i(\zeta(t), U(t), \theta_d) - \partial_t U_i) \\
&= \sum_{i \in I} \lambda_i (g_i(\zeta(t), U(t), \tilde{\theta}_d) - \partial_t U_i) \\
&= \sum_{i \in I} \lambda_i B_i(\tilde{\theta}_d) U_i,
\end{aligned}$$

which leads to

$$\sum_{i \in I} \lambda_i (d_i - \tilde{d}_i) A U_i = 0.$$

Thus, $V := \sum_{i \in I} \lambda_i (d_i - \tilde{d}_i) U_i$ is an eigenvector of A associated with zero eigenvalue. Thus, V is constant. Since, for all $t \in (t_\nu, t_{\nu+1})$, $(U_i(t, \cdot))_{i \in I}$ is linearly independent up to an additive constant in Ω, we deduce that for all $i \in I$

$$\lambda_i (d_i - \tilde{d}_i) = 0,$$

which leads to the result since $\lambda_i \neq 0$.

It remains to obtain the identifiability with respect to θ_c. To this end, Propositions 3.1 and 3.2 can be used. However, in order to test the linear independence of the family $(m_k(y_b))_{k=1,\ldots,n}$, the calculus of the wronskian can not be possible due to the lack of regularity of the solutions. In the following lemma, we propose to substitute this test by another one.

Lemma 3.2. *Let $\tilde{P} := \langle P \rangle$. Assume that*

1. *(Γ_b) is identifiable with respect to θ_d,*
2. *the polynomial P defined in (7) with $\theta := \theta_c$ satisfy, for all $k = 1, \ldots, n$,*

$$\gamma_k(\theta_c) = \gamma_k(\tilde{\theta}_c) \implies \theta_c = \tilde{\theta}_c,$$

3. *the family of functions $(< m_k(y_b) >)_{k=1,\ldots,n}$ are linearly independent.*

Then (Γ_b) is identifiable with respect to θ_c.

Proof 3.5. *The relation $\tilde{P}(y_b, \theta_c) - \tilde{P}(y_b, \tilde{\theta}_c)$ gives:*

$$\sum_{k=1}^{n} (\gamma_k(\theta_c)) - \gamma_k(\tilde{\theta}_c)) \langle m_k(y_b) \rangle = 0. \tag{14}$$

A linear system of solutions in the block of parameters $\gamma_k(\theta_c) - \gamma_k(\tilde{\theta}_c)$ is deduced. According to Assumption 3, we obtain that $\gamma_k(\theta_c) = \gamma_k(\tilde{\theta}_c)$ and according to Assumption 2, (Γ_b) is identifiable with respect to θ_c.

Remark 3.5. 1. *If the relation $\tilde{P}$ obtained from (7) by taken its mean value is not well-defined with respect to the time variable, it can be considered in the distribution sense. In that case, for Assumption 3, it is sufficient to prove the linear independence of the family $(\langle m_k(y_b) \rangle)_{k=1,\ldots,n}$. Indeed, if the family $(\langle m_k(y_b) \rangle)_{k=1,\ldots,n}$ is linearly independent, then the family $(T_{\langle m_k(y_b) \rangle})_{k=1,\ldots,n}$ is also linearly independent.*

2. *Another way to deal with the linear independence assumption is to suppose that there exist n distinct points $t_1, \ldots, t_n$ such that the determinant*

$$
\begin{vmatrix}
\langle m_1(y_b) \rangle (t_1) & \ldots & \langle m_n(y_b) \rangle (t_1) \\
\langle m_1(y_b) \rangle (t_2) & \ldots & \langle m_n(y_b) \rangle (t_2) \\
\vdots & & \vdots \\
\langle m_1(y_b) \rangle (t_n) & \ldots & \langle m_n(y_b) \rangle (t_n)
\end{vmatrix}
\tag{15}
$$

is not zero.

Indeed, from relation (14), the following linear system in the block of parameters composed of n equations is obtained:

$$
\sum_{k=1}^{n} (\gamma_k(\theta_c)) - \gamma_k(\tilde{\theta}_c)) \, \langle m_k(y_b) \rangle (t_j) = 0, \quad \text{for } j = 1, \ldots, n.
$$

Thus, since the determinant (15) is not zero, following the same argumentation, the identifiability of (Γ_b) at θ_c is deduced.
In the numerical applications, the n distinct points $t_1, \ldots, t_n$ can be chosen randomly to evaluate this determinant.

4. Application to an epidemiological model

The identifiability method presented at the previous section is applied on a coupling model describing the transmission and the propagation of the chikungunya disease by *Aedes* mosquitoes to the human population (See. [20]).

4.1. Chikungunya transmission model

The model of [20] couples two sub-systems: the mosquito dynamics model and the transmission virus model between mosquitoes and humans populations. The first one describes the biological mosquito life cycle so that three stages are concerned: E_m the number of eggs, L_m the number of larvae/pupae and A_m the number of adult females. This model is the following

$$
\begin{cases}
E'_m(t) = bA_m(t)(1 - \dfrac{E_m(t)}{K_E}) - (s+d)E_m(t), \\[2mm]
L'_m(t) = sE_m(t)(1 - \dfrac{L_m(t)}{K_L}) - (s_L + d_L)L_m(t), \\[2mm]
A'_m(t) = s_L L_m(t) - d_m A_m(t),
\end{cases}
\tag{16}
$$

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where $K_E > 0$ (resp. $K_L = K_E/2$) is the carrying capacity of E_m (resp. carrying capacity of L_m), $s_L > 0$ (resp. $s > 0$) is transfer rate from L_m to A_m (resp. from E_m to L_m), $b > 0$ is the intrinsic rate, $d > 0$, $d_L > 0$ and $d_m > 0$ are the mortality rate for E_m, L_m and A_m respectively.

To construct the second model, that is the transmission virus one, the human and mosquito populations had been first considered in [20] and divided in sub-populations before doing a change of variables to obtain densities. In this paper, only the final version concerning densities is studied. In this model, three stages are considered: I_m the density of infective mosquitoes; S_H the density of susceptible humans; I_H the density of infected humans. The transmission virus model is

$$
\begin{cases}
I'_m(t) = -(s_L \dfrac{L_m(t)}{A_m(t)} + \beta_m I_H(t)) I_m(t) + \beta_m I_H(t), \\[2mm]
S'_H(t) = -(b_H + \beta_H I_m(t)) S_H(t) + b_H, \\[2mm]
I'_H(t) = \beta_H I_m(t) S_H(t) - (\gamma + b_H) I_H(t),
\end{cases}
\tag{17}
$$

where $\beta_H > 0$ (resp. $\beta_m > 0$) is the infectious contact rate between susceptible humans and vectors (resp. susceptible mosquitoes and infected humans), $\gamma > 0$ is the human recovery rate, $b_H > 0$ is the human birth rate.

Under the same conditions as in [21], a continuous model in space is proposed in this paper. Contrary to the displacement of mosquitoes limited to a few meters, human mobility is considered using diffusion terms (See e.g. [22]). Hence, Model (17) is rewritten as follows:

$$
\begin{cases}
\begin{cases}
\partial_t E_m(t,x) = b A_m(t,x)(1 - \dfrac{E_m(t,x)}{K_E(t,x)}) - (s+d) E_m(t,x), \\[2mm]
\partial_t L_m(t,x) = s E_m(t,x)(1 - \dfrac{L_m(t,x)}{K_L(t,x)}) - (s_L + d_L) L_m(t,x), \\[2mm]
\partial_t A_m(t,x) = s_L L_m(t,x) - d_m A_m(t,x),
\end{cases} & (a) \\[6mm]
\begin{cases}
\partial_t I_m(t,x) = -(s_L \dfrac{L_m(t,x)}{A_m(t,x)} + \beta_m I_H(t,x)) I_m(t,x) + \beta_m I_H(t,x), \\[2mm]
\partial_t S_H(t,x) = -(b_H + \beta_H I_m(t,x)) S_H(t,x) + b_H + d_1 \Delta S_H(t,x), \\[2mm]
\partial_t I_H(t,x) = \beta_H I_m(t,x) S_H(t,x) - (\gamma + b_H) I_H(t,x) + d_2 \Delta I_H(t,x),
\end{cases} & (b)
\end{cases}
\tag{18}
$$

where $d_1, d_2 > 0$ are diffusion coefficients, x is in a bounded domain $\Omega \subset \mathbb{R}^n$ with C^2-boundary and $t > 0$. The model is completed with the following initial

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conditions

$$(E_m(0,x), L_m(0,x), A_m(0,x)) = (E_0(x), L_0(x), A_0(x)),$$
$$(I_m(0,x), S_H(0,x), I_H(0,x)) = (I_0^m(x), S_0^H(x), I_0^H(x)).$$

Furthermore, we assume that there there is no population flux across the boundary $\partial\Omega$ of Ω, thus the model is completed by homogeneous Neumann boundary conditions:
$$\frac{\partial S_H}{\partial \nu} = \frac{\partial I_H}{\partial \nu} = 0 \text{ in } \mathbb{R}_+ \times \partial\Omega,$$
where ν is the unit outward normal at $\partial\Omega$.

An identifiability study of this model was proposed in [37] but with constant carrying capacities and continuous initial conditions and consequently in the framework of continuous solutions. In this paper, we generalize the results of [37] to the L^2 framework. More precisely, we make the following assumptions:

1. $(E_0, L_0, A_0) \in C(\overline{\Omega})^3$, $I_0^m \in C(\Omega)$ and $(S_0^H, I_0^H) \in L^2(\Omega)^2$.
2. The carrying capacities of mosquitoes stages K_E and K_L satisfy

$$K_E, K_L \in L^\infty([0,\infty)\times\Omega) \quad \text{with} \quad K_L(t,x) = K_E(t,x)/2 \neq 0, \quad \text{a.e. } (t,x) \in \mathbb{R}_+\times\Omega.$$

3. Moreover, K_E and K_L are piecewise constant functions in time that can correspond to a brutal change in the environment.

4.2. Existence and uniqueness of the solutions

4.2.1. The ODE system

We set

$$\Sigma := \left\{ (E,L,A) \in C(\overline{\Omega})^3 \,\Big|\, 0 \leq E \leq k,\ 0 \leq L \leq \frac{k}{2},\ 0 \leq A \leq \frac{s_L\, k}{2d_m} \right\},$$

where, to simplify notations, we set $k := \|K_E\|_\infty > 0$.

A simple adaptation of Lemmas 4.2 and 4.3 of [20], from the case K_E constant to the case K_E depending of x and piecewise constant function in time, leads to the following result:

Proposition 4.1. *Let* $(E_0, L_0, A_0) \in \Sigma$. *We set*

$$R := \frac{s_L}{d_m} \frac{b}{s+d} \frac{s}{s_L + d_L}.$$

Then, if $R > 1$, system (18)-(a) admits a unique solution (E_m, L_m, A_m) in the space of differentiable piecewise functions $C_l^1\left([0, \infty); int(\Sigma)\right)^3$ where $int(\Sigma)$ is the interior of Σ.

Remark 4.1.

1. *Note that the discontinuous points of E_m, L_m and A_m are the same and are those of K_E.*
2. *From [20], the condition of survival of eggs, larvae and adults populations of mosquitoes is given by $R > 1$. Afterwards, we suppose that $R > 1$ so that $E_m, L_m, A_m > 0$. In particular, we make the following assumption:*

$$(\mathcal{H})\ R > 1 \text{ and there exists } c > 0 \text{ such that, for any } t \geq 0,$$
$$\zeta_3(t) := A_m(t, \cdot) > c.$$

4.2.2. The PDE system

Since $(\mathcal{H})$ is satisfied, we have

$$r := \frac{L_m}{A_m} \in C_l^1\left([0, \infty); C(\overline{\Omega})\right).$$

By setting $U := (I_m, S_H, I_H)$, system (18)-(b) is of the form (2) where the Banach space X is given by

$$X := \left\{(u_1, u_2, u_3) \mid u_1 \in C(\overline{\Omega}),\ u_2,\ u_3 \in L^2(\Omega)\right\},$$

and the operator B is defined by

$$B := \mathrm{diag}(I, -d_1 A + b_H, -d_2 A + \gamma + b_H),$$

where A is the realization of the Laplacian in $L^2(\Omega)$ with Neuman homogeneous boundary condition on $\partial\Omega$, and I is the identity operator of $C(\overline{\Omega})$. Furthermore, the nonlinear operator $G(t, \cdot)$ is given by

$$G(t, U) := (-(s_L r(t) + \beta_m u_3 - 1)u_1 + \beta_m u_3, -\beta_H u_1 u_3 + b_H, \beta_H u_1 u_2).$$

We prove in the appendix, section 7, that G satisfies (3) and thus (18)-(b) admits a unique local solution

$$U \in C_l([0, T_{U_0}]; D(B)) \cap C_l^1((0, T_{U_0}]; X)$$

where $U_0 := (I_0^m, S_0^H, I_H^0)$.

Moreover, setting

$$X_+ := \left\{(u_1, u_2, u_3) \in X \mid u_1, u_2, u_3 \geq 0\right\}, \tag{19}$$

we have the following theorem which states that the solution is global.

Theorem 4.1. *Under the assumption* $(\mathcal{H})$*, for any* $(I_0^m, S_0^H, I_0^H) \in X_+$*, (18)-(b)
possesses a unique non-negative global solution such that*

$$\begin{cases} I_m \in C_l^1([0, \infty); C(\overline{\Omega})), \\ S_H, \ I_H \in C_l([0, \infty); H_N^2(\Omega)) \cap C_l^1((0, \infty); L^2(\Omega)). \end{cases}$$

The proof of the theorem is given in the appendix, section 7.

4.3. Identifiability result

   The parameters whose values are not directly accessible from the field are s, s_L for the system (18)-(a) and β_H, β_m, d_1, d_2 for the system (18)-(b).

   In the case of the ODEs model (16)-(17), an identifiable study had been done in [27] and a procedure based on input-output polynomials had been proposed in [32]. In [37], the identifiability model (18) was studied but in the case of very regular functions. Namely, for system (18)-(a), the solutions were C^∞ and for system (18)-(b) the solutions were continuous. We consider the same assumptions on the measured outputs, that is L_m, S_H, I_H can be measured.

   Indeed, some weekly informations on the number of mosquitoes larvae can be obtained owing to the use of water tanks in which the mosquitoes female lay their eggs. Then, institutes for Health Care can collect periodically data on the number of new infections. Thus, we assume that the number of susceptible humans S_H, infected humans I_H and larvae L_m can be considered as measured variables in Ω during a finite time interval.

   The main result of the paper is the following:

Theorem 4.2. *Assume the constants* $b, d, d_L, d_m, b_H, \gamma$ *are known and there exists* $\nu \in \mathbb{N}$ *such that*

   - *for all* $(t, x) \in (t_\nu, t_{\nu+1}) \times \Omega$*,* $L_m(t, x)$*,* $S_H(t, x)$ *and* $I_H(t, x)$ *are the outputs of the model,*

   - *for any* $t \in (t_\nu, t_{\nu+1})$*,* $S_H(t, \cdot)$ *and* $I_H(t, \cdot)$ *are linearly independent up to an additive constant in* Ω*.*

We recall that the notation $< ., . >$ *is the mean on all the space* Ω*. Then, system (18) is identifiable with respect to* s, s_L, A_0, d_1 *and* d_2*.*

   Let $\tilde{I}_m := \beta_H \, I_m$*. Under the same assumptions, if there exists* $\tilde{t} \in (t_\nu, t_{\nu+1})$ *such that* $\langle I_H S_H^2 \rangle (\tilde{t}) \neq 0$ *and* $\left\langle \tilde{I}_m I_H S_H^2 \right\rangle (\tilde{t}) \neq 0$*, then system (18) is identifiable with respect to* β_m *and* β_H*.*

Remark 4.2.

1. *According to equation (18)-(b), $\tilde{I}_m$ can be expressed almost everywhere only in function of the measured variable S_H (or I_H) and of the identifiable parameter d_1 (or d_2). Consequently, $\tilde{I}_m$ is considered as a measured variable almost everywhere.*

2. *Note that a supplementary result is obtained on the identifiability of the initial condition $A_0 \in C(\overline{\Omega})$. Therefore, by an optimization procedure based on the identifiability study, the values of A_0 and the other unknown parameters can be obtained in a unique way from the knowledge of L_m, S_H and I_H.*

3. *An example of the estimation of d_1 and d_2 is given at section 5.*

4.4. Proof of Theorem 4.2

We proceed in two steps. In the first step, we show that (18)-(a) is identifiable with respect to $\theta_a := (s, s_L, A_0)$. In the second step, we show that (18)-(b) is identifiable with respect to $\theta_b := (\beta_m, \beta_H, d_1, d_2)$.

First step. For x fixed in Ω, let us introduce the following notations:

$$\forall\, t \in [0, \infty), \quad \zeta_1(t) := \frac{E_m(t, x)}{K_E(t, x)}, \quad \zeta_2(t) := \frac{L_m(t, x)}{K_E(t, x)}, \quad \zeta_3(t) := \frac{A_m(t, x)}{K_E(t, x)}.$$

In all the sequel, we denote by $(t_\nu)_\nu$ the finite increasing family of discontinuity time points of K_E (and so of ζ_1, ζ_2 and ζ_3). First, to obtain simpler polynomials, the third equation of system (18)-(a) is integrated before using the package `DifferentialAlgebra` of Maple.

Integration of the third equation of system (18)-(a) on any interval $(t_\nu, t_{\nu+1})$ yields

$$\forall\, t \in (t_\nu, t_{\nu+1}), \quad \zeta_3(t) = \zeta_3(0)e^{-d_m t} + s_L \int_{t_\nu}^{t_{\nu+1}} \zeta_2(s, x)e^{-d_m(t-s)}\, ds.$$

Then, we set

$$\forall\, t \in (t_\nu, t_{\nu+1}), \quad \tilde{\zeta}_{2,\nu}(t, x) := \int_{t_\nu}^{t_{\nu+1}} \zeta_2(s, x)e^{-d_m(t-s)}\, ds \quad \text{and} \quad \lambda(t) := e^{-d_m t}.$$

To simplify the notations, we let $\tilde{\zeta}_{2,\nu} = \tilde{\zeta}_2$. Since $\tilde{\zeta}_2$ depends only on d_m and the measured variable ζ_2, it can be also considered as a measured variable. Thus, we have three observations

$$y_{a,1} := \zeta_2, \quad y_{a,2} := \tilde{\zeta}_2 \quad \text{and} \quad y_{a,3} := \lambda.$$

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Then, system (18)-(a) can be rewritten:

$$\begin{cases} \partial_t \zeta_1 &=& b\zeta_3(1 - \zeta_1) - (s + d)\zeta_1 \\ \partial_t \zeta_2 &=& s\zeta_1(1 - 2\zeta_2) - (s_L + d_L)\zeta_2 \\ \zeta_3 &=& \zeta_3(0)\lambda + s_L\tilde{\zeta}_2 \\ \partial_t \tilde{\zeta}_2 &=& \zeta_2 - d_m\tilde{\zeta}_2 \\ \partial_t \lambda &=& -d_m\lambda \\ y_{a,1} &=& \zeta_2, \quad y_{a,2} = \tilde{\zeta}_2, \quad y_{a,3} = \lambda \end{cases} \tag{20}$$

with the initial conditions:

$$(\zeta_1(0, x), \zeta_2(0, x), \zeta_3(0, x), \tilde{\zeta}_2(0, x), \lambda(0)) = (\zeta_{1,0}(x), \zeta_{2,0}(x), \zeta_{3,0}(x), 0, 1).$$

The Rosenfeld-Groebner algorithm[1] is then applied with (20) and the elimination order [2]

$$[\zeta_{3,0}, s, s_L] \prec [y_{a,1}, y_{a,2}, y_{a,3}] \prec [\zeta_1, \zeta_2, \zeta_3, \tilde{\zeta}_2, \lambda]$$

The software gives the characteristic presentation composed of the following polynomials:

$$Q_1 = -\zeta_{3,0}y_{a,3} - s_L y_{a,2} + \zeta_3, \quad Q_2 = \zeta_1 (2 \, y_{a,1} - 1) \, s + y_{a,1} \, s_L + d_L \, y_{a,1} + \partial_t y_{a,1}$$

and

$$P = -2 \, \partial_t(y_{a,1}^2) - \partial_t^2 y_{a,1} + 2 \, y_{a,1} \, \partial_t^2 y_{a,1} + b \, s \, \zeta_{3,0} \, y_{a,3} + (d \, d_L + d \, s_L + \, d_L \, s$$

$$+ s \, s_L) \, (2 \, y_{a,1}^2 - y_{a,1}) + (2 \, b \, d_L \, \zeta_{3,0} + 4 \, b \, s \, \zeta_{3,0} + 2 \, b \, s_L \, \zeta_{3,0}) \, y_{a,1}^2 \, y_{a,3}$$

$$+ (-b \, d_L \, \zeta_{3,0} - 4 \, b \, s \, \zeta_{3,0} - b \, s_L \, \zeta_{3,0}) \, y_{a,1} \, y_{a,3} + b \, s \, s_L \, y_{a,2}$$

$$+ (-b \, d_L \, s_L - 4 \, b \, s \, s_L - b \, s_L^2) \, y_{a,1} \, y_{a,2} + (2 \, b \, d_L \, s_L + 4 \, b \, s \, s_L + 2 \, b \, s_L^2) \, y_{a,1}^2 \, y_{a,2}$$

$$+ b \, \zeta_{3,0} \, (-y_{a,3} \, \partial_t y_{a,1} + 2 \, y_{a,1} \, y_{a,3} \, \partial_t y_{a,1}) + (2 \, d + 2 \, s) \, y_{a,1} \, \partial_t y_{a,1}$$

$$- (d + d_L + s + s_L) \, \partial_t y_{a,1} + b \, s_L \, (2 \, y_{a,1} \, \partial_t y_{a,1} \, y_{a,2} - \partial_t y_{a,1} \, y_{a,2}).$$

From the two first polynomials Q_1, Q_2, ζ_1 and ζ_3 can be expressed according to $y_{a,1}, y_{a,2}, y_{a,3}$. The third one, P, links the outputs and the parameters s, s_L and

---

[1] This algorithm is implemented in in the package DifferentialAlgebra of Maple.

[2] Note that the equations $\dot{\xi}_{3,0} = 0$, $\dot{s} = 0$ and $\dot{s}_L = 0$ had been added to (Γ_a) before the elimination procedure.

$\zeta_{3,0}$ of the model, it is also an input-output polynomial. Since solutions of (18) are in $C_l^1([0,\infty);\mathcal{C})$ and P contains derivatives of second order in time, P is not well-defined with respect to the regularity of the solution. Let us show how to obtain a regular relation.

In considering P in the distribution sense and in changing the term $y_{a,1}\,\partial_t^2 y_{a,1}$ to $\partial_t(y_{a,1}\,\partial_t y_{a,1}) - (\partial_t y_{a,1})^2$ the following polynomial $\tilde{P}$ in the distribution sense is obtained:

$$\tilde{P} = -2\,T_{\partial_t(y_{a,1}^2)} - T''_{y_{a,1}} + 2T'_{y_{a,1}\,\partial_t y_{a,1}} - 2T_{(\partial_t y_{a,1})^2} + \gamma_1(\theta_a)\,T_{y_{a,3}} + \gamma_2(\theta_a)\,T_{2\,y_{a,1}^2 - y_{a,1}}$$

$$+\gamma_2(\theta_a)\,T_{y_{a,1}} + \gamma_3(\theta_a)\,T_{y_{a,1}^2\,y_{a,3}} + \gamma_4(\theta_a)\,T_{y_{a,1}\,y_{a,3}} + \gamma_5(\theta_a)\,T_{y_{a,2}} + \gamma_6(\theta_a)\,T_{y_{a,1}\,y_{a,2}}$$

$$+\gamma_7(\theta_a)\,T_{y_{a,1}^2\,y_{a,2}} + \gamma_8(\theta_a)\,T_{-y_{a,3}\,\partial_t y_{a,1} + 2\,y_{a,1}\,y_{a,3}\,\partial_t y_{a,1}}$$

$$+\gamma_9(\theta_a)\,T_{y_{a,1}\,\partial_t y_{a,1}} - \gamma_{10}(\theta_a)\,T'_{y_{a,1}} + \gamma_{11}(\theta_a)\,T_{2\,y_{a,1}\,\partial_t y_{a,1}\,y_{a,2} - \partial_t y_{a,1}\,y_{a,2}},$$

where

$$\begin{aligned}
\gamma(\theta_a) \;&:=\; (\gamma_k(\theta_a))_{1\leq k\leq 11}\\
&:=\; \big(b\,s\,\zeta_{3,0}\,,\; d\,d_L + d\,s_L + d_L\,s + s\,s_L\,,\\
&\quad\; 2\,b\,d_L\,\zeta_{3,0} + 4\,b\,s\,\zeta_{3,0} + 2\,b\,s_L\,\zeta_{3,0}\,,\; -b\,d_L\,\zeta_{3,0}\\
&\quad\; -4\,b\,s\,\zeta_{3,0} - b\,s_L\,\zeta_{3,0}\,,\, b\,s\,s_L\,,\, -b\,d_L\,s_L - 4\,b\,s\,s_L - b\,s_L^2\,,\\
&\quad\; 2\,b\,d_L\,s_L + 4\,b\,s\,s_L + 2\,b\,s_L^2\,,\, b\,\zeta_{3,0}\,,\, 2\,d + 2\,s\\
&\quad\; -(d + d_L + s + s_L)\,,\, b\,s_L\big).
\end{aligned}$$

Remark 4.3. *From the observation L_m and by using $\tilde{P}$, the unknown parameters s, s_L and $A_0(x)$ can be estimated for all $x \in \Omega$.*

Let us prove that the model is identifiable with Proposition 3.2. Using Maple, we obtain that the functional determinant of the functions $\{y_{a,3}, 2\,y_{a,1}^2 - y_{a,1},$ $y_{a,1}^2 y_{a,3},\; y_{a,1}y_{a,3},\; y_{a,2},\; y_{a,1}y_{a,2},\; y_{a,1}^2 y_{a,2},\; -y_{a,3}\dot{y}_{a,1} + 2y_{a,1}y_{a,3}\dot{y}_{a,1},\; y_{a,1}\dot{y}_{a,1},\; \dot{y}_{a,1},$ $2y_{a,1}\dot{y}_{a,1}y_{a,2} - \dot{y}_{a,1}y_{a,2}\}$ is not identically equal to zero. Then, solving the algebraic system $\gamma(\theta_a) = \gamma(\tilde{\theta}_a)$ with the Groebner basis implemented in maple leads to $\theta_a = \tilde{\theta}_a$. Consequently, applying Proposition 3.2, the model is identifiable at the parameters s, s_L, and $\zeta_{3,0}(x)$ for each $x \in \Omega$.

Second step. Since S_H and I_H are assumed to be known for all $(t,x) \in (t_\nu, t_{\nu+1}) \times \Omega$, the equalities $y_{b,1} = S_H$ and $y_{b,2} = I_H$ are added to system (18)-(b) which is

rewritten in the following form:

$$
\begin{cases}
\partial_t I_m = -(s_L r + \beta_m I_H) I_m + \beta_m I_H, \\[4pt]
\partial_t S_H = -(b_H + \beta_H I_m) S_H + b_H + d_1 \Delta S_H, \\[4pt]
\partial_t I_H = \beta_H I_m S_H - (\gamma + b_H) I_H + d_2 \Delta I_H, \\[4pt]
y_{b,1} = S_H,\ y_{b,2} = I_H.
\end{cases}
$$

where $r := \frac{\zeta_2}{\zeta_3}$ is known according to the previous subsection.

The parameters to identify being β_m, β_H, d_1, d_2, we denote $\theta_b := (\beta_m, \beta_H, d_1, d_2)$. The initial conditions are in that case $(I_m(0, \cdot), S_H(0, \cdot), I_H(0, \cdot)) = (I_0^m, S_0^H, I_0^H)$.

Following section 3.3, the identifiability of the parameters is done in two steps: first the identifiability study of d_1 and d_2 by using Lemma 3.1, then the identifiability study of β_m and β_H by using Proposition 3.3.

Identifiability of d_1 and d_2.

Summing the second equation and the third equation of (Γ_b) yields:

$$
\begin{aligned}
d_1 \Delta y_{b,1}(t, \cdot) + d_2 \Delta y_{b,2}(t, \cdot) \ =\ & \partial_t y_{b,1}(t, \cdot) + \partial_t y_{b,2}(t, \cdot) + b_H(y_{b,1}(t, \cdot) - 1) \\
& + (\gamma + b_H) y_{b,2}(t, \cdot).
\end{aligned}
\tag{21}
$$

The right hand-side of (21) does not depend on d_1 and d_2, and the functions $y_{b,1}$ and $y_{b,2}$ are supposed to be linearly independent. According to Lemma 3.1, the model is identifiable with respect to d_1 and d_2.

Identifiability of β_m and β_H.

From the package `DifferentialAlgebra` of Maple, we obtain the following input-output polynomial:

$$
\begin{aligned}
&-(-b_H s_L r - s_L r \gamma) y_{b,2} y_{b,1} - (\gamma + b_H) y_{b,2} \partial_t y_{b,1} - (-s_L r - b_H - \gamma) y_{b,1} \partial_t y_{b,2} \\
&- d_2 r s_L y_{b,1} \Delta y_{b,2} - (d_2 \partial_t \Delta y_{b,2} - \partial_{tt} y_{b,2}) y_{b,1} - \partial_t y_{b,2} \partial_t y_{b,1} + d_2 \partial_t y_{b,1} \Delta y_{b,2} \\
&= \beta_m \left((-\gamma - b_H) y_{b,2}^2 y_{b,1} - y_{b,2} y_{b,1} \partial_t y_{b,2} + d_2 y_{b,2} y_{b,1} \Delta y_{b,2} \right) + \beta_H \beta_m\, y_{b,2} y_{b,1}^2
\end{aligned}
\tag{22}
$$

Since the function $y_{b,1} = S_H$ and $y_{b,2} = I_H$ are in $C_l^1((0, \infty), L^2(\Omega))$, the previous polynomial is considered in the distribution sense.

We apply Lemma 3.2. Since the model is identifiable with respect to d_1 and d_2, Assumption 1 of Lemma 3.2 is satisfied. The exhaustive summary of the input-output relation (22) being $(\beta_m, \beta_H \beta_m)$, Assumption 2 of Lemma 3.2 is easily verified.

It remains to show Assumption 3. We set

$$m_1 := (-\gamma - b_H)y_{b,2}^2 y_{b,1} - y_{b,2}y_{b,1}\partial_t y_{b,2} + d_2 y_{b,2}y_{b,1}\Delta y_{b,2} \quad \text{and} \quad m_2 := y_{b,2}y_{b,1}^2.$$

m_1 can be rewritten:

$$m_1 = y_{b,2}y_{b,1}\left((-\gamma - b_H)y_{b,2} - \partial_t y_{b,2} + d_2\Delta y_{b,2}\right) = -y_{b,2}y_{b,1}^2 \tilde{I}_m.$$

Thus, the Wronksian of $(\langle m_1\rangle, \langle m_2\rangle)$ is equal to:

$$\left\langle y_{b,2}y_{b,1}^2 \right\rangle \left\langle (\partial_t \tilde{I}_m)y_1^2 y_2 \right\rangle.$$

By assumption, there exists a time point $\tilde{t} \in (t_\nu, t_{\nu+1})$ such that this Wronskian does not vanish. Thus, from Lemma 3.2 and Remark 3.5, the model is identifiable with respect to β_m and β_H.

Remark 4.4. *The proof of Proposition 4.2 provides two input-output polynomials (21) and (22). To illustrate a way to use them in a parameter estimation procedure, we propose, in the following section, a method to estimate d_1 and d_2 based on (21). The procedure does not require any knowledge of the parameter values. This first estimate of d_1 and d_2 can be used by a local algorithm to improve their estimation.*

5. Example of the estimation of the two parameters d_1 and d_2

This part is devoted to a numerical simulation estimating the parameters d_1 and d_2 based on (21). We follow the following procedure:

- We solve (18) with known parameters and thus we obtain approximations of S_H and I_H.

- These approximations permit to simulate measured states S_H^{meas} (resp. I_H^{meas}) as normal distributions around S_H (resp. I_H) with variance $(\sigma S_H)^2$ (resp. $(\sigma I_H)^2$), where $\sigma \in \mathbb{R}_+$. The constant σ is chosen in order to obtain the desired error between S_H and S_H^{meas}, and also between I_H and I_H^{meas}.

- We apply the parameter estimation procedure with the measured states S_H^{meas} and I_H^{meas} to recover the parameters d_1 and d_2.

Let us first present the simulations data.

Parameters	Description	Value
b	Oviposition rate	6
K_E	Egg carrying capacity	1000
s	Egg transformation rate	0.7
s_L	Larva transformation rate	0.5
d	Egg mortality rate	0.2
d_L	Larva mortality rate	0.2
d_m	Female adult mortality rate	0.25
b_H	Human birth/death rate	0.0000457
β_H	Infection rate: vector to human	0.75
β_m	Infection rate: human to vector	0.5
γ	Human recovery rate	0.1428

Table 1: Parameters values

5.1. Simulations

We use the parameters values from Table 1 of [19] (see also [21]) and recalled in Table 1. Moreover, we set $d_1 = 0.1$ and $d_2 = 0.01$ so that susceptible populations diffuse through the domain faster than the infected populations. The domain considered is $\Omega := (0,1)^2$ and the final time is $T = 20$.

At the initial time, the variables ζ_i are taken constant while the infected humans are supposed to be concentrated in the center of the domain, which can correspond for example to an hospital, and the susceptible humans are located at the extremities of the domain. More precisely, the initial conditions are given by:

$$
\begin{cases}
\zeta_1(t=0,x,y) = 0.1,\ \zeta_2(t=0,x,y) = 0.04,\ \zeta_3(t=0,x,y) = 0.01, \\
I_m(t=0,x,y) = 0.2, \\
S_H(t=0,x,y) = 1 - z(x,y), \\
I_H(t=0,x,y) = z(x,y),
\end{cases}
$$

where

$$
z(x,y) := \begin{cases}
e^{-\frac{\frac{1}{4}}{\frac{1}{4}-(x-\frac{1}{2})^2-(y-\frac{1}{2})^2}}, & \text{if } (x-\tfrac{1}{2})^2 + (y-\tfrac{1}{2})^2 < \tfrac{1}{4} \\
0 & \text{else.}
\end{cases}
$$

Then, we compute approximations of S_H and I_H by solving the system (18), with the exact parameter values, by an explicit finite difference method.

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The measured states S_H^{meas} and I_H^{meas} are constructed by using the function *randn* of Matlab, where the coefficient σ is chosen in order to have a maximal value of the relative error between S_H and S_H^{meas} (and between I_H and I_H^{meas}) equal to 1%, 5%, 10% and 20%.

5.2. The numerical input-output method for estimating d_1 and d_2

The relation (21) is given in distribution sense by:

$$
d_1 \int_\Omega S_H(t,x)\Delta\psi(x)\,dx + d_2 \int_\Omega I_H(t,x)\Delta\psi(x)\,dx
$$
$$
= \int_\Omega \Big(\partial_t S_H(t,x) + \partial_t I_H(t,x) \Big) \psi(x)\,dx
$$
$$
+(\gamma + b_H) \int_\Omega I_H(t,x)\,\psi(x)\,dx - b_H \int_\Omega \Big(1 - S_H(t,x)\Big)\psi(x)\,dx,
$$

for all $\psi \in C_c(\Omega)$. Integrating this relation on $(0,t)$, we obtain

$$
d_1 \int_0^t \left(\int_\Omega S_H(\tau,s)\Delta\psi(s)\,ds \right) d\tau + d_2 \int_0^t \left(\int_\Omega I_H(\tau,s)\Delta\psi(s)\,ds \right) d\tau
$$
$$
= \int_\Omega \Big(S_H(t,s) + I_H(t,s) \Big)\psi(s)\,ds - \int_\Omega \Big(S_H(0,s) + I_H(0,s) \Big)\psi(s)\,ds
$$
$$
+(\gamma + b_H) \int_0^t \left(\int_\Omega I_H(\tau,s)\,\psi(s)\,ds \right) d\tau
$$
$$
-b_H \int_0^t \left(\int_\Omega \Big(1 - S_H(\tau,s)\Big)\psi(s)\,ds \right) d\tau,
$$

$$\tag{23}$$

for all $\psi \in C_c(\Omega)$ and all $t > 0$.

We consider the following test function:

$$
\psi(x,y) := \begin{cases} e^{\frac{1}{1-x^2-y^2}} & \text{if } (x,y) \in \Omega, \\ 0 & \text{else,} \end{cases}
$$

and a discretization $0 = t_1 < t_2 < \ldots < t_{M+1} = T$ of $[0,\ T]$. For $k = 1, 2, \ldots, M$, we set

$$
A(k,1) := \int_0^{t_{k+1}} \left(\int_\Omega S_H(\tau,s)\Delta\psi(s)\,ds \right) d\tau,
$$

$$
A(k,2) := \int_0^{t_{k+1}} \left(\int_\Omega I_H(\tau,s)\Delta\psi(s)\,ds \right) d\tau,
$$

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and

$$B(k) := \int_\Omega \Big(S_H(t_{k+1}, s) + I_H(t_{k+1}, s) \Big) \psi(s) \, ds - \int_\Omega \Big(S_H(0, s) + I_H(0, s) \Big) \psi(s) \, ds$$

$$+ (\gamma + b_H) \int_0^{t_{k+1}} \left(\int_\Omega I_H(\tau, s) \, \psi(s) \, ds \right) d\tau - b_H \int_0^{t_{k+1}} \left(\int_\Omega \Big(1 - S_H(\tau, s) \Big) \psi(s) \, ds \right) d\tau.$$

Then, we obtain the following approximation of (23):

$$Ad = B, \text{ where } d := (d_1, d_2)^T.$$

We solve this system by the standard least squares method based upon QR factorization to obtain the parameters approximations d_1^a and d_2^a.

The results are summarized in Table 2 where λ is the relative error between (S_H, I_H) and (S_H^{meas}, I_H^{meas}), while re is the relative error between (d_1, d_2) and (d_1^a, d_2^a).

λ	1%	5%	10%	20%
d_1^a	0.1019	0.1011	0.0836	0.1153
d_2^a	0.0186	0.0159	0.0102	0.0191
re	0.0880	0.0595	0.1636	0.1773

Table 2: Calculation results and errors

One can see that the method gives good approximations of d_1 and d_2. Moreover, this method also works with a strong noise.

6. Conclusion

In this paper, we have investigated an identifiability method applied up to now to ordinary differential equations systems to partial differential equations systems. Furthermore, some generalization results on the L^2 framework had been obtained. This method based on algebra tools had proved to provide interesting relations after regularizing them in using the distribution theory. As shown on the two examples describing the chikungunya disease, these relations permit to provide identifiability results. Furthermore, a numerical method deduced from the differential relations had been proposed and permitted to give a first initial guess of the unknown parameters. Future works concern the exploration of the proposed method to parameters in L^p and for other class of systems.

7. Appendix

In this appendix we give the proof of Theorem 4.1. To this end it suffices to show that (3) is satisfied so that a local solution U exists and then to show that U is non negative and satisfies (4).

We restrict ourselves to the case $r \in C^1\left([0, +\infty); C(\overline{\Omega})\right)$. The case r piecewise differentiable in time is a simple adaptation by considering only compact time intervals on which r is C^1. Thus, since we assume $(\mathcal{H})$ satisfied, in all the sequel we have

$$r := \frac{L_m}{A_m} \in C^1\left([0, \infty); C(\overline{\Omega})\right).$$

Set $\eta \in (3/4, 1)$. The domain of the fractional power B^η of B is given by (see theorem 16.7 of [35]):

$$D(B^\eta) = \{(u_1, u_2, u_3)^T;\ u_1 \in \mathcal{C},\ u_2,\ u_3 \in H_N^{2\eta}(\Omega)\} \tag{24}$$

and there exists $c > 0$ such that for $i = 1, 2$

$$\frac{1}{c}\|f\|_{H_N^{2\eta}(\Omega)} \leq \|B_i^\eta f\|_{L^2(\Omega)} \leq c\|f\|_{H_N^{2\eta}(\Omega)}, \tag{25}$$

for all $f \in D(B_i^\eta)$. Moreover, since $2\eta > 1$ and Ω is bounded, from Sobolev embedding theorem, we have

$$H_N^{2\eta}(\Omega) \subset C(\bar{\Omega}) \subset L^\infty(\Omega) \subset L^2(\Omega), \tag{26}$$

with continuous embedding.

First step. *Existence and uniqueness of a local solution.*

In all the sequel, C will denote a positive constant whose value can change from line to line. Set $U := (u_1, u_2, u_3) \in D(B^\eta)$, $V := (v_1, v_2, v_3) \in D(B^\eta)$, $T > 0$ and $s, t \in [0, T]$. We have

$$\begin{aligned}
\|G(t, U) - G(s, \tilde{U})\|_2 \leq \| &- (s_L r(t) + \beta_m u_3 - 1)u_1 + \beta_m u_3 \\
&+ (s_L r(s) + \beta_m v_3 - 1)\tilde{u}_1 - \beta_m v_3\|_{L^2} \\
&+ \beta_H \|u_1 u_3 - v_1 v_3\|_{L^2} + \beta_H \|u_1 u_2 - v_1 v_2\|_{L^2}. \tag{27}
\end{aligned}$$

From (25) and (26), we deduce

$$
\begin{aligned}
\|u_1 u_2 - v_1 v_2\|_{L^2} &\leq \|u_1 u_2 - u_1 v_2 + u_1 v_2 - v_1 v_2\|_{L^2} \\
&\leq \|u_1(u_2 - v_2)\|_{L^2} + \|(u_1 - v_1)v_2\|_{L^2} \\
&\leq \|u_1\|_\infty \|u_2 - v_2\|_{L^2} + \|v_2\|_\infty \|u_1 - v_1\|_{L^2} \\
&\leq C\|u_1\|_{H^{2\eta}} \|u_2 - v_2\|_{L^2} + \|v_2\|_{H^{2\eta}} \|u_1 - v_1\|_{L^2} \\
&\leq C(\|B^\eta U\|_{L^2} + \|B^\eta V\|_{L^2})\|U - V\|_{L^2}. \qquad (28)
\end{aligned}
$$

In the same way, we also have

$$
\|u_1 u_3 - v_1 v_3\|_{L^2} \leq C(\|B^\eta U\|_{L^2} + \|B^\eta V\|_{L^2})\|U - V\|_{L^2}. \qquad (29)
$$

Moreover, since $r \in C^1\big([0, \infty); C(\overline{\Omega})\big)$, arguing as previously we obtain

$$
\begin{aligned}
\| -(s_L r(t) &+ \beta_m u_3 - 1)u_1 + \beta_m u_3 + (s_L r(s) + \beta_m v_3 - 1)v_1 - \beta_m v_3\|_{L^2} \\
&\leq (s_L\|r\|_\infty\| + 1)\|u_1 - v_1\|_{L^2} + s_L\|r'\|_\infty\|u_1\|_{L^2}|t - s| \\
&\quad + \beta_m\|u_1 u_3 - v_1 v_3\|_{L^2} + \beta_m\|u_3 - v_3\|_{L^2} \\
&\leq C\left(\|B^\eta(U - V)\|_{L^2} + (\|B^\eta U\|_{L^2} + \|B^\eta V\|_{L^2} + 1)\left(|t - s| + \|U - V\|_2\right)\right).
\end{aligned}
$$
$$(30)$$

From inequalities (27), (28), (29) and (30), we get (3).

Set $U_0 \in X_+$, where X_+ is given by (19). From the first step and Theorem 4.4 of [35], we obtain that there exists $T_{U_0} > 0$ such that (18)-(b) admits a unique local solution:

$$
U := (u_1, u_2, u_3) \in C\left([0, T_{U_0}]; D(B)\right) \cap C^1\left((0, T_{U_0}]; X\right).
$$

Second step. *Non negativity of the local solution.*

This proof is quite standard and can be found in [35] (e.g. page 197), we set it here for the reader convenience. Let $\chi(f)$ be a cutoff function defined by $\chi(f) = 0$ for $f \in (-\infty, 0)$ and $\chi(f) = f$ for $f \in [0, +\infty)$. We set

$$
\tilde{G}(t, \tilde{U}) := (-(s_L r(t) + \beta_m \tilde{u}_3 - 1)\tilde{u}_1 + \beta_m \tilde{u}_3, -\beta_H \chi(\tilde{u}_1)\tilde{u}_3 + b_H, \beta_H \chi(\tilde{u}_1)\tilde{u}_2).
$$
$$(31)$$

Then, we consider the following problem

$$
\begin{cases}
\partial_t \tilde{U} + B\tilde{U} &= \tilde{G}(t, \tilde{U}), \quad \text{in } (0, \infty), \\
\tilde{U}(0) &= U_0.
\end{cases}
\qquad (32)
$$

Using similar arguments as in step 1, one can prove that there exists $\tilde{T}_{U_0}$ such that (32) admits a unique local solution

$$\tilde{U} := (\tilde{u}_1, \tilde{u}_2, \tilde{u}_3) \in C\left([0, \tilde{T}_{U_0}]; D(B)\right) \cap C^1\left((0, \tilde{T}_{U_0}]; X\right).$$

Consider $H(s) := \frac{1}{2}s^2$ for $s \in (-\infty, 0)$ and $H(s) := 0$ for $s \in [0, +\infty)$. This function satisfies

$$H(s) \geq 0, \ H'(s) \leq 0 \quad \text{and} \quad H'(s)s \geq 0, \ H'(s)s \leq 2H(s). \tag{33}$$

We set

$$\phi_1(t) := \int_\Omega H(\tilde{u}_2(t, x))\, dx.$$

Since $x \mapsto H(\tilde{u}_2(t, x))$ is continuous for all $t \in (0, \tilde{T}_{U_0}]$, if $\phi_1 \equiv 0$ then $\tilde{u}_2 \geq 0$. Since ϕ_1 is continuously differentiable and from (32), we have:

$$\phi_1'(t) = \int_\Omega H'(\tilde{u}_2(t, x))\partial_t \tilde{u}_2(t, x)dx$$

$$= d_1 \int_\Omega H'(\tilde{u}_2)\Delta\tilde{u}_2 dx + \int_\Omega H'(\tilde{u}_2)(b_H - (b_H + \beta_H \chi(\tilde{u}_1))\tilde{u}_2)dx$$

$$- b_H \int_\Omega H'(\tilde{u}_2)\tilde{u}_2 dx - \beta_H \int_\Omega H'(\tilde{u}_2)\, \tilde{u}_2\, \chi(\tilde{u}_1)dx.$$

Since $\partial_\nu \tilde{u}_2 = 0$ on $\partial\Omega$, we get

$$\int_\Omega H'(\tilde{u}_2)\Delta\tilde{u}_2 dx = -\int_\Omega \nabla(H'(\tilde{u}_2)).\nabla\tilde{u}_2 dx = -\int_\Omega |\nabla\tilde{u}_2|^2\, dx \leq 0.$$

Owing to (33), one gets that $\int_\Omega H'(\tilde{u}_2)dx \leq 0$, $\int_\Omega H'(\tilde{u}_2)\tilde{u}_2 dx \geq 0$ and consequently that $\phi_1'(t) \leq 0$. Thus, for any $t \in [0, \tilde{T}_{U_0}]$, $0 \leq \phi_1(t) \leq \phi_1(0)$. Since $U_0 \in X_+$, $\tilde{u}_0 \geq 0$ and so $\phi_1(0) = 0$. We deduce that $\tilde{u}_2 \geq 0$ in $[0, \tilde{T}_{U_0}]$.

In the same way, we obtain that $\tilde{u}_1 \geq 0$ and $\tilde{u}_3 \geq 0$ in $[0, \tilde{T}_{U_0}]$. Set $T := \min(T_{U_0}, \tilde{T}_{U_0})$. Since $\tilde{u}_1 \geq 0$ in $[0, T]$, we deduce from the definition (31) of $\tilde{G}$ that $\tilde{G}(\tilde{U}(t)) = G(U(t))$ in $[0, T]$. By uniqueness of the solution of (18)-(b), this leads to $\tilde{U} = U$ in $[0, T]$. Thus, $u_1, u_2, u_3 \geq 0$ in $[0, T]$.

Third step. *Global non negative solution.*

To prove that the solution is global, it suffices to show that the inequality (4) is satisfied.

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1. Let us prove first that u_1 is bounded . Suppose that there exists t such that $u_1(t, x) > 1$ and consider

$$t_1 := \inf\{t \mid u_1(t, x) = 1 \text{ and } u_1(t + \varepsilon, x) > 1, \ \forall \varepsilon > 0\},$$

then

$$\forall t \in [0, \ t_1], \quad u_1(t, x) \leq 1, \ u_1(t_1, x) = 1.$$

Since

$$\partial_t u_1(t_1, x) = -\left(s_L \frac{\zeta_2(t_1, x)}{\zeta_3(t_1, x)} + \beta_m u_3(t_1, x)\right) u_1(t_1, x) + \beta_m u_3(t_1, x))$$

$$= -s_L \frac{\zeta_2(t_1, x)}{\zeta_3(t_1, x)} \leq 0.$$

If $\partial_t u_1(t_1, x) = 0$, then $\zeta_2(t_1, x) = 0$ so $\partial_t \zeta_2(t_1, x) = s\zeta_1(t_1, x) \geq 0$. Recall that $\zeta_3(t_1, x) \neq 0$.

- $\partial_t \zeta_2(t_1, x) > 0$, by continuity, there exists δ_1 such that $\zeta_2(t, x)$ is strictly increasing on $(t_1 - \delta_1, \ t_1 + \delta_1)$, then $\zeta_2(t, x) < \zeta_2(t_1, x) = 0$, $t \in (t_1 - \delta_1, \ t_1)$, which contradicts the positivity of ζ_2.

- $\partial_t \zeta_2(t_1, x) = 0$, then $\zeta_1(t_1, x) = 0$ and $\partial_t \zeta_1(t_1, x) = b\zeta_3(t_1, x) > 0$, so by continuity, there exists δ_2 such that $\zeta_1(t, x)$ is strictly increasing on $(t_1 - \delta_2, \ t_1 + \delta_2)$, then $\zeta_1(t, x) < \zeta_1(t_1, x) = 0$, $t \in (t_1 - \delta_2, \ t_1)$, which contradicts the positivity of ζ_1.

So we have $\partial_t u_1(t_1, x) < 0$, by continuity, there exists δ_3 such that $u_1(t, x)$ is strictly decreasing on $(t_1 - \delta_3, \ t_1 + \delta_3)$, then

$$u_1(t_1 - \delta_3, x) > u_1(t, x) > u_1(t_1, x), \ t \in (t_1 - \delta_3, \ t_1).$$

Since $u_1(t, x) > u_1(t_1, x) = 1$, $t \in (t_1 - \delta_3, \ t_1)$, which contradicts the definition of t_1. So we obtain

$$\forall t \in [0, T], \quad \|u_1(t)\|_\infty \leq 1. \tag{34}$$

2. Let $t \in [0, T]$. Multiplying $\partial_t u_2 = -(b_H + \beta_H u_1)u_2 + b_H + d_1 \Delta u_2$ by u_2 and integrating by parts over Ω, we get

$$\frac{1}{2}\frac{d}{dt}\|u_2(t)\|_{L^2}^2 = -b_H\|u_2(t)\|_{L^2}^2 - \beta_H \int_\Omega u_1(t)u_2^2(t)\, dx + \int_\Omega b_H u_2(t)\, dx$$

$$- d_1 \int_\Omega |\nabla u_2(t)|^2\, dx.$$

Since $u_1 \geq 0$, $d_1 > 0$ and $b_H u_2(t) \leq \frac{b_H}{2} + \frac{b_H}{2} u_2^2(t)$, we obtain

$$\frac{d}{dt}\|u_2(t)\|_{L^2}^2 + b_H\|u_2(t)\|_{L^2}^2 \leq b_H\,|\Omega|.$$

Solving this differential inequality leads to

$$\forall t \in [0, T], \quad \|u_2(t)\|_{L^2}^2 \leq C. \tag{35}$$

3. In the same way, from (34), we obtain that u_3 satisfies

$$\frac{1}{2}\frac{d}{dt}\|u_3(t)\|_{L^2}^2 \leq \beta_H \int_\Omega u_1 u_2 u_3\, dx - (\gamma + b_H)\|u_3(t)\|_{L^2}^2$$

$$\leq \beta_H \int_\Omega u_2\, u_3\, dx - (\gamma + b_H)\|u_3(t)\|_{L^2}^2.$$

From Cauchy-Schwarz inequality and Young's inequality, for any $\varepsilon > 0$, we get

$$\frac{1}{2}\frac{d}{dt}\|u_3(t)\|_{L^2}^2\, dx \leq \beta_H\|u_2(t)\|_{L^2}\,\|u_3(t)\|_{L^2} - (\gamma + b_H)\|u_3(t)\|_{L^2}^2$$

$$\leq \frac{\beta_H}{2\varepsilon}\|u_2(t)\|_{L^2}^2 + \frac{\beta_H \varepsilon}{2}\|u_3(t)\|_{L^2}^2 - (\gamma + b_H)\|u_3(t)\|_{L^2}^2$$

$$\leq \frac{\beta_H C_1}{4\varepsilon} + (\beta_H \varepsilon - \gamma - b_H)\int_\Omega u_3^2\, dx.$$

Taking $\varepsilon := (\gamma + b_H)/\beta_H$, from (35), we obtain

$$\frac{d}{dt}\|u_3(t)\|_{L^2}^2\, dx + (\gamma + b_H)\|u_3(t)\|_{L^2}^2 \leq C.$$

Solving this differential inequality leads to

$$\forall t \in [0, T], \quad \|u_3(t)\|_{L^2}^2 \leq C. \tag{36}$$

From (34), (35) and (36) we obtain that U satisfies (4), which leads to the result.

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