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Abstract

We investigate the parameter identifiability problem for a system of nonlinear integro-partial differential equations of transport type, representing the spread of a disease with a long infectious but undetectable period in an animal population. After obtaining the expression of the model input-output (IO) relationships, we give sufficient conditions on the initial and boundary conditions of the system that guarantee the parameter identifiability on a finite time horizon. We finally illustrate our findings with numerical simulations.

Keywords: inverse problem,identifiability, PDE, transport equations, epidemiological model.

AMS keywords: 35R30, 35L60, 93B30, 92D30.

Contents

1 Introduction

Epidemiological models are useful tools to describe the spread of a disease in a population, to predict its evolution and control its outbreak. They usually derive from the classical SIR model, a compartmental model in which the population is structured in susceptible, infected and recovered individuals. Depending on the interactions between host and pathogen, as well as their time and space scales, several models have been built, dating back to Kermack-McKendrick [1, 2].

The model we investigate in this paper is a SI-like model, a simplified version of a model developed to study the spread of scrapie in a sheep flock [3]. It is characterised by a long and variable incubation period, during which individuals are infectious but cannot be detected. At the end of this period, either they are culled, or they recovered and become immune. In both cases, they do not participate in the infection process anymore and need not be represented in the model. The flock is assumed to be a well-mixed population confined on a limited territory, so the space dimension can be omitted. It is however structured in age ($a \in [0, A]$) and infection load ($\theta \in [0, 1]$). Newly infected individuals are distributed along θ according to a probability density function Θ (support $[0, 1]$). The infection load θ then grows exponentially with time during the incubation period, which ends when θ reaches 1. An alternative option would have been to structure the infected population according to an age of infection instead, leading to a model similar to [4]. Whatever the modelling, it yields a distributed delay structure. The resulting susceptible (S) and infected (I) population densities evolve with time ($t \in [0, +\infty[$) according to the following nonlinear integro-partial differential dynamical system of transport reaction type

$$\left(\frac{\partial}{\partial t} + \frac{\partial}{\partial a}\right) S(t, a) = -\mu S(t, a) - \beta S(t, a)\mathbf{I}(t), \tag{1}$$

$$\left(\frac{\partial}{\partial t} + \frac{\partial}{\partial a} + c\theta\frac{\partial}{\partial \theta}\right) I(t, a, \theta) = -(\mu + c)I(t, a, \theta) + \Theta(\theta)\beta S(t, a)\mathbf{I}(t), \tag{2}$$

where positive parameters μ, β, and c correspond to, respectively, the basic mortality rate, the transmission rate, and the infection load growth rate ($\frac{d\theta}{dt} = c\theta$). $\mathbf{I}(t) = \int_0^A \int_0^1 I(t, a, \theta)\, d\theta\, da$ denotes the total number of infected individuals at time t. Boundary conditions are given by

$$S(t, 0) = B(t), \quad I(t, 0, \theta) = 0, \quad I(t, a, 0) = 0, \tag{3}$$

where B is the birth function, and initial conditions by

$$S(0, a) = S_0(a), \quad I(0, a, \theta) = I_0(a, \theta). \tag{4}$$

The system input is the birth function B. The system outputs are observed on a given finite time horizon $T > 0$ and consist of the total population density given by

$$N(t, a) = S(t, a) + \int_0^1 I(t, a, \theta)\ d\theta, \tag{5}$$

and the incidence given by

$$\imath(t, a) = c\, I(t, a, 1), \tag{6}$$

which corresponds either to the disease-induced mortality, or to the recovery outflow. Indeed, infected individuals cannot be distinguished from susceptible individuals during their infectious incubation period. Unlike the demographic parameter μ and function B which are estimated [5] or known, epidemiological parameters c, β and function Θ need to be identified from output observations.

An important issue is therefore to check whether these epidemiological parameters are identifiable, i.e. whether they can be uniquely determined from the input, initial conditions and observed outputs. It is an inverse problem that consists in establishing that the map from parameters to outputs is into, the input and initial conditions being known. This property is a prerequisite to the model identification, in which parameters are estimated from observed data.

There is a well-established theory for the identifiability of controlled and uncontrolled dynamical systems described by ordinary differential equations [6, 7]. Three main approaches have been used: (i) the state isomorphism method [8, 9]; (ii) the Taylor series expansion method [10]; (iii) the algebro-differential elimination method [11, 12, 13], aiming at obtaining and exploiting algebro-differential relations between the input and output of the system.

In infinite dimension, identifiability results exist for fairly general classes of linear problems. Results concerning convolutive systems, which include the delay-differential equations, can be found in [14, 15, 16]. Identifiability results derived from the use of spectral theory are given in [17] for the 1-D heat and wave equations with boundary observations as well as for abstract homogeneous evolution equations with whole state observation. Results on various classes of linear models with point-wise observation where obtained using Carleman estimates, for instance for the Schrödinger equation [18] or for a non-stationary particle transport equation (see [19] and references therein). In the nonlinear case, we only found results dealing with parabolic equations using Carleman estimates [20, 21, 22].

To our knowledge, the identifiability of nonlinear transport reaction models, such as the model presented here, has never been considered before. Our aim is to check the identifiability of this model, which is therefore an original study. Our approach is adapted from the finite dimensional elimination method.

The document is organised as follows: identifiability results are stated in Section 2; Section 3 establishes an input-output (IO) relation for the model; the proofs, based on algebro-differential elimination are given in Sections 4 and 5. Results are illustrated by simulations in Section 6. Finally, we conclude in Section 7.

2 Identifiability results

As mentioned in the introduction, the parameters of interest are the epidemiological parameters. They are gathered into a vector $p = (c, \beta, \Theta)^T$ belonging to $\mathbf{P} = (\mathbb{R}^{+*})^2 \times \mathcal{A}_0$, where $\mathcal{A}_0$ is the set of real-analytic functions on $]0, 1[$, continuous on $[0, 1]$, with zero values at 0 and 1.

Denoting $H_S^+ = L^2([0, A], \mathbb{R}^+)$, $H_I^+ = L^2([0, A] \times [0, 1], \mathbb{R}^+)$ and $C_p(J_1, J_2)$ the set of piecewise continuous functions from J_1 to J_2 it has been shown in [23] that for $T > 0$, $(S_0, I_0) \in H_S^+ \times H_I^+$, $B \in C_p([0, T], \mathbb{R}^+)$, and $p \in \mathbf{P}$ system (1-4) has a unique mild solution in $C([0, T], H_S^+ \times H_I^+)$ and outputs in $C([0, T], H_S^+)^2$. Moreover, with stronger regularity assumptions on the initial conditions $(S_0, I_0) \in C_p([0, A], \mathbb{R}^+) \times C_p([0, A] \times [0, 1], \mathbb{R}^+)$, solutions satisfy $(S(t), I(t)) \in C_p([0, A], \mathbb{R}^+) \times C_p([0, A] \times [0, 1], \mathbb{R}^+)$. Consequently, the outputs $N(t, \cdot)$ and $\mathfrak{i}(t, \cdot)$ are both in $C_p([0, A], \mathbb{R}^+)$. We assume in the sequel that all these assumptions are verified. We also assume that the initial conditions (S_0, I_0) are fixed and known. Hence the parameter to output map O is defined from $\mathbf{P}$ to the set

$$\{(N, \mathfrak{i}) \in C([0, T], H^+)^2 \; / \forall\, t \in [0, T], (N(t), \mathfrak{i}(t)) \in C_p([0, A], \mathbb{R}^+)^2\}.$$

A subset $\mathbf{Q}$ of $\mathbf{P}$ is said to be identifiable if the restriction $\mathcal{O}|_{\mathbf{Q}}$ is into.

We are now in a position to state our first identifiability result.

Let $\theta^\star$, $c^\star$, $\underline{B}$, $\mathcal{B}$, $\mathbf{Q}^\star$ and $\mathbf{R}^\star$ be defined as

$$\begin{aligned}
\theta^\star &= \sup\{\theta \in]0,1[,\ \exists a^\star \in]0,A[,\ I_0(a^\star,\theta) > 0\},\\
c^\star &= -\frac{1}{\underline{m}} \ln\theta^\star, \quad \text{where } \underline{m} = \min(A,T),\\
\mathcal{B} &= \{t \in [0,T],\ B(t) \neq 0\}, \quad \underline{B} = \inf\mathcal{B},\\
\mathbf{Q}^\star &=]c^\star, +\infty[\times \mathbb{R}^{+*} \times \mathcal{A}_0, \quad \mathbf{R}^\star =]0, c^\star[\times \mathbb{R}^{+*} \times \mathcal{A}_0,
\end{aligned} \tag{7}$$

Consider the following conditions on (3,4),

(H_1) The birth function B is such that $\mathcal{B}$ is a *finite* union of disjointed intervals (not reduced to singleton sets since B is piecewise continuous).

(H_2) $\exists\, t' \in [0,\underline{m}]$ such that $]\underline{B}, t'] \subset \mathcal{B}$ and $t \mapsto S_0(A-t)$ has two discontinuity points $t_1 < t_2 \in \mathcal{B} \cap [0, t'[$.

Theorem 1.

1. *$\mathbf{Q}^\star$ is identifiable if either $\underline{B} = 0$ and (H_1) holds or if $\underline{B} > 0$ and (H_1) and (H_2) hold,*
2. *$\mathbf{R}^\star$ is not identifiable.*

Theorem 1 shows that $\mathbf{Q}^\star$ is identifiable under realistic hypotheses on the input B and the initial condition (S_0, I_0). Hypothesis (H_1) includes seasonal birth functions, that correspond to real situations in many animal populations. Hypothesis (H_2) is a technical assumption that is not too restrictive on the initial conditions. We are convinced that it could be made more realistic, or even unnecessary in future work.

Moreover, in the definition of $\mathbf{Q}^\star$, a condition on the infection load growth rate appears, stating that it should be bigger than a threshold value $c^\star$ that depends on the initial condition I_0. The biological interpretation of this condition is clear: for such growth rates, some initially infected animals necessarily die of the disease (i.e. their load reaches value 1) during the observation period.

In order to obtain Theorem 1, we assumed that the initial conditions were fixed and known. However, whatever the time, getting to know the state of the system is not easy in practical situations, unless perhaps in an experimental setting. When restricting Θ to a suitable parametric family, it is possible to prove the identifiability of the epidemiological parameters on the whole parameter space with weaker assumptions on the initial conditions, as stated in the two following theorems.

We now assume that the initial conditions (S_0, I_0) are fixed, but they are not known. Then we have

Theorem 2. *Assume that (H_1) holds and let $\mathcal{G} \subset \mathcal{A}_0$ be such that for all $(\Theta, \bar\Theta) \in \mathcal{G}^2$, $\forall (c, \bar c) \in (\mathbb{R}^{+*})^2$, $\forall(\alpha, \bar\alpha) \in (\mathbb{R}^{+*})^2$,*

$$(\forall\theta \in [0,1],\ \bar c\theta^{\bar c}\bar\Theta(\theta^{\bar c}) = c\theta^c\Theta(\theta^c)) \Rightarrow (\bar c = c,\ \bar\Theta = \Theta) \tag{8}$$

and

$$\begin{gathered}
\forall\theta \in [0,1],\ \frac{\bar c}{\alpha}\theta^{\bar c}\bar\Theta(\theta^{\bar c}) - \frac{c}{\bar\alpha}\theta^c\Theta(\theta^c) = \mathcal{F}(\theta^c) - \bar{\mathcal{F}}(\theta^{\bar c})\\
\Downarrow\\
(\alpha = \bar\alpha,\ c = \bar c \text{ and } \Theta = \bar\Theta),
\end{gathered} \tag{9}$$

where $\mathcal{F}$ and $\bar{\mathcal{F}}$ denote the cumulative distribution function of Θ and $\bar{\Theta}$.

Then $\mathbf{Q}^{\star}_{\mathcal{G}} = (\mathbb{R}^{+*})^2 \times \mathcal{G}$ is identifiable.

Theorem 2 ensures that, given a suitable parametric family for the first infection load distribution, $\mathbf{Q}^{\star}_{\mathcal{G}}$ is identifiable under the realistic hypothesis (H_1). This theorem has a very strong practical interest, because when dealing with parameter identification on experimental data, Θ is indeed restricted to a parametric family of p.d.f., such as for instance the two-parameter family of Beta p.d.f. with support in $[0,1]$. For this family, it is easily checked that conditions (8) and (9) hold.

Note that in Theorem 2, the initial conditions are assumed to be fixed but unknown. Assuming now that they are not fixed, they have to be included in the unknown parameter vector. Hence the "extended parameter" to output map is now defined on $\mathbf{P_E} = \mathbf{P} \times C_p([0,A], \mathbb{R}^+) \times C_p([0,A] \times [0,1], \mathbb{R}^+)$.

Theorem 3. *Let $\mathcal{G} \subset \mathcal{A}_0$ be as in Theorem 2, and assume that $\underline{B} = 0$. Then for all $p = (c, \beta, \Theta, S_0, I_0)^T \in \mathbf{P_E}$, $\bar{p} = (\bar{c}, \bar{\beta}, \bar{\Theta}, \bar{S}_0, \bar{I}_0)^T \in \mathbf{P_E}$ such that $\mathbf{I}(0) = \bar{\mathbf{I}}(0)$,*

$$\mathcal{O}(p) = \mathcal{O}(\bar{p}) \;\Rightarrow\; (c = \bar{c},\ \beta = \bar{\beta},\ \Theta = \bar{\Theta}).$$

3 Input-Output relationships

A standard strategy to investigate identifiability problems is to seek differential IO relationships of the model. To this end, we use an alternative expression of the incidence (6). It can be deduced from the mild solution of (1-4) given in [23] by

$$S(t,a) = \begin{cases} S_0(a-t)e^{-(\mu t + \beta \int_0^t \mathbf{I}(s)\ ds)} & \text{for } a \geqslant t, \\ B(t-a)e^{-(\mu a + \beta \int_{t-a}^t \mathbf{I}(s)\ ds)} & \text{for } a \leqslant t, \end{cases} \tag{10}$$

$$I(t,a,\theta) = \begin{cases} S_0(a-t)e^{-\mu t} \int_0^t e^{c(s-t)} \Theta\left(\theta e^{c(s-t)}\right) \beta \mathbf{I}(s) e^{-\beta \int_0^s \mathbf{I}(u) du} ds & \\ \quad + I_0(a-t, \theta e^{-ct}) e^{-(\mu+c)t} & \text{for } a \geqslant t, \\ B(t-a)e^{-\mu a} \int_{t-a}^t e^{c(s-t)} \Theta\left(\theta e^{c(s-t)}\right) \beta \mathbf{I}(s) e^{-\beta \int_{t-a}^s \mathbf{I}(u) du} ds & \text{for } a \leqslant t. \end{cases} \tag{11}$$

Let us define the non-negative real-analytic function on $\mathbb{R}^{+*}$, continuous on $\mathbb{R}^+$

$$X(\tau) = c\, e^{-c\tau} \Theta(e^{-c\tau}), \tag{12}$$

Note that X is the p.d.f. corresponding to the incubation period ($\tau = \frac{-1}{c} \ln \theta$). Then, for $(t,a) \in [0,T] \times [0,A]$ and $t \leqslant a$, one has

$$\begin{aligned} \mathfrak{i}(t,a) = S_0(a-t)e^{-\mu t} \int_0^t X(t-s) \beta \mathbf{I}(s) e^{-\beta \int_0^s \mathbf{I}(u) du} ds \\ + c I_0(a-t, e^{-ct}) e^{-(\mu+c)t}, \end{aligned} \tag{13}$$

and, for $(t,a) \in [0,T] \times [0,A]$ and $t \geqslant a$,

$$\mathfrak{i}(t,a) = B(t-a)e^{-\mu a} \int_{t-a}^t X(t-s) \beta \mathbf{I}(s) e^{-\beta \int_{t-a}^s \mathbf{I}(u) du} ds. \tag{14}$$

We now define $\mathcal{D} = \{(t,a) \in [0,T] \times [0,A],\ a \leqslant t\}$ and introduce the function y defined on $\mathcal{D}$ by

$$y(t,a) = \int_{t-a}^t X(t-s) \beta \mathbf{I}(s) e^{-\beta \int_{t-a}^s \mathbf{I}(u) du}\ ds. \tag{15}$$

In the sequel we shall also denote

$$\mathcal{D}_{\mathcal{B}} = \{(t,a) \in \mathcal{D},\, t-a \in \mathcal{B}\}, \quad D = \partial_a + \partial_t \,.$$

Therefore, y is known on $\mathcal{D}_{\mathcal{B}}$ since $y(t,a) = \frac{\mathrm{i}(t,a)}{B(t-a)e^{-\mu a}}$ on $\mathcal{D}_{\mathcal{B}}$. Moreover, the following key result holds.

Proposition 1. *On $\mathcal{D}$, y and Dy are C^1, $\partial_a y$ is differentiable and*

$$D\partial_a y(X(a) - y) = \partial_a y(X'(a) - Dy). \tag{16}$$

On $\mathcal{D}_{\mathcal{B}}$, Eq. (16) defines an IO relation for the system.

Proof 1. *Consider $\tilde{y}$ defined on $\mathcal{D}$ by*

$$\tilde{y}(t,a) = c\int_{t-a}^{t} e^{2c(s-t)}\,\Theta'(e^{c(s-t)})\,\beta\,\mathbf{I}(s)\,e^{-\beta\int_{t-a}^{s}\mathbf{I}(u)du}\,ds.$$

From Eq. (11) the function $t \mapsto \mathbf{I}(t)$ is differentiable on $[0,T]$ and has a piecewise continuous derivative. Consequently, $t \mapsto e^{-\beta\int_0^t \mathbf{I}(u)du} \in C^1([0,T])$ and $y(t,a)$ has partial derivatives in a and t on $\mathcal{D}$, expressed as

$$\begin{aligned}\partial_a y &= X(a)\beta\mathbf{I}(t-a) - \beta\mathbf{I}(t-a)\int_{t-a}^{t} X(t-s)\beta\mathbf{I}(s)e^{-\beta\int_{t-a}^{s}\mathbf{I}(u)du}ds\\ &= X(a)\beta\mathbf{I}(t-a) - \beta\mathbf{I}(t-a)y(t,a) = \beta\mathbf{I}(t-a)\left(X(a)-y\right),\end{aligned} \tag{17}$$

and

$$\begin{aligned}\partial_t y =& -X(a)\beta\mathbf{I}(t-a) - c\int_{t-a}^{t} X(t-s)\beta\mathbf{I}(s)e^{-\beta\int_{t-a}^{s}\mathbf{I}(u)du}ds\\ &- c^2\int_{t-a}^{t} e^{2c(s-t)}\,\Theta'(e^{c(s-t)})\,\beta\,\mathbf{I}(s)\,e^{-\beta\int_{t-a}^{s}\mathbf{I}(u)du}\,ds\\ &+ \beta\mathbf{I}(t-a)\int_{t-a}^{t} X(t-s)\beta\mathbf{I}(s)e^{-\beta\int_{t-a}^{s}\mathbf{I}(u)du}ds\\ &= -X(a)\beta\mathbf{I}(t-a) - cy + \beta\mathbf{I}(t-a)y - c\tilde{y}.\end{aligned} \tag{18}$$

Moreover, standard results on integrals depending on parameters imply that the functions y and $\tilde{y}$ are continuous on $\mathcal{D}$. From Eq. (17,18) we deduce that $\partial_a y$ and $\partial_t y$ are continuous functions on $\mathcal{D}$ and consequently y is C^1 on this set. Similar arguments prove that $\tilde{y}$ is also C^1. Summing (17) and (18) leads to $Dy = -c\,y - c\,\tilde{y}$, which proves that Dy is C^1. Since y is C^1 and $t \mapsto \mathbf{I}(t)$ is differentiable, Eq. (17) implies that $\partial_a y$ is differentiable. Applying the operator D to (17), since $D\big(\mathbf{I}(t-a)\big) = 0$, leads to

$$D\partial_a y = \beta\,\mathbf{I}(t-a)\,(X'(a) - Dy). \tag{19}$$

Eq. (16) is obtained by combination on $\mathcal{D}$ of Eq. (17) and (19).

4 Proof of Theorem 1

Let (S_0, I_0) and B be given and consider $(p,\bar{p}) \in \mathbf{P}^2$ such that

$$\mathcal{O}(p) = \mathcal{O}(\bar{p}). \tag{20}$$

The theorem is proved by directly checking that $\mathcal{O}$ is (or is not) injective, that is by showing that under the the given hypothesis, (20) implies (or not) $p = \bar{p}$.

In the sequel, the population densities, the p.d.f. of first infection load and incubation period, the output vector associated to $\bar{p}$ shall be denoted as $\bar{S}$, $\bar{I}$, $\bar{\Theta}$, $\bar{X}$, $\bar{\imath}$ and $\bar{N}$; more generally, all the quantities wearing a bar will be related to $\bar{p}$. The same quantities without bar will be related to p. Note that (20) implies $\bar{y} = y$ on $\mathcal{D}_{\mathcal{B}}$.

As mentioned in the introduction, we start with an algebro-differential elimination step where $\bar{y} = y$ is combined with Eq. (16) in order to obtain some relationships between p and $\bar{p}$.

4.1 Algebro-differential elimination

Algebro-differential elimination between $\bar{y} = y$ and Eq. (16) in Proposition 1 leads to the following fundamental result.

Proposition 2. *If (20) holds, then*

$$\begin{aligned} &\textit{either} \quad X = \bar{X} \ \textit{on } \mathbb{R}^+, \\ &\textit{or} \qquad \exists\,(\alpha, \bar{\alpha}) \in (\mathbb{R}^{+*})^2 \ / \qquad \alpha \neq \bar{\alpha} \ \textit{and } \frac{1}{\alpha}\bar{X}' - \frac{1}{\bar{\alpha}}X' = X - \bar{X} \ \textit{on } \mathbb{R}^{+*}. \end{aligned}$$

In this last case, $t \mapsto \beta\mathbf{I}(t)$ and $t \mapsto \bar{\beta}\bar{\mathbf{I}}(t)$ are non zero constant functions on $\mathcal{B}$, whose values are α and $\bar{\alpha}$ respectively.

Let us define $M_y(t, a) = (Dy,\, y)^T$, and also $M_{\partial_a y}$, $Y(a) = (X'(a),\, X(a))^T$ and $\bar{Y}(a) = \left(\bar{X}'(a),\, \bar{X}(a)\right)^T$ and finally for $x > 0$,

$$R(x) = \begin{vmatrix} X'(x) & \bar{X}'(x) & \Delta(x) \\ X^{(2)}(x) & \bar{X}^{(2)}(x) & \Delta'(x) \\ X^{(3)}(x) & \bar{X}^{(3)}(x) & \Delta^{(2)}(x) \end{vmatrix}, \tag{21}$$

where we set $\Delta = X - \bar{X}$ on $\mathbb{R}^+$.

Note that from (20), $M_y(t, a) = M_{\bar{y}}(t, a)$ and $M_{\partial_a y} = M_{\partial_a \bar{y}}$ on $\mathcal{D}_{\mathcal{B}}$. The proof of proposition 2 starts with three technical lemmas that make an extensive use of the following remark.

Remark 1. *Since Θ and $\bar{\Theta}$ are analytic on $]0, 1[$, X, $\bar{X}$, Δ and all their derivatives are real-analytic functions on $\mathbb{R}^{+*}$. Consequently, either they have isolated zeros in $\mathbb{R}^{+*}$ or they are identically equal to zero.*

Lemma 1. *If (20) holds one gets for all $(t, a) \in \mathcal{D}_{\mathcal{B}}$*

$$D\partial_a y(X(a) - \bar{X}(a)) - \partial_a y(X'(a) - \bar{X}'(a)) = 0 \tag{22}$$

$$[X'\bar{X} - X\bar{X}'] - y\,[X' - \bar{X}'] + Dy\,[X - \bar{X}] = 0. \tag{23}$$

Proof 2. *Let $(t, a) \in \mathcal{D}_{\mathcal{B}}$. Then either $M_{\partial_a y}(t, a) \neq 0$ or $M_{\partial_a y}(t, a) = 0$.*

In the first case, as Eq. (16) implies that $M_{\partial_a y}(t, a)$ and $(Y(a) - M_y(t, a))$ are colinear, and so are $M_{\partial_a \bar{y}}(t, a)$ and $(\bar{Y}(a) - M_{\bar{y}}(t, a))$. It follows that $(Y(a) - \bar{Y}(a))$ and $M_{\partial_a y}(t, a)$ are colinear, which yields (22). Moreover, $Y(a) - M_y(t, a)$ and $\bar{Y}(a) - M_{\bar{y}}(t, a)$ are also colinear and consequently (23) holds.

In the second case, Eq. (17) yields $\beta\,\mathbf{I}(t - a)(X(a) - y(t, a)) = 0$. It can be easily checked that when starting from a positive (> 0) infected population at time zero, $\mathbf{I}$ remains positive on $[0, T]$, so $X(a) = y(t, a) = \bar{X}(a)$. Using (19) we similarly obtain $X'(a) = \bar{X}'(a)$, so (22) and (23) also hold.

Lemma 2. *If* (20) *holds one gets for all* $(t,a) \in \mathcal{D}_{\mathcal{B}}$

$$\begin{aligned} &[X'\bar{X} - X\bar{X}'][X' - \bar{X}'] - [X^{(2)}\bar{X} - X\bar{X}^{(2)}][X - \bar{X}] \\ &-y\left([X' - \bar{X}']^2 - [X^{(2)} - \bar{X}^{(2)}][X - \bar{X}]\right) = 0. \end{aligned} \tag{24}$$

Proof 3. *Consider* $(t,a) \in \mathcal{D}_{\mathcal{B}}$*. Since* B *is piecewise continuous, there exists an interval* $\mathcal{V}(a)$ *such that* $\{a\} \subsetneq \mathcal{V}(a) \subset [0,A]$*, and* $\{t\} \times \mathcal{V}(a) \subset \mathcal{D}_{\mathcal{B}}$*. Therefore we differentiate Eq.* (23) *w.r.t.* a*, which yields, for all* $(t,a) \in \mathcal{D}_{\mathcal{B}}$*,*

$$[X^{(2)}\bar{X} - X\bar{X}^{(2)}] - \partial_a y[X' - \bar{X}'] - y[X^{(2)} - \bar{X}^{(2)}] + Dy\,[X' - \bar{X}'] + \partial_a Dy\,[X - \bar{X}] = 0.$$

Using (22) *to eliminate* $\partial_a y$ *we obtain*

$$[X'^{(2)}\bar{X} - X\bar{X}^{(2)}] - y[X^{(2)} - \bar{X}^{(2)}] + Dy\,[X' - \bar{X}'] = 0 \quad \forall (t,a) \in \mathcal{D}_{\mathcal{B}}. \tag{25}$$

Combining (23) *and* (25) *one gets* (24) *on* $\mathcal{D}_{\mathcal{B}}$*.*

Lemma 3. *If* (20) *holds then* $R(x) = 0$ *for all* $x \in \mathbb{R}^{+*}$ *.*

Proof 4. *We perform algebro-differential elimination of* y *in* (23) *and* (24) *using operator* D *to obtain the following equality*

$$\begin{aligned} (X - \bar{X})^3 \Big(&-\bar{X}\bar{X}^{(2)}X^{(3)} + \bar{X}X^{(2)}\bar{X}^{(3)} - X^{(2)}\bar{X}^{(2)}X' + (\bar{X}')^2X^{(3)} \\ &+ X\bar{X}^{(2)}X^{(3)} - X'\bar{X}'X^{(3)} + \bar{X}^{(3)}(X')^2 + X'(\bar{X}^{(2)})^2 \\ &- X^{(2)}X\bar{X}^{(3)} - \bar{X}^{(2)}X^{(2)}\bar{X}' - \bar{X}^{(3)}X'\bar{X}' + (X^{(2)})^2\bar{X}'\Big) = 0, \end{aligned}$$

which rewrites after some calculation

$$(\Delta(x))^3\, R(x) = 0. \tag{26}$$

Using similar arguments as in the proof of Lemma 24, Eq. (26) *is valid on an open interval of* $[0,A]$ *and can be extended to* $\mathbb{R}^{+*}$ *consequently to Remark 1. The proof is ended by contradiction: assume there exists* $x_0 > 0$ *such that* $R(x_0) \neq 0$*. By continuity, this is still valid on a neighbourhood* $\mathcal{V}(x_0) \subset \mathbb{R}^{+*}$ *and equality* (26) *implies that* $\Delta(x) = 0$ *for all* $x \in \mathcal{V}(x_0)$ *and finally, since the third column of the determinant is null,* $R(x) = 0$ *on* $\mathcal{V}(x_0)$ *which is impossible.*

We now proceed with the proof of Proposition 2. Lemma 3 and (20) imply that, for all $x > 0$, there exists $\lambda(x), \mu(x), \nu(x) \in \mathbb{R}$ such that

$$\begin{cases} \lambda X' + \mu\bar{X}' + \nu\Delta = 0, \\ \lambda X^{(2)} + \mu\bar{X}^{(2)} + \nu\Delta' = 0, \\ \lambda X^{(3)} + \mu\bar{X}^{(3)} + \nu\Delta^{(2)} = 0, \end{cases} \tag{27}$$

where λ, μ, ν are minors of determinant (21). We can choose ν associated to $\Delta^{(2)}$, given by $\nu = X'\bar{X}^{(2)} - \bar{X}'X^{(2)}$. Then two cases may arise.

Case 1. Assume that $\nu(x) = 0$ *for all* $x > 0$*.* The function $\bar{X}'$ is a non zero function on $\mathbb{R}^{+*}$, otherwise, by continuity, $\bar{X}$ would be constant and equal to zero on $\mathbb{R}^+$. Therefore, we can find $x_1 > 0$ such that $\bar{X}'(x_1) \neq 0$. By continuity, this is still true in a neighbourhood $\mathcal{V}(x_1)$ of x_1. Then, for all $x \in \mathcal{V}(x_1)$,

$$\left(\bar{X}'(x)\right)^2 \times \frac{d}{dx}\left(\frac{X'}{\bar{X}'}\right) = 0,$$

which implies that there exists a constant c_0 such that $X' = c_0\,\bar X'$ on $\mathcal{V}(x_1)$. From Remark 1, we get $X' = c_0\,\bar X'$ on $\mathbb{R}^{+*}$ and $X = c_0\,\bar X$ on $\mathbb{R}^{+*}$ since $X(0) = \bar X(0) = 0$. Taking into account that $\int_0^{+\infty} X(x)dx = \int_0^{+\infty} \bar X(x)dx = 1$, we have $c_0 = 1$ and finally $X = \bar X$ on $\mathbb{R}^{+*}$.

Case 2. Assume that there exists $x_2 > 0$ and a neighbourhood $\mathcal{V}(x_2) \subset \mathbb{R}^{+*}$ such that $\nu(x) \neq 0$ for all $x \in \mathcal{V}(x_2)$. Then, from system (27), we deduce that the following equations are satisfied on $\mathcal{V}(x_2)$,

$$\tilde\lambda X' + \tilde\mu \bar X' = \Delta, \tag{28}$$

$$\tilde\lambda X^{(2)} + \tilde\mu \bar X^{(2)} = \Delta', \tag{29}$$

$$\tilde\lambda X^{(3)} + \tilde\mu \bar X^{(3)} = \Delta^{(2)}, \tag{30}$$

where $\tilde\lambda = -\frac{\lambda}{\nu}$, $\tilde\mu = -\frac{\mu}{\nu}$. Differentiating (28) and subtracting (29) yields, for $x \in \mathcal{V}(x_2)$,

$$\tilde\lambda' X' + \tilde\mu' \bar X' = 0. \tag{31}$$

In the same way, differentiating (28) twice and subtracting (30) yields

$$\tilde\lambda^{(2)} X' + \tilde\mu^{(2)} \bar X' + 2(\tilde\lambda' X^{(2)} + \tilde\mu' \bar X^{(2)}) = 0. \tag{32}$$

Finally, differentiating (31) and combining it (32), we get

$$\tilde\lambda^{(2)} X' + \tilde\mu^{(2)} \bar X' = 0 \text{ on } \mathcal{V}(x_2). \tag{33}$$

From (31) and (33), we have $W = 0$ on $\mathcal{V}(x_2)$ where

$$W = \begin{vmatrix} \tilde\lambda' & \tilde\mu' \\ \tilde\lambda^{(2)} & \tilde\mu^{(2)} \end{vmatrix}.$$

Otherwise, there would exist an open subset $\mathcal{V} \subset \mathcal{V}(x_2)$ such that $W(x) \neq 0$ for $x \in \mathcal{V}$. The unique solution of system (31,33) would be $\big(X', \bar X'\big) = (0,0)$ on $\mathcal{V}$. This would imply $\nu(x) = 0$ on $\mathcal{V}$, which is impossible. We now distinguish the two following subcases.

Case 2.1. If there exists an open subset $\mathcal{V} \subset \mathcal{V}(x_2)$ on which $\tilde\lambda'(x) \neq 0$, then $W = 0$ on $\mathcal{V}(x_2)$ implies that $\frac{d}{dx}(\tilde\mu'/\tilde\lambda') = 0$ in $\mathcal{V}$. Consequently, there exists a constant c_0 such that $X' = c_0\,\bar X'$ on $\mathcal{V}$ and we can conclude as in *Case 1* that $X = \bar X$ on $\mathbb{R}^+$.

Case 2.2. If $\tilde\lambda' = 0$ on $\mathcal{V}(x_2)$, then $\tilde\lambda$ is a constant function on $\mathcal{V}(x_2)$ whose value is denoted $\tilde\lambda_0$. Since $\bar X'$ has isolated zeros, Remark 1 and (31) imply that $\tilde\mu$ is also a constant function on $\mathcal{V}(x_2)$ whose value is denoted $\tilde\mu_0$. Consequently, on $\mathcal{V}(x_2)$, equalities (28) and (29) become respectively

$$\begin{aligned} \tilde\lambda_0 X' + \tilde\mu_0 \bar X' &= \Delta, \\ \tilde\lambda_0 X^{(2)} + \tilde\mu_0 \bar X^{(2)} &= \Delta'. \end{aligned} \tag{34}$$

By Remark 1, these equalities can be extended to $\mathbb{R}^{+*}$ and can be used to simplify (24). On $\mathcal{D}_{\mathcal{B}}$ one therefore has

$$[X'\bar X - X\bar X']\Delta' - [X^{(2)}\bar X - X\bar X^{(2)}]\Delta = (\tilde\lambda_0 X + \tilde\mu_0 \bar X)(\bar X^{(2)} X' - \bar X' X^{(2)}),$$
$$(\Delta')^2 - \Delta\,\Delta^{(2)} = (\tilde\lambda_0 + \tilde\mu_0)\,(\bar X^{(2)} X' - \bar X' X^{(2)}),$$

and

$$\Big(-y(\tilde\lambda_0 + \tilde\mu_0) + \tilde\lambda_0 X + \tilde\mu_0 \bar X\Big)\Big(\bar X^{(2)} X' - \bar X' X^{(2)}\Big) = 0.$$

By Remark 1, since $\nu \neq 0$, we conclude that

$$-y(\tilde\lambda_0 + \tilde\mu_0) + \tilde\lambda_0 X + \tilde\mu_0 \bar X = 0 \quad \text{on } \mathcal{D}_{\mathcal{B}}. \tag{35}$$

Then, either $\tilde{\lambda}_0 + \tilde{\mu}_0 = 0$, and integrating (34) yields $\Delta = X - \bar{X} = 0$. Or $\tilde{\lambda}_0 + \tilde{\mu}_0 \neq 0$ and consequently for all $(t, a) \in \mathcal{D}_{\mathcal{B}}$

$$y(t, a) = \frac{\tilde{\lambda}_0 X(a) + \tilde{\mu}_0 \bar{X}(a)}{\tilde{\lambda}_0 + \tilde{\mu}_0}.$$

This expression used in (17) yields, for all $(t, a) \in \mathcal{D}_{\mathcal{B}}$,

$$\tilde{\lambda}_0 X'(a) + \tilde{\mu}_0 \bar{X}'(a) = \tilde{\mu}_0 \, \beta \, \mathbf{I}(t-a) \, (X(a) - \bar{X}(a)). \tag{36}$$

Denoting $\mathcal{J} = \{a \in [0, A], \, \Delta(a) \neq 0\}$, we easily check that 0 is in the closure of $\mathcal{J}$. Moreover, equation (36) implies that $(t, a) \mapsto \beta \, \mathbf{I}(t-a)$ is a constant on $\{(t, a) \in \mathcal{D}_{\mathcal{B}}, \, a \in \mathcal{J}\}$ and consequently, for all $a \in \mathcal{J} \cap [0, T]$, $t \mapsto \beta \, \mathbf{I}(t)$ is constant on $\mathcal{B} \cap [0, T-a]$. Since 0 is in the closure of $\mathcal{J}$, we conclude that $t \mapsto \beta \, \mathbf{I}(t)$ is constant on $\mathcal{B}$. We denote α this constant, which is positive, as already mentioned. By the same arguments we also prove that $t \mapsto \bar{\beta} \, \bar{\mathbf{I}}(t)$ is a positive constant on $\mathcal{B}$ that we denote $\bar{\alpha}$. Then (28) and (36) yield $\alpha = \frac{1}{\tilde{\mu}_0}$. Similarly, $\bar{\alpha}$ is positive and such that $\bar{\alpha} = -\frac{1}{\tilde{\lambda}_0}$. Substituting these values in (34) yields the desired result.

4.2 Proof of theorem 1, part 1

We assume in this section that (20) is satisfied.

4.2.1 Case where (H_1) holds and $\underline{B} = 0$

Step 1: proof of $X = \bar{X}$. By contradiction, assume that there exists $x_0 > 0$ such that $X(x_0) - \bar{X}(x_0) \neq 0$. Then, from Proposition 2, $t \mapsto \beta \, \mathbf{I}(t)$ and $t \mapsto \bar{\beta} \, \bar{\mathbf{I}}(t)$ are constant positive functions on $\mathcal{B}$ with values

$$\alpha \neq \bar{\alpha}. \tag{37}$$

Therefore, Eq. (5) can be rewritten as

$$\int_0^A S(t, a) \, da + \frac{\alpha}{\beta} = \int_0^A \bar{S}(t, a) \, da + \frac{\bar{\alpha}}{\bar{\beta}}, \quad \forall t \in \mathcal{B}. \tag{38}$$

Since $\underline{B} = 0$ and $S_0 = \bar{S}_0$, letting t tend to 0 in (38) yields $\frac{\alpha}{\beta} = \frac{\bar{\alpha}}{\bar{\beta}}$ and

$$\int_0^A S(t, a) \, da = \int_0^A \bar{S}(t, a) \, da \quad \forall \, t \in \mathcal{B}. \tag{39}$$

From hypothesis (H_1), let $t' > 0$ be such that $]0, t'[\subset \mathcal{B}$.
Then, on $]0, t'[\times [0, A]$, S satisfies $\partial_t S + \partial_a S = -\mu \, S - \alpha \, S$. Integrating w.r.t. a on $[0, A]$ leads to

$$\frac{\partial}{\partial t} \int_0^A S(t, a) \, da + S(t, A) - B(t) = -(\mu + \alpha) \int_0^A S(t, a) \, da, \quad \forall t \in]0, t'[.$$

The same holds for $\bar{S}$. Using (39) and its derivative on $]0, t'[$ one gets

$$S(t, A) - \bar{S}(t, A) = (\bar{\alpha} - \alpha) \int_0^A S(t, a) \, da, \quad \forall t \in \mathcal{B}.$$

Letting t tend to 0, one has $\alpha = \bar{\alpha}$, which contradicts (37) and ends the proof.

Step 2: proof of $\beta = \bar{\beta}$ and $\mathbf{I}(t) = \bar{\mathbf{I}}(t)$ for all $t \in [0, T]$. Substituting $X = \bar{X}$ in Eq. (17), one has for all $(\xi, a) \in \mathcal{B} \times [0, A]$

$$\partial_a y(\xi + a, a) = \beta \mathbf{I}(\xi) \big(X(a) - y(\xi + a, a)\big),$$
$$\partial_a y(\xi + a, a) = \bar{\beta} \bar{\mathbf{I}}(\xi) \big(X(a) - y(\xi + a, a)\big).$$

Term to term subtraction yields

$$\big(\beta \mathbf{I}(\xi) - \bar{\beta} \bar{\mathbf{I}}(\xi)\big) \big(X(a) - y(\xi + a, a)\big) = 0. \tag{40}$$

By contradiction, assume that there exists $\xi_0 \in \mathcal{B}$ such that $\beta \mathbf{I}(\xi_0) \neq \bar{\beta} \bar{\mathbf{I}}(\xi_0)$. Since B is piecewise continuous and $\xi \mapsto (\beta \mathbf{I} - \bar{\beta} \bar{\mathbf{I}})(\xi)$ is continuous, there exists an interval $\mathcal{V}(\xi_0)$ included in $\mathcal{B}$, containing ξ_0, not reduced to a singleton set, such that $(\beta \mathbf{I} - \bar{\beta} \bar{\mathbf{I}})(\xi) \neq 0$ for all $\xi \in \mathcal{V}(\xi_0)$. Therefore, (40) reduces to

$$X(a) = y(\xi + a, a), \quad \forall (\xi, a) \in \mathcal{V}(\xi_0) \times [0, A]. \tag{41}$$

This implies that $\partial_t y(\xi + a, a) = 0$ for $(\xi, a) \in \mathcal{V}(\xi_0) \times [0, A]$. Consequently,Eq.(17) becomes $\partial_a y(\xi + a, a) = 0$ on $\mathcal{V}(\xi_0)$ and differentiating (41) w.r.t a yields

$$X'(a) = \partial_t y(\xi + a, a) + \partial_a y(\xi + a, a) = 0,$$

for all $a \in [0, A]$. It follows that $X \equiv 0$ on $[0, A]$. Then Remark 1 implies that X is null on $\mathbb{R}^+$, which contradicts its definition as a p.d.f., and consequently yields

$$\beta \, \mathbf{I}(t) = \bar{\beta} \, \bar{\mathbf{I}}(t), \quad \forall t \in \mathcal{B}. \tag{42}$$

As $\underline{B} = 0$, then 0 is in the closure of $\mathcal{B}$ and we deduce successively from Eq. (42) that $\beta = \bar{\beta}$ and then $\mathbf{I}(t) = \bar{\mathbf{I}}(t)$ for all $t \in \mathcal{B}$.

We now prove that $\mathbf{I}(t) = \bar{\mathbf{I}}(t)$ for all $t \in [0, T]$. Consider $E = \{t \in [0, T] / \forall s \in [0, t],\ \mathbf{I}(s) = \bar{\mathbf{I}}(s)\}$. From hypothesis (H_1), there exists $t' > 0$ be such that $]0, t'[\subset \mathcal{B}$, hence E is nonempty. Since $\mathbf{I}$ and $\bar{\mathbf{I}}$ are continuous on $[0, T]$, E is a closed subset of $[0, T]$. Let $s \in E$. Using hypothesis (H_1), we can choose $\varepsilon > 0$ small enough so that either $B > 0$ on $]s, s + \varepsilon[\cap [0, T]$ or B is identically equal to 0 on $]s, s + \varepsilon[\cap [0, T]$. We show that $\mathbf{I} = \bar{\mathbf{I}}$ on $[s, s + \varepsilon[\cap [0, T]$. In the first case $(B > 0)$, since $\mathbf{I} = \bar{\mathbf{I}}$ on $\mathcal{B}$, the desired result is obviously true. In the second case $(B = 0)$, from (20) and (5), we have

$$\mathbf{I}(t) - \bar{\mathbf{I}}(t) = \int_0^A \bar{S}(t, a) \; da - \int_0^A S(t, a) \; da, \; \forall t \in [0, T]. \tag{43}$$

Using (10) and performing the change of variables $b = t - a$, it follows that for $t \in]s, s + \varepsilon[\cap [0, T]$

$$\begin{aligned}(\mathbf{I} - \bar{\mathbf{I}})(t) = \int_0^t & \left(B(b) \, e^{-\mu(t-b)} \, f\left(\int_b^t \beta \bar{\mathbf{I}}(\xi) d\xi, \int_b^t \beta \mathbf{I}(\xi) d\xi \right) \right. \\ & \left. \times \int_b^t \beta \, (\mathbf{I} - \bar{\mathbf{I}})(\xi) d\xi \right) db + \left(\int_0^{A - \min(t, A)} S_0(a) da \right) \\ & \times f \left(\int_0^t \beta \bar{\mathbf{I}}(\xi) d\xi, \int_0^t \beta \mathbf{I}(\xi) d\xi \right) \int_0^t \beta \, (\mathbf{I} - \bar{\mathbf{I}})(\xi) d\xi,\end{aligned}$$

where the continuous function $f : \mathbb{R}^2 \rightarrow]0, 1]$ is defined by

$$f : (x, y) \mapsto \begin{cases} -\frac{e^{-x} - e^{-y}}{x - y} \text{ if } x \neq y, \\ e^{-x} \text{ if } x = y, \end{cases} \tag{44}$$

Since $\mathbf{I} = \bar{\mathbf{I}}$ on $[0, s]$, we get for $t \in]s, s + \varepsilon[\cap [0, T]$,

$$
\begin{aligned}
(\mathbf{I} - \bar{\mathbf{I}})(t) = \int_0^s & \left(B(b)\, e^{-\mu(t-b)}\, f\left(\int_b^t \beta\bar{\mathbf{I}}(\xi)d\xi, \int_b^t \beta\mathbf{I}(\xi)d\xi \right) \right. \\
& \times \int_s^t \beta\, (\mathbf{I} - \bar{\mathbf{I}})(\xi)d\xi \left. \vphantom{\int} \right) db + \left(\int_0^{A-\min(t,A)} S_0(a)da \right) \\
& f\left(\int_0^t \beta\bar{\mathbf{I}}(\xi)d\xi, \int_0^t \beta\mathbf{I}(\xi)d\xi \right) \int_s^t \beta\, (\mathbf{I} - \bar{\mathbf{I}})(\xi)d\xi,
\end{aligned}
$$

and finally for $t \in]s, s + \varepsilon[\cap [0, T]$,

$$
\mathbf{I}(t) - \bar{\mathbf{I}}(t) = H_0(t) \int_s^t \left(\mathbf{I}(\xi) - \bar{\mathbf{I}}(\xi) \right) \, d\xi, \tag{45}
$$

where H_α is defined for $0 \leq \alpha \leq \underline{B}$ by

$$
\begin{aligned}
H_\alpha : t \mapsto \beta & \left(\int_\alpha^s B(b)\, e^{-\mu(t-b)}\, f\left(\int_b^t \beta\bar{\mathbf{I}}(\xi)d\xi, \int_b^t \beta\mathbf{I}(\xi)d\xi \right) \, db \right. \\
& + \left. \left(\int_0^{A-\min(t,A)} S_0(a)da \right) f\left(\int_0^t \beta\bar{\mathbf{I}}(\xi)d\xi, \int_0^t \beta\mathbf{I}(\xi)d\xi \right) \right).
\end{aligned}
$$

Since $(\mathbf{I} - \bar{\mathbf{I}})(s) = 0$, by a standard Gronwall argument, $\mathbf{I} = \bar{\mathbf{I}}$ on $[s, s + \varepsilon[\cap [0, T]$. Therefore E is also an open subset of $[0, T]$ and $E = [0, T]$.

Step 3: $c = \bar{c}$ and $\Theta = \bar{\Theta}$. Eq. (13) and (20) imply that for $(t, a) \in [0, T] \times [0, A]$, $a \geqslant t$

$$
cI_0(a - t, e^{-ct})\, e^{-(\mu+c)t} = \bar{c}I_0(a - t, e^{-\bar{c}t})\, e^{-(\mu+\bar{c})t}.
$$

Performing the coordinate change $(t, a) \to (t, u = a - t)$ and dividing each member by $e^{-\mu t}$, this equality rewrites

$$
cI_0(u, e^{-ct})\, e^{-ct} = \bar{c}I_0(u, e^{-\bar{c}t})\, e^{-\bar{c}t}, \text{ for } (t, u) \in [0, T] \times [0, A].
$$

Note that for $u > A - t$, both members are zero in the above equation. Using the change of variable $v = e^{-ct}$, one gets $\int_{e^{-\bar{c}t}}^{e^{-ct}} I_0(u, v)\, dv = 0$. Denoting $\theta = e^{-\bar{c}t}$, one has

$$
\int_\theta^{\theta^{\bar{c}/c}} I_0(u, v)\, dv = 0, \ \forall\, \theta \in]e^{-\bar{c}T}, 1[, \ \forall\, u \in [0, A]. \tag{46}
$$

Moreover, from the definition of $c^\star$ and the piecewise continuity of I_0, we deduce the existence of a sequence $\{\theta_n\}_{n\in\mathbb{N}}$ and a sequence of open intervals $\{V_n\}_{n\in\mathbb{N}}$ verifying:

$$
\forall\, n \in \mathbb{N}, \theta_n \in V_n \subset]0, e^{-c^\star \underline{m}}[, \tag{47}
$$

$$
\theta_n \xrightarrow[n\to+\infty]{} e^{-c^\star \underline{m}}, \tag{48}
$$

$$
\forall\, n \in \mathbb{N}, \ \exists\, a_n \in]0, A[, \ \forall\, \theta \in V_n, \ I_0(a_n, \theta) > 0. \tag{49}
$$

Since $\bar{c} > c^\star$ and $T \geq \underline{m}$, $]0, e^{-c^\star \underline{m}}[\cap]e^{-\bar{c}T}, 1[$ is nonempty and from (47, 48), one can choose n_0 big enough such that $V_{n_0} \cap]e^{-\bar{c}T}, 1[$ is nonempty. From (46, 49), we deduce that

$$
\int_\theta^{\theta^{\bar{c}/c}} I_0(a_{n_0}, v)\, dv = 0, \ I_0(a_{n_0}, \theta) > 0, \ \forall\, \theta \in V_{n_0} \cap]e^{-\bar{c}T}, 1[,
$$

which implies $c = \bar{c}$. It easily follows, since $X = \bar{X}$ on $\mathbb{R}^+$, that $\Theta = \bar{\Theta}$ on $[0, 1]$, which proves that $\mathbf{Q}^\star$ is identifiable.

4.2.2 Case where (H_1) and (H_2) hold and $\underline{B} > 0$

Step 1: proof of $X = \bar{X}$. The proof (by contradiction) is the same as in previous subsection until Eq. (38). Then Eq. (2) can be integrated w.r.t. a and θ so as to obtain the following integro-differential equation for $\mathbf{I}$ on $[0, T]$

$$\frac{d}{dt}\mathbf{I}(t) + \int_0^1 I(t, A, \theta d\theta + \int_0^A \mathfrak{i}(t, a)da = -\mu\mathbf{I}(t) + \beta\mathbf{I}(t)\int_0^A S(t, a)da.$$

Substituting the constant value $\beta\mathbf{I} = \alpha$, one gets

$$\int_0^1 I(t, A, \theta)\ d\theta + \int_0^A \mathfrak{i}(t, a)\ da = -\frac{\mu\,\alpha}{\beta} + \alpha\int_0^A S(t, a)\ da, \quad \forall t \in \mathcal{B}.$$

The same holds for $\bar{\mathbf{I}}$. Subtracting these two equations and using (5,20) yields

$$(\bar{S} - S)(t, A) = \alpha\left(\int_0^A S(t, a)\ da - \frac{\mu}{\beta}\right) - \bar{\alpha}\left(\int_0^A \bar{S}(t, a)\ da - \frac{\mu}{\bar{\beta}}\right), \tag{50}$$

for $t \in \mathcal{B}$. Integrating Eq. (10) in age, we obtain

$$\begin{aligned}\int_0^A S(t, a)da = &\int_0^{\min(t,A)} B(t-a)e^{-\mu a - \beta\int_{t-a}^t \mathbf{I}(u)du}da \\ &+ \int_{\min(t,A)}^A S_0(a - \min(t, A))e^{-\mu t - \beta\int_0^t \mathbf{I}(u)du}da.\end{aligned}$$

From hypothesis (H_1), let $t < A$ be such that $]\underline{B}, t] \subset \mathcal{B}$. Then $S(t, A) = S_0(A-t)G(t)$ and

$$\begin{aligned}&\int_0^t B(t-a)e^{-\mu a - \beta\int_{t-a}^t \mathbf{I}(u)du}da = \int_{\underline{B}}^t B(u)e^{-(\mu+\alpha)(t-u)}du, \\ &\int_t^A S_0(a-t)\,e^{-\mu t - \beta\int_0^t \mathbf{I}(u)du}\ da = \left(\int_0^{A-t} S_0(u)\ du\right)G(t),\end{aligned}$$

where $G(t) = e^{-\left(\mu t + \beta\int_0^t \mathbf{I}(u)du\right)}$. $\bar{G}(t)$ is similarly defined for $\bar{p}$. Eq. (50) rewrites, for all t such that $]\underline{B}, t] \subset \mathcal{B}$,

$$\begin{aligned}S_0(A-t)(G - \bar{G})(t) = &\,\alpha\int_{\underline{B}}^t B(u)e^{-(\mu+\alpha)(t-u)}du - \bar{\alpha}\int_{\underline{B}}^t B(u)e^{-(\mu+\bar{\alpha})(t-u)}du \\ &+ (\alpha G(t) - \bar{\alpha}\bar{G}(t))\int_0^{A-\min(t,A)} S_0(u)du + \mu\left(\frac{\alpha}{\beta} - \frac{\bar{\alpha}}{\bar{\beta}}\right).\end{aligned} \tag{51}$$

Thanks to hypothesis (H_2), (51) is valid on a neighbourhood of $[t_1, t_2]$. Moreover, the right member of (51) is a continuous function of t and so is $t \mapsto (G - \bar{G})(t)$. Hence the discontinuity of $t \mapsto S_0(A-t)$ at t_1 and t_2 implies that

$$G(t_1) = \bar{G}(t_1), \quad G(t_2) = \bar{G}(t_2).$$

Since $[t_1, t_2] \subset \mathcal{B}$, $G(t) = G(t_1)e^{-(\mu+\alpha)(t-t_1)}$ and $\bar{G}(t) = \bar{G}(t_1)e^{-(\mu+\alpha)(t-t_1)}$ for all $t \in [t_1, t_2]$, so $e^{-(\mu+\alpha)(t_2-t_1)} = e^{-(\mu+\bar{\alpha})(t_2-t_1)}$ and consequently $\alpha = \bar{\alpha}$. This contradicts Eq. (37).

Step 2: proof of $\beta = \bar{\beta}$ and $\mathbf{I}(t) = \bar{\mathbf{I}}(t)$ for all $t \in [0,T]$. As in previous subsection we obtain Eq. (42). Eq. (43) holds on $[0, \underline{B}]$; therefore, since for $a \in [0,t]$, $B(t-a) = 0$, multiplying Eq. (43) by β and using Eq. (10), one gets

$$\beta(\mathbf{I} - \bar{\mathbf{I}})(t) = \beta e^{-\mu t} \left(\int_0^{A-\min(t,A)} S_0(a) da \right) \left(e^{-\bar{\beta} \int_0^t \bar{\mathbf{I}}(\xi) d\xi} - e^{-\beta \int_0^t \mathbf{I}(\xi) d\xi} \right). \tag{52}$$

Consider the continuous functions $g : [0,T] \rightarrow]0,1]$ defined by

$$g(t) = \exp\left(- \int_0^t \beta e^{-\mu s} \left(\int_0^{A-\min(s,A)} S_0(a) da \right) f\left(\int_0^s \bar{\beta} \bar{\mathbf{I}}(\xi) d\xi, \int_0^s \beta \mathbf{I}(\xi) d\xi \right) ds \right),$$

where f is defined in (44). Eq. (52) can be rewritten as

$$\beta \left(\mathbf{I}(t) - \bar{\mathbf{I}}(t) \right) = \frac{g'(t)}{g(t)} \left(\int_0^t \bar{\beta} \bar{\mathbf{I}}(\xi) d\xi - \int_0^t \beta \mathbf{I}(\xi) d\xi \right). \tag{53}$$

By contradiction, let us assume that $\beta > \bar{\beta}$. Then we have

$$\beta \big(\mathbf{I} - \bar{\mathbf{I}})(t) \big) \leqslant (\beta \mathbf{I} - \bar{\beta} \bar{\mathbf{I}})(t),$$

and, consequently to (53), we get

$$-\frac{g'(t)}{g(t)} \left(\int_0^t \beta \mathbf{I}(\xi) d\xi - \int_0^t \bar{\beta} \bar{\mathbf{I}}(\xi) d\xi \right) \leqslant \beta \mathbf{I}(t) - \bar{\beta} \bar{\mathbf{I}}(t), \tag{54}$$

which implies that $t \mapsto g(t) \int_0^t \left(\beta \mathbf{I} - \bar{\beta} \bar{\mathbf{I}} \right)(\xi) d\xi$ is increasing on $[0, \underline{B}]$. At $t = 0$, one has $(\beta \mathbf{I} - \bar{\beta} \bar{\mathbf{I}})(0) = (\beta - \bar{\beta}) \mathbf{I}(0) > 0$ and, by a continuity argument, there exists $0 < \varepsilon_0 < \underline{B}$ such that $\beta \mathbf{I} - \bar{\beta} \bar{\mathbf{I}}$ is positive on $[0, \varepsilon_0]$. Since $0 < g < 1$, for all $t \in [\varepsilon_0, \underline{B}]$

$$\int_0^t \left(\beta \mathbf{I} - \bar{\beta} \bar{\mathbf{I}} \right)(\xi) \; d\xi \geqslant g(t) \int_0^t \left(\beta \mathbf{I} - \bar{\beta} \bar{\mathbf{I}} \right)(\xi) \; d\xi \geqslant \Lambda_0,$$

where $\Lambda_0 = g(\varepsilon_0) \int_0^{\varepsilon_0} \left(\beta \mathbf{I}(\xi) - \bar{\beta} \bar{\mathbf{I}}(\xi) \right) d\xi > 0$. Using this inequality and the expression of $-\frac{g'(t)}{g(t)}$ in (54), we deduce that for all $t \in [\varepsilon_0, \underline{B}]$

$$\beta e^{-\mu t} \left(\int_0^{A-\min(t,A)} S_0(a) da \right) f \left(\bar{\beta} \int_0^t \bar{\mathbf{I}}(\xi) d\xi, \beta \int_0^t \mathbf{I}(\xi) d\xi \right) \Lambda_0 \leqslant (\beta \mathbf{I} - \bar{\beta} \bar{\mathbf{I}})(t).$$

Evaluating the above expression at $t = \underline{B}$ yields a contradiction with Eq. (42), and then $\beta = \bar{\beta}$.

We now prove that $\mathbf{I}(t) = \bar{\mathbf{I}}(t)$ for all $t \in [0,T]$. We first show that $\mathbf{I} = \bar{\mathbf{I}}$ on $[0, \underline{B}]$. Eq. (53) rewrites, for all $t \in [0, \underline{B}]$,

$$\mathbf{I}(t) - \bar{\mathbf{I}}(t) = \frac{g'(t)}{g(t)} \left(\int_0^t \mathbf{I}(\xi) d\xi - \int_0^t \bar{\mathbf{I}}(\xi) d\xi \right),$$

and, therefore,

$$\int_0^t \mathbf{I}(\xi) d\xi - \int_0^t \bar{\mathbf{I}}(\xi) d\xi = \left(\mathbf{I}(0) - \bar{\mathbf{I}}(0) \right) \, e^{\int_0^t \frac{g'}{g}(s) ds} = 0.$$

After differentiating the above equation w.r.t. t, one gets $\mathbf{I} = \bar{\mathbf{I}}$ on $[0, \underline{B}]$. This result is extended to $[0,T]$ by the same argument as in previous section, where (45) is given with $H_{\underline{B}}$ instead of H_0.

Step 3 Proving $c = \bar{c}$ is similar to Step 3 in previous section, which proves that $\mathbf{Q}^\star$ is identifiable.

4.3 Proof of Theorem 1, part 2

To prove that the restriction $\mathcal{O}|_{\mathbf{R}^\star}$ is not into, we build a counter example, that is two parameter vectors $p \neq \bar{p} \in \mathbf{R}^\star$ such that $\mathcal{O}(p) = \mathcal{O}(\bar{p})$. These vectors are such that $\beta = \bar{\beta}$, $0 < \bar{c} < c < c^\star$ and Θ and $\bar{\Theta}$ are p.d.f. in $\mathcal{A}_0$ related by

$$\bar{\Theta}(\theta) = \frac{c}{\bar{c}}\theta^{\frac{c-\bar{c}}{\bar{c}}}\Theta\left(\theta^{\frac{c}{\bar{c}}}\right). \tag{55}$$

This relationship ensures that the two incubation time p.d.f. X and $\bar{X}$ are identical, and after an easy computation, that the cumulative distribution functions of Θ and $\bar{\Theta}$, denoted $\mathcal{F}$ and $\bar{\mathcal{F}}$ satisfy

$$\mathcal{F}(e^{-ct}) = \bar{\mathcal{F}}(e^{-\bar{c}t}),\ \forall t \geq 0. \tag{56}$$

Let us prove that $\mathbf{I} = \bar{\mathbf{I}}$ on $[0, T]$. From the semigroup property in [23], setting $r(t) = A - \min(t, A)$, $f_0(t) = \int_0^{r(t)} S_0(u)du$ and $g_0(t, v) = \int_0^{r(t)} I_0(u, v)du$, integration of (11) shows that $\mathbf{I}$ is the unique solution of the integral equation

$$\begin{aligned}\mathbf{I}(t) = e^{-\mu t}\int_0^{e^{-ct}} g_0(t,v)dv + e^{-\mu t}f_0(t)\int_0^t \beta\mathcal{F}(e^{c(x-t)})\mathbf{I}(x)e^{-\beta\int_0^x \mathbf{I}(\xi)d\xi}dx,\\ + \int_{\max(t-A,0)}^t B(u)e^{-\mu(t-u)}\int_u^t \beta\mathcal{F}(e^{c(x-t)})\mathbf{I}(x)e^{-\beta\int_u^x \mathbf{I}(\xi)d\xi}dxdu,\end{aligned} \tag{57}$$

We now check that $\bar{\mathbf{I}}$ is also a solution of this equation to complete the proof.

Assume first that $t \leqslant T \leqslant A$, then $\underline{m} = T$ and, since $0 < c < \bar{c} < c^\star$, $e^{-ct} > e^{-c^\star \underline{m}}$ for $t \leqslant T$, and similarly for $\bar{c}$. By definition of $c^\star$, we have

$$\int_0^{e^{-ct}} g_0(t,v)dv = \int_0^{A-t}\int_0^{e^{-c^\star \underline{m}}} I_0(u,v)\,dv\,du = \int_0^{e^{-\bar{c}t}} g_0(t,v)dv. \tag{58}$$

If $t \leqslant A < T$, then $\underline{m} = A$ and $e^{-ct} > e^{-c^\star \underline{m}}$, and similarly for $\bar{c}$ and Eq. (58) is still true. Finally, if $A < t \leqslant T$, we also have

$$\int_0^{e^{-ct}} g_0(t,v)dv = 0 = \int_0^{e^{-\bar{c}t}} g_0(t,v)dv,$$

which shows that in all cases, Eq. (58) holds on $[0, T]$. Therefore, from Eq. (56) and Eq. (58), it follows that $\bar{\mathbf{I}}$ is a solution of (57).

From the definition of $c^\star$ and Eq. (13), when $t \leqslant a$ the incidence expression for p reduces to

$$\mathfrak{i}(t,a) = S_0(a-t)e^{-\mu t}\int_0^t c\,e^{c(s-t)}\,\Theta\left(e^{c(s-t)}\right)\beta\mathbf{I}(s)e^{-\beta\int_0^s \mathbf{I}(u)du}\,ds,$$

and similarly for $\bar{p}$. Since $\mathbf{I} = \bar{\mathbf{I}}$ on $[0, T]$ and (56) is satisfied, we obtain $\mathfrak{i}(t, a) = \bar{\mathfrak{i}}(t, a)$ when $t \leqslant a$. In the same way we can easily check that $\mathfrak{i}(t, a) = \bar{\mathfrak{i}}(t, a)$ when $t > a$.

We now prove that the populations N and $\bar{N}$ are equal. From (1) and (2) N satisfies $\frac{\partial N}{\partial t}(t, a) + \frac{\partial N}{\partial a}(t, a) = -\mu\, N(t, a) - \mathfrak{i}(t, a)$. Subtracting the corresponding equation for $\bar{N}$ we deduce that

$$\frac{\partial(N-\bar{N})}{\partial t}(t,a) + \frac{\partial(N-\bar{N})}{\partial a}(t,a) = -\mu\,(N-\bar{N})(t,a),$$

with initial and boundary condition $(N - \bar{N})(0, a) = 0$ and $(N - \bar{N})(t, 0) = 0$. Consequently, $N = \bar{N}$ on $[0, T]$, which ends the proof of the theorem.

5 Proof of Theorems 2 and 3

The proof of Proposition 2 does not make use of any assumption on the initial conditions, hence it is still true. Therefore, the assumptions on $\mathcal{G}$ immediately yield $c = \bar{c}$ and $\Theta = \bar{\Theta}$. Moreover, Eq. 42 is satisfied.

If (H_1) is true and the initial conditions are fixed, the same steps as in Step 2 of 4.2.1 and Step 2 of 4.2.2 prove that $\beta = \bar{\beta}$, and Theorem 2 holds.

When the initial conditions are not fixed, using 42 and $\underline{B} = 0$, we get $\beta \mathbf{I}(0) = \bar{\beta}\bar{\mathbf{I}}(0)$. If $\mathbf{I}(0) = \bar{\mathbf{I}}(0)$, it follows that $\beta = \bar{\beta}$, which proves Theorem 3.

6 Numerical simulations

In this section, we illustrate our identifiability results through two simulation scenarios. Scenario 1 corresponds to the non identifiability case under the assumptions of Theorem 1. Scenario 2 represents Theorem 2 for the Beta distribution family.

For both scenarios, system (1, 2, 3, 4) is integrated with parameter values given in Table 1. The birth function B is constant. The initial susceptible population density follows an exponential distribution $S_0(a) \propto e^{-\mu a}$. The initial infected population density $I_0(a, \theta)$ is uniformly distributed over $[a^{\min}, a^{\max}] \times [\theta^{\min}, \theta^{\max}]$. Scaling coefficients are adjusted to obtain the initial population sizes given in Table 1. Parameter values are chosen to mimic realistic epidemiological situations.

Table 1: Parameter values used for the simulations.

Parameter definition	symbol	value
initial population size	–	600 indiv.
initial infected population size	–	30 indiv.
— age range	$[a^{\min}, a^{\max}]$	$[0.625, 1, 04]$ years
basic mortality rate	μ	0.15 year^{-1}
horizontal transmission rate	β	$3\,10^{-3}$ $(\text{indiv. year})^{-1}$
birth rate	B	70 indiv./year
maximum lifespan	A	13 years
observation period	T	4 years
	Scenario 1 specific parameters	
initial infection load range	$[\theta_1^{\min}, \theta_1^{\max}]$	$[0.125, 0.18]$
infection load growth rates	$(c_1, \bar{c}_1)$	$(0.35, 0.28)$ year^{-1}
first infection load distribution Θ_1: mean	m_{Θ_1}	0.35
— : standard deviation	σ_{Θ_1}	0.05
	Scenario 2 specific parameters	
initial infection load range	$[\theta_2^{\min}, \theta_2^{\max}]$	$[0.68, 0.73]$
infection load growth rates	$(c_2, \bar{c}_2)$	$(0.35, 0.12)$ year^{-1}
first infection load distribution Θ_2: mean	m_{Θ_2}	0.35
— : standard deviation	σ_{Θ_2}	0.05
first infection load distribution $\bar{\Theta}_2$: mean	$m_{\bar{\Theta}_2}$	0.7
— : standard deviation	$\sigma_{\bar{\Theta}_2}$	0.05

6.1 Scenario 1

We build two parameter vectors $p_1 \neq \bar{p}_1$ of $\mathbf{R}^\star$ for which the observed incidences $\mathfrak{i}(t,a)$ are the same on the observation time interval $[0,T]$. The only differences between the two parameter vectors p_1 and $\bar{p}_1$ are the infection load growth rates c_1 and $\bar{c}_1$, and the first infection load distributions Θ_1 and $\bar{\Theta}_1$. Θ_1 is a Beta distribution with mean m_{Θ_1} and standard deviation σ_{Θ_1}. The first infection load distribution $\bar{\Theta}_1$ is related to Θ_1 by (55). Parameter values ensure that c_1 and $\bar{c}_1$ are in $]0, c_1^\star[$, $c_1^\star = 0.42$ being defined in (7).

As a consequence of Theorem 1 the model is not identifiable on $[0,T]$. This is illustrated in Figure 1, that represents the total incidence $\int_0^A \mathfrak{i}(t,a)da$ over time for both parameter vectors p_1 and $\bar{p}_1$. The two incidence curves coincide up to time T, but become different on a longer time horizon.

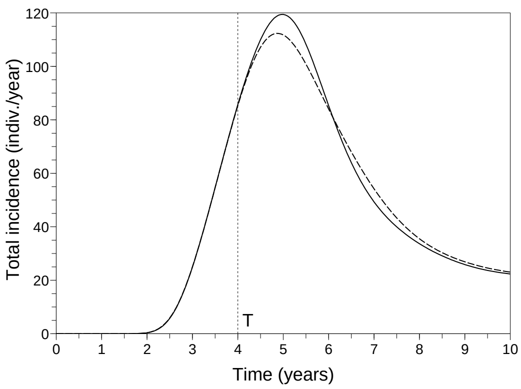


Figure 1: Scenario 1 – Total incidence $\int_0^A \mathfrak{i}(t,a)da$ over time t for the two parameter sets given in Table 1: (c_1, Θ_1) plain line & $(\bar{c}_1, \bar{\Theta}_1)$ dashed line. Up to time $T = 4$, the model is not identifiable and the incidence outputs coincide.

Moreover, the proof of Theorem 1 states that $\mathbf{I} = \bar{\mathbf{I}}$ on $[0,T]$. However, the infected densities are different, as shown in Figure 2.

6.2 Scenario 2

The differences between the parameter vectors p_2 and $\bar{p}_2$ are again the infection load growth rates c_2 and $\bar{c}_2$, and the first infection load distributions Θ_2 and $\bar{\Theta}_2$. They are both Beta distributions with the same standard deviations $\sigma_{\Theta_2} = \sigma_{\bar{\Theta}_2}$, but different means $m_{\Theta_2} \neq m_{\bar{\Theta}_2}$. Parameters c_2 and $\bar{c}_2$ are adjusted to obtain the same mean incubation period of 3 years for the distribution given in (12). First infection load and incubation period distributions are represented in Figure 3.

With such similar incubation period distributions, one could fear the model not to be identifiable. However, theorem 2 guarantees that the model is identifiable. This is illustrated in Figure 4 that represents the total incidence for both parameter sets. Total incidences, which are instantaneous flow measurements, exhibit notable differences. It is even more obvious on the yearly cumulated incidences, which are closer to the data collected in realistic situations.

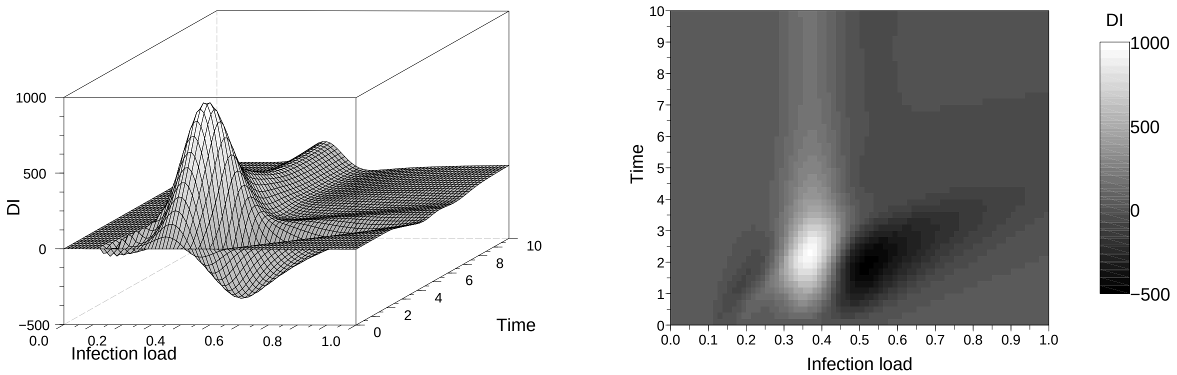


Figure 2: Scenario 1 – Difference $DI(t,\theta) = \int_0^A (I - \bar{I})(t,a,\theta)da$ between the two infected densities obtained with the two parameter sets given in Table 1. Up to time $T = 4$, the model is not identifiable, but the infected densities differ.

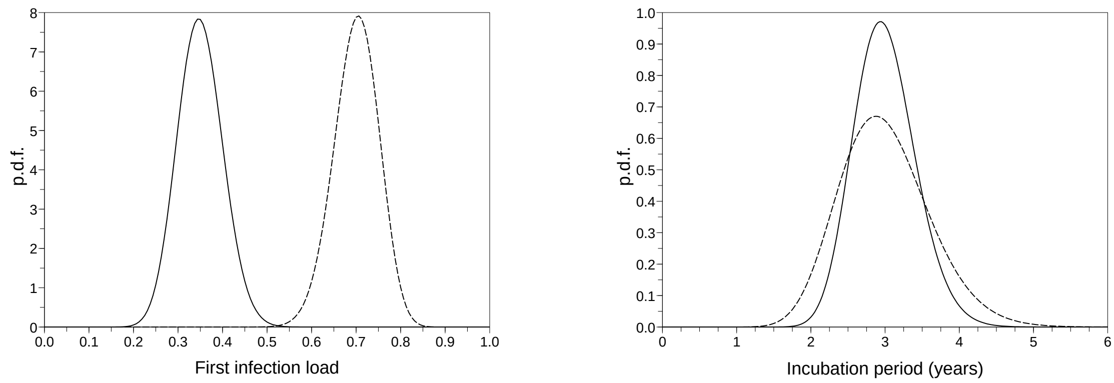
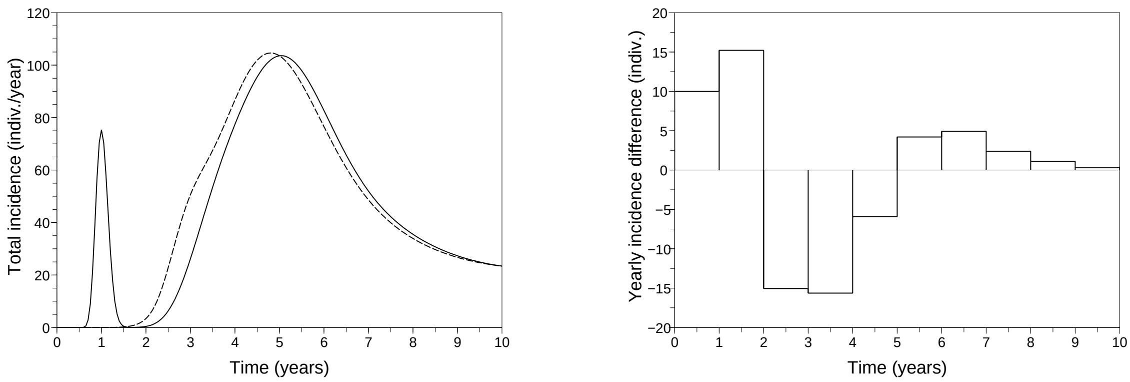


Figure 3: Scenario 2 – Distributions represented for the two parameter sets given in Table 1: (c_2, Θ_2) plain line & $(\bar{c}_2, \bar{\Theta}_2)$ dashed line.



(a) Total incidence $\int_0^A \mathrm{i}(t,a)da$.

(b) Difference between the yearly cumulated incidences.

Figure 4: Scenario 2 – Incidence outputs correspond to the two parameter sets given in Table 1: (c_2, Θ_2) plain line & $(\bar{c}_2, \bar{\Theta}_2)$ dashed line. The model is identifiable.

7 Conclusion

We proved identifiability results for a nonlinear transport reaction model representing the spread of a disease in a structured population in several cases. The first case, corresponding to Theorem 1, holds for any analytic p.d.f. of the first infection load Θ. This might seem restrictive, but in practical situations, parametric p.d.f. such as the Beta or log-Gamma distributions are used, which satisfy this assumption. The (non) identifiable region has a clear biological interpretation: cases must (not) be observed among the initial infected population. Therefore, the initial conditions need to be known. These results were obtained under several fairly realistic assumptions. Hypothesis (H_1) on the birth function B is not restrictive at all since it covers situations like seasonal birth. Hypothesis $\underline{B} = 0$ amounts to knowing the state of the system at a time when birth occurs, in our case the initial time. When $\underline{B} > 0$, the sufficient technical hypothesis (H_2) needs to be verified to obtain the parameter identifiability. However, whatever the time, getting to know the state of the system is not easy in practical situations, unless perhaps in an experimental setting.

The second and third cases, corresponding to Theorems 2 and 3 respectively, are valid when restricting Θ to a suitable parametric family. In the second case, we proved the identifiability of the epidemiological parameters on the whole parameter space with fixed but not necessarily known initial conditions and hypothesis (H_1). In the third case, initial conditions are not known but the total number of initially infected individuals is fixed. Then, assuming that birth occurs at the initial time ($\underline{B} = 0$), we proved the identifiability of the epidemiological parameters.

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