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Modelling, Analysis, Observability and Identifiability of Epidemic Dynamics with Reinfections

Marcel Fang and Pierre-Alexandre Bliman

Abstract—We consider in this paper a general SEIRS model describing the dynamics of an infectious disease including latency, waning immunity and infection-induced mortality. We derive an infinite system of differential equations that provides an image of the same infection process, but counting also the reinfections. Existence and uniqueness of the corresponding Cauchy problem is established in a suitable space of sequence valued functions, and the asymptotic behavior of the solutions is characterized, according to the value of the basic reproduction number. This allows to determine several mean numbers of reinfections related to the population at endemic equilibrium. We then show how using jointly measurement of the number of infected individuals and of the number of primo-infected provides observability and identifiability to a simple SIS model for which none of these two measures is sufficient to ensure on its own the same properties.

I. INTRODUCTION

Since their introduction by Kermack and McKendrik in 1927 [16], compartmental models have been massively used in mathematical epidemiology in order to study epidemic dynamics. The obtained dynamical models may be analyzed and simulated, with parameter values estimated by fitting to observed data. The inverse problem consisting of this estimation process is essential for realistic replication of the phenomenon. It is thus important to look beforehand if the obtained parameter estimates are meaningful, and first of all whether perfect, error-free, measurement of the system actually contains information on the unknown parameters — in other terms whether the model is identifiable [14]. Identifiability is only a recent topic in mathematical epidemiology, with few works addressing that issue. A survey on this topic has been recently published [13]. Xia and Moog [22] were among the first who considered this question, in a paper on an intra-host model of HIV. Structural identifiability [14], [18] for the classical SIR and SEIR models, based on prevalence measurement, has been studied by Tuncer et al. [20]. One may also cite Evan et al. [10] who addressed the identifiability problem for a SIR model with seasonal forcing, with either prevalence or incidence measured; or [9] for a SIR model for waterborne disease.

At the same time, the phenomena of reinfection, and particularly the counting of the number of reinfections, have been little studied to date. Among the works addressing that question, Andreasen et al. [2] and Abu-Raddad & Ferguson [1] studied models with reinfections by different strains.

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1Marcel Fang and Pierre-Alexandre Bliman are with Sorbonne Université, Laboratoire Jacques-Louis Lions, CNRS and with Inria, France. {marcel.fang,pierre-alexandre.bliman}@inria.fr

Arino et al. [3] presented a SVIRS model in order to analyze the efficiency of vaccination. With the same goal, Gomes et al. [12] studied systematically different SIRS models with vaccination, partial and temporary immunity. In addition, Katriel [15] highlighted a threshold condition for endemicity for a SIRS system borrowed from [12]. This author also proposed in the same paper a modified SIRS system with an infinite set of differential equations capable of counting the number of reinfections — to our knowledge, the only contribution made from this perspective.

In the present article, we draw inspiration from Katriel’s modelling approach, with the general aim of analyzing whether measuring the number of reinfections may provide more information for observability and identifiability than the usual perspective, which only considers all the infections globally. For this, we propose and analyze a SEIRS differential system with infinite number of equations that takes into account the reinfections. The model is presented in Section II and its well-posedness is established in Section III. The asymptotic convergence of the solutions is then studied in Section IV, while quantities of interest related to the asymptotic mean numbers of reinfections at the endemic equilibrium are computed in Section V. Simulations illustrating the behavior of the system are presented in Section VI. Finally, we present in Section VII results that demonstrate how the supplementary information on the number of reinfections may render observable and identifiable a SIS model which otherwise possesses none of these properties. For sake of space, all proofs are omitted and may be found in [11].

II. A SEIRS MODEL COUNTING REINFECTIONS

We begin by introducing the classical SEIRS system, presented e.g. in the recent paper [19] by Bjørnstad et al. and depicted in Figure 1. It is written as follows:

\[
\begin{align*}
\dot{S} &= bN - \beta S \frac{I}{N} + \omega R - \mu S, \\
\dot{E} &= \beta S \frac{I}{N} - (\sigma + \mu)E, \\
\dot{I} &= \sigma E - (\gamma + \mu + \nu)I, \\
\dot{R} &= \gamma I - (\omega + \mu)R,
\end{align*}
\]

where \(N(t) = S(t) + E(t) + I(t) + R(t)\). Here the variables \(S(t), E(t), I(t), R(t)\) represent respectively the number of individuals that are susceptible; exposed to the disease, but still not infectious; infectious; and recovered and subject, at least transiently, to immunity. The number \(N(t)\) is the total population size. All the model coefficients are nonnegative, with \(b\) and \(\mu\) representing the birth and natural mortality.
rates, while the other coefficients are characteristic of the considered disease. The coefficient $\beta$ is the contact rate, and $\omega^{-1}$, $\sigma^{-1}$, $\gamma^{-1}$ correspond respectively to the period of immunity, the period of latency when the subject is infected but not yet contagious, and the period of infection. Last, the constant $\nu$ is the infection-induced mortality rate.

Remark 1: Note that generally speaking, the total population $N = S + E + I + R$ may vary, as $N = (b - \mu)N - \nu I$. In particular, when $\nu = 0$, the solution of (1) diverges, resp. vanishes, as $t$ tends to $+\infty$ when $b > \mu$, resp. $b < \mu$. The variable $N$ may also vary when $b = \mu$ and $\nu > 0$. \(\Box\)

For non-permanent immunity, that is when $\omega > 0$, individuals recovered become newly susceptible after healing. We now want to account for these reinfections, by keeping track of their number. Denoting, for any $i \in \mathbb{N}$, $E_i(t)$ the number of individuals exposed after having been ill $i - 1$ times; $I_i(t)$ the number of individuals infected for the $i$-th time; $R_0(t)$ the number of individuals immune after having recovered $i$ times; and $S_i(t)$ the number of susceptible individuals that lost their transitory immunity after $i - 1$ recoveries, we expand system (1) along the idea used in [15], by dividing the compartments and adding an index associated to the number of reinfections. The corresponding system is schematized on Figure 2, and the following equations are obtained:

\[
\begin{align*}
\dot{S}_i &= \omega R_{i-1} - \beta S_i \frac{I_i}{N} - \mu S_i, \quad i \geq 1, \\
\dot{E}_i &= \beta S_i \frac{I_i}{N} - (\sigma + \mu) E_i, \quad i \geq 1, \\
\dot{I}_i &= \sigma E_i - (\gamma + \mu + \nu) I_i, \quad i \geq 1, \\
\dot{R}_i &= \gamma I_i - (\omega + \mu) R_i, \quad i \geq 1,
\end{align*}
\]  

(2a), (2b), (2c), (2d)

with $S(t) := \sum_{i\geq1} S_i(t)$, $E(t) := \sum_{i\geq1} E_i(t)$, $I(t) := \sum_{i\geq1} I_i(t)$, $R(t) := \sum_{i\geq1} R_i(t)$, $N(t) := S(t) + E(t) + I(t) + R(t)$. Furthermore by convention one puts

$$\omega R_0(t) = b N(t),$$

representing the recruitment term. Finally, the initial condition for the Cauchy problem associated to (2) is given by the quantities $S_i(0) = S_i^0, E_i(0) = E_i^0, I_i(0) = I_i^0, R_i(0) = R_i^0$, for $i \geq 1$. As depicted by the unwrapping of Figure 1 in Figure 2, the central difference is that, after an $i$-th recovery, the individuals enter a new susceptible compartment $S_{i+1}$, instead of coming back to a unique reservoir $S$ as in (1).

Notice that summing up the equations in (2) and the initial conditions, one formally recovers system (1). This property will be elucidated afterwards. In the sequel, we call (1) the macroscopic system and (2) the microscopic one, as (2) disentangles the hidden reinfection structure of the former.

Let us now introduce some notations. For $n \in \mathbb{N}$, define respectively by $X^n, X^n_+, X^n_{++}$ the spaces of sequences : $l^1 \times \cdots \times l^1, l^1_+ \times \cdots \times l^1_+, l^1_{++} \times \cdots \times l^1_{++}$, where $l^1$ is the Banach space of summable sequence, $l^1_+ \subset l^1$ the subspace of $l^1$ sequences of nonnegative numbers and $l^1_{++} \subset l^1_+$ the subspace of sequences of positive numbers. The space $X^n$ is endowed with the norm $\|x\|_{X^n} := \sum_{1 \leq i \leq n} \|x_i\|_{l^1}$ for $x = (x_1, x_2, \ldots, x_n) \in X^n$. We assume in the whole paper that the initial condition $(S^0_i, E^0_i, I^0_i, R^0_i)_{i\geq1} \in X^4_+$ belongs to $X^4_+$, and moreover that the system contains initially some infected (without which the solution is trivial), that is

$$\|I^0_i\|_{l^1} + \|E^0_i\|_{l^1} = \sum_{i\geq1} (I^0_i + E^0_i) > 0.$$  

(3)

III. WELL-POSEDNESS

Due to the infinite dimension of system (2), proving its well-posedness is not completely evident. We follow here an approach employed for example for the study of the Becker-Döring system, see e.g. [4], [17], [8]. One first defines an adequate notion of solution for the Cauchy problem associated to (2).

Definition 1: Let $0 < T \leq \infty$ and $x_0 := (S^0_i, E^0_i, I^0_i, R^0_i)_{i\geq1} \in X^4_+$ verifying (3). We call solution of (2) on $[0, T)$ any function $x : [0, T) \to X^4_+$, $t \mapsto x(t) := (S(t), E(t), I(t), R(t))_{i\geq1}$ such that:

1) each function $S_i, E_i, I_i, R_i : [0, T) \to \mathbb{R}_+ \times \mathbb{R}_+$, $i \geq 1$, is continuous and $\sup_{t \in [0,T)} \|x(t)\|_{X^4} < \infty$,

2) For all $t \in [0, T)$, $i \geq 1$,

$$S_i(t) = S_i(0) + \int_{0}^{t} (\omega R_{i-1}(s) - \beta S_i(s) \frac{I_i(s)}{N(s)} + \mu S_i(s)) ds,$$

$$E_i(t) = E_i(0) + \int_{0}^{t} (\beta S_i(s) \frac{I_i(s)}{N(s)} - (\sigma + \mu) E_i(s)) ds,$$

$$I_i(t) = I_i(0) + \int_{0}^{t} (\sigma E_i(s) - (\gamma + \mu + \nu) I_i(s)) ds,$$

$$R_i(t) = R_i(0) + \int_{0}^{t} (\gamma I_i(s) - (\omega + \mu) R_i(s)) ds. \quad \Box$$

Notice that the condition $\sup_{t \in [0,T]} \|x(t)\|_{X^4} < \infty$ implies that the functions $I$, and $N$ are bounded, and by
\[ \text{then easily obtains, by dividing the solution of (2) by } N(t), \]

existence and uniqueness result for the normalized system (4).

**Remark 2:** Let the set \( \Gamma = \{ \bar{x} \in X_+^4 : \| \bar{x} \|_{X^4} = 1 \} \). As \( \dot{S} + \dot{E} + \dot{I} + \dot{R} = (b - \nu I)(1 - S - E - I - R) \equiv 0 \), the set \( \Gamma \) is positively invariant for the normalized system (4), as expected. \( \square \)

**Remark 3:** Notice that the normalized systems (4) and (5) do not depend upon the value of \( \mu \). \( \square \)

The local stability of the disease-free population, and therefore the propensity of the infection to grow or to go extinct, is usually characterized by the basic reproduction number, see e.g. [6]. This is the number of secondary infections resulting from a single primary infection into an otherwise susceptible population. See [7] for interpretation in terms of dominant eigenvalue of a positive linear (“next generation”) operator, and [21] for its computation.

We have the following result for systems (4) and (5).

**Theorem 2:** The basic reproduction number of system (5) is \( R_0 := \frac{\sigma}{\sigma + b} \frac{\beta}{\gamma + \nu + b} \).

Moreover, for any \( \bar{x}_0 \in \Gamma \) verifying (3), the solutions of (4) and (5) are such that:

1. if \( R_0 < 1 \), denoting \( \delta \) the Kronecker delta, one has for any \( i \geq 1 \),
\[
\lim_{t \to +\infty} (\bar{S}(t), \bar{E}(t), \bar{I}(t), \bar{R}(t)) = \delta_1^i (1,0,0,0),
\]
\[
\lim_{t \to +\infty} (\bar{S}(t), \bar{E}(t), \bar{I}(t), \bar{R}(t)) = (0,1,0,0),
\]

2. if \( R_0 > 1 \), there exists a unique nonzero equilibrium \((\bar{S}^*, \bar{E}^*, \bar{I}^*, \bar{R}^*)\) of (5), which is indeed positive. The quantity \( \bar{I}^* \) satisfies:
\[
\left( \frac{\beta - \nu}{b} + 1 \right) \left( 1 - \frac{\nu \bar{I}^*}{\sigma + b} \left( 1 - \frac{\nu \bar{I}^*}{\gamma + \nu + b} \right) \right) = R_0 \left( 1 + \frac{\gamma}{\omega} \frac{b}{\omega + b - \nu \bar{I}^*} \right),
\]

and the three other quantities \( \bar{S}^*, \bar{E}^*, \bar{R}^* \) are given as
\[
\bar{S}^* = \frac{\gamma + b + \nu - \nu \bar{I}^* \sigma + b - \nu \bar{I}^* \beta}{\sigma}, \quad \bar{R}^* = \frac{\gamma}{\omega + b - \nu \bar{I}^* \bar{I}},
\]
\[
\bar{E}^* = \frac{\gamma + \nu + b - \nu \bar{I}^*}{\sigma}. \quad \tag{6b}
\]

Furthermore, let
\[
\phi := \frac{\omega}{\beta - \nu} \frac{\gamma}{\bar{I}^*} \frac{\bar{I}^*}{\bar{S}^*}
\]
then \( 0 < \phi < 1 \) and the following asymptotic convergence property holds, for every \( i \geq 1 \):
\[
\lim_{t \to +\infty} \left( S_i(t), E_i(t), I_i(t), R_i(t) \right) = \phi^{i-1} \left( S_1^*, E_1^*, I_1^*, R_1^* \right),
\]
\[
\lim_{t \to +\infty} \left( S(t), E(t), I(t), R(t) \right) = \left( \bar{S}^*, \bar{E}^*, \bar{I}^*, \bar{R}^* \right),
\]

with
\[
\bar{S}_1^* = \frac{b}{(\beta - \nu)\bar{I}^* + b}, \quad \bar{E}_1^* = \frac{\beta \bar{I}^*}{\sigma + b - \nu \bar{I}^* \bar{S}_1^*},
\]
\[
\bar{I}_1^* = \frac{\bar{I}^*}{\bar{S}_1^*}, \quad \bar{R}_1^* = \frac{\gamma}{\omega + b - \nu \bar{I}^* \bar{S}_1^*}. \quad \tag{7}
\]
Theorem 2 shows in particular that $R_0 = 1$ constitutes a threshold condition, which determines if the disease will eventually die out or remain in an endemic state with persistent (re)infections.

When $R_0 < 1$, then the infection goes extinct: asymptotically the whole population becomes susceptible, with zero previous infections.

When $R_0 > 1$, the infection settles at global endemic level, uniquely defined by the positive solution of (6a). Moreover, in this situation the asymptotic proportion $\bar{A}$ of the population with epidemiological status $\bar{A} \in \{\bar{S}, \bar{E}, \bar{I}, \bar{R}\}$, is a geometric progression with common ratio $\phi$, and for any $\bar{A}, \bar{B} \in \{\bar{S}, \bar{E}, \bar{I}, \bar{R}\}$, any $i, j \in \mathbb{N}$, one has $\frac{\bar{A}_i}{\bar{B}_j} = \phi^{-i-j} \frac{\bar{A}}{\bar{B}}$.

The case $\nu = 0$ yields simpler formulas, given now.

**Corollary 1:** When $\nu = 0$ and $R_0 > 1$, then

$$R_0 = \frac{\beta}{\gamma + b\sigma + b}, \quad \phi = \frac{\gamma \omega}{(\omega + b) - \gamma \omega} (R_0 - 1).$$

Moreover, we have an explicit formula for the value of $\bar{I}^*$:

$$\bar{I}^* = \frac{R_0 - 1}{\bar{\zeta}} = \frac{1}{\bar{\zeta}}, \quad \bar{\zeta} = \frac{\gamma + b)(\sigma + b)(\omega + b) - \gamma \omega \sigma}{\sigma(b(\omega + b))} > 1.$$

The constant $\bar{\zeta}$ is called number of critical stability [5].

We now derive from Theorem 2 a complete picture of the asymptotic behavior of the total size of the (non-normalized) population.

**Theorem 3:** Let $N(t)$ be the total population size at time $t$ of the solution of system (2) corresponding to a given initial condition fulfilling (3). The following properties hold.

1) If $b < \mu$, then $N(t)$ converges to 0 when $t \to +\infty$.

2) If $b = \mu$,
   a) If $\nu = 0$, then $N(t) = N(0)$ for all $t$.
   b) If $\nu > 0$,
      i) $N(t)$ converges asymptotically to a positive finite limit when $R_0 < 1$.
      ii) $N(t)$ converges asymptotically to 0 when $R_0 > 1$.

3) If $b > \mu$,
   a) If $b - \mu > \nu \bar{I}^*$, then $N(t)$ tends to $+\infty$.
   b) If $R_0 > 1$ and $b - \mu < \nu \bar{I}^*$, then $N(t)$ converges to 0.

As $\bar{I}^*$ does not depend upon $\mu$ (see Remark 3), there exist parameter sets fulfilling the case 2a, resp. 3b.

**V. MEAN NUMBERS OF REINFECTIONS**

Based on the convergence properties previously established, we now obtain significant quantities, related to the asymptotic mean numbers of reinfections at endemic equilibrium.

**Theorem 4:** Let $R_0 > 1$, then

$$\frac{\sum_{i \geq 1} (i - 1)S_i^* + i(\bar{I}^* + \bar{I}^* + \bar{R}^*))}{\sum_{i \geq 1} S_i^*} = \frac{\phi}{1 - \phi},$$

$$\frac{\sum_{i \geq 1} i\bar{E}_i}{\sum_{i \geq 1} E_i} = \frac{1}{1 - \phi},$$

where all diagonal blocks of the block-triangular Jacobian matrix of the truncated system (4), corresponding to the evolution of a finite number of microscopic modes, are worth

$$\begin{pmatrix} -\beta \bar{I}^* - b & 0 & -\beta \bar{S}^* & \omega \\ \beta \bar{I}^* - (\sigma + b) & \beta \bar{S}^* + \bar{E}^* & 0 \\ 0 & \sigma & -\gamma & 0 \\ 0 & 0 & \gamma & -\omega + b \end{pmatrix}.$$
The latter matrix is diagonal, its spectrum is real, and is numerically approximated to \{-1.01, -1.87, -26.08, -52.17\}. One computes numerically the spectrum of the former matrix, which appears to be complex, and approximately equal to \{-1.28 \times 10^{-2}, -68.62, -6.24 \pm 3.16i\}. Both matrices are Hurwitz, and the largest real part of the eigenvalues is associated to the macroscopic evolution, as foreseen.

VII. OBSERVABILITY AND IDENTIFIABILITY OF A SIMPLIFIED SIS MODEL

In order to illustrate the interest of the previous study for system identifiability, we consider here the following SIS system, formally obtained from (4) by putting \(\nu = 0\) and \(\sigma, \omega \to +\infty\): for any \(i \geq 1\),

\[
\begin{align*}
\dot{S}_i &= \gamma I_{i-1} - \beta S_i I - \mu S_i, & S_i(0) &= S_i^0, \\
\dot{I}_i &= \beta S_i I - (\mu + \gamma) I_i, & I_i(0) &= I_i^0.
\end{align*}
\]

One checks easily that the results obtained above are valid for this system. Let us now show that the knowledge of the two positive limits \(I^*\) and \(I_1^*\) allows to compute all parameters of the system, provided the mortality rate \(\mu\) is known.

Theorem 5: Suppose the coefficient \(\mu\) is known and that the limits of the numbers of infected \(I^* > 0\) and primoinfected \(I_1^* > 0\) are measured. Then

\[
R_0 = \frac{1}{1 - I^*},
\]

and by posing

\[
\theta := \frac{I_1^*}{\sum_{i \geq 1} I_i^*} = \frac{I_1^*}{I^*},
\]

the infection rate \(\beta\) and the recovery rate \(\gamma\) are given by:

\[
\beta = \frac{\mu}{R_0 - 1} \left(\frac{R_0^2}{\theta} - 1\right), \quad \gamma = \frac{\mu}{R_0 - 1} \left(\frac{R_0}{\theta} - 1\right).
\]

Theorem 5 provides a way to identify the coefficients \(\beta\) and \(\gamma\) of the system, when \(\mu\) and the limit quantities \(I_1^*\) and \(I^*\) are measured. Clearly, the knowledge of the two measurements brings more information than any of them does alone.
Remark 4: The ratio $\theta$ is the proportion of primo-infected in the total infected population at endemic equilibrium. It is as well the proportion of susceptible individuals never previously infected in the total susceptible population, see the explanations given after the statement of Theorem 2. □

Theorem 5 suggests to study the observability and identifiability properties of the system. To tackle this point, we study the following 4-dimensional system, obtained as subsystem of (8) (see the comment following Theorem 1):

\[
\begin{align*}
\dot{S} &= \mu - \beta SI - \mu S + \gamma I, \\
\dot{S}_1 &= \mu - \beta S_1 I - \mu S_1, \\
\dot{I} &= \beta SI - (\mu + \gamma) I, \\
y &= \alpha I, \\
y_1 &= \alpha I_1.
\end{align*}
\]

We assume through (9c) that the measurements of a portion $y$ of the infected individuals $I$ is available (as done e.g. in [10]), as well as of a portion $y_1$ of the primo-infected $I_1$, with the same proportion $\alpha$. The coefficient $\alpha$ lies in $[0, 1]$. It is supposed to represent the proportion of infected individuals detected by the Public health system. It typically depends upon the performance of the latter (say through testing policies...) and the infection itself (existence of asymptomatic cases...).

As before, the mortality rate $\mu$ is supposed known, as well as the total population size, taken to 1 for simplicity. The parameters $\alpha, \beta, \gamma$ are unknown.

**Theorem 6:** When the measurement $y$ is available, then system (9) is neither observable, nor identifiable. When both measurements $y$ and $y_1$ are available, then system (9) is both observable and identifiable.

The properties established here [11] are more precisely algebraic observability and algebraic identifiability [22].

**VIII. CONCLUSIONS**

We proposed in this article a SEIRS model with an infinite set of differential equations, allowing to enumerate the number of reinfections. The well-posedness of this system has been established in an appropriate functional setting, and the asymptotic convergence to either the disease-free equilibrium (when the basic reproduction number $R_0$ is smaller than 1) or the endemic equilibrium (when $R_0 > 1$) has been shown. We also provided in the latter case several formulas related to mean numbers of reinfections. Last, we have shown that the joint measurement of the number of infected and of primo-infected is sufficient to render observable and identifiable a system that is not when only the infected are measured. This result demonstrates the interest of the reinfection data for analyzing the communicable diseases. Based on this first step, further research will now consider the key issues of observation and identification. We also plan to investigate the extension of the observability and identifiability results to the general SEIRS system.

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