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Kwassi H. Degue & Jerome Le Ny

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Estimation and outbreak detection with interval observers for uncertain discrete-time SEIR epidemic models*

Kwassi H. Degue and Jerome Le Ny

Department of Electrical Engineering, Polytechnique Montreal and GERAD, Montreal, QC, Canada

ABSTRACT

According to the World Health Organization, infectious diseases are among the top ten causes of death worldwide. To prepare intervention strategies in a timely manner, tracking the evolution of these diseases is critical. For this purpose, public health services have access to noisy counts of infected people, which we use here to design a state estimator for a nonlinear discrete-time Susceptible-Exposed-Infected-Recovered (SEIR) epidemic model. We consider the practical case in which only sets of admissible values are known for the model's disturbances, uncertainties and parameters. Moreover, no bounds are available for the uncertain transmission rate from the 'susceptible' to the 'exposed' stage of the illness. We estimate the set of possible values of the state using an interval observer and characterise the stability and size of the estimation errors using linear programming. Furthermore, we propose an epidemic outbreak detector that leverages these state interval estimates. We demonstrate the observer's performance in numerical simulations.

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1. Introduction

About 31.1 million to 43.9 million people were living with HIV in 2017 (World Health Organization, 2018), while seasonal influenza epidemics usually cause three to five million cases of severe illness and result in about 250,000 to 500,000 deaths worldwide every year, according to the World Health Organization (Vaillant, La Ruche, Tarantola, & Barboza, 2009). Infectious disease surveillance plays a major role in analysing the origins, dynamics and spread of such epidemics. Public Health Services (PHS) rely on surveillance data, e.g. records of infected people collected by agencies such as the Centers for Disease Control and Prevention in the United States, to estimate these infectious diseases' activity levels, prepare intervention strategies and design policy recommendations.

Mathematical modelling of epidemics has become an essential tool in the sentinel role played by early outbreak detection systems and for public health response planning (Dukic, Lopes, & Polson, 2012; Fallas-Monge, Chavarría-Molina, & Alpízar-Brenes, 2016, November; Grassly & Fraser, 2008; Kaplan, Craft, & Wein, 2002; Keeling & Rohani, 2008). Kermack and McKendrick (1927) proposed the first modern mathematical epidemiology model, namely, a Susceptible-Infectious-Recovered (SIR) model for the plague (London 1665–1666, Bombay 1906) and cholera (London 1865) epidemics. The basic SIR model assumes that a fixed population, at any time, can be divided into three compartments: susceptible people (those who are not infected but could become infected), infectious people (those who have the disease and are able to infect others), and recovered people (those who were infected by the disease and are now immune). The model assumes that the total number of people remains constant as well as homogeneous mixing, that is, each individual is equally likely to come in contact with any other (Dukic et al., 2012). The proportions of the population in each compartment form the states of an SIR model.

In the case of some infectious diseases such as tuberculosis (Feng, Huang, & Castillo-Chavez, 2001), HIV/AIDS (Castillo-Chavez, Cooke, Huang, & Levin, 1989) or influenza-like illnesses (Dukic et al., 2012), one needs to extend the standard SIR model and introduce a fourth compartment and state corresponding to the disease's latency period, when a person is infected but not yet able to infect others. This extension is called the Susceptible-Exposed-Infected-Recovered (SEIR) model (Hethcote, 2000). Several estimators have been previously designed to track the states of SEIR models (Alonso-Quesada, De la Sen, Agarwal, & Ibeas, 2012; Dukic et al., 2012; Ibeas, de la Sen, Alonso-Quesada, Zamani, & Shafiee, 2014, December). Strong assumptions on the disturbances or uncertain parameters in these models enable the design of estimators converging to the true state values. However, the problem of observer design for SEIR models becomes very challenging in practice, when one has to take into account the presence of disturbances or uncertain parameters whose values are only known to belong to an interval or polytope. An interval estimation approach can address such problems (Degue, Efimov, & Iggidr, 2016; Efimov, Perruquetti, Raïssi, & Zolghadri, 2013; Efimov, Polyakov, Fridman, Perruquetti, & Richard, 2015; Efimov, Raïssi, & Zolghadri, 2013; Gouzé, Rapaport, & Hadj-Sadok, 2000; Gucik-Derigny, Raïssi,

CONTACT Kwassi H. Degue kwassi-holali.degue@polymtl.ca Department of Electrical Engineering, Polytechnique Montreal and GERAD, Montreal, QC H3T-1J4, Canada

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& Zolghadri, 2015; Mazenc, Dinh, & Niculescu, 2012). Using input and output measurements, an observer has to estimate the set of admissible values (interval) for the states at each instant of time (Degue, Efimov, & Richard, 2018; Mazenc, Dinh, & Niculescu, 2013, 2014; Moisan & Bernard, 2005; Rotondo, Cristofaro, Johansen, Nejjari, & Puig, 2017; Yousfi, Raïssi, Amairi, Gucik-Derigny, & Aoun, 2017). A major advantage of the interval estimation methodology is that it allows us to take into account many types of uncertainties in the system (Efimov & Raïssi, 2015; Mazenc & Bernard, 2010, 2011).

Contributions. This article presents a strategy based on interval estimation to track the four states of a discrete-time SEIR epidemic model in the presence of uncertainty, and to compute a decision variable that helps predict epidemic outbreaks. An interval observer was proposed for the first time for an epidemic model by Diaby, Iggidr, and Sy (2015). Their approach showed reasonable accuracy in simulation but the result was not optimal since the observer gain was selected manually. Instead, we use efficient methods to compute optimal interval observer gains that minimise the L_∞-gain of the estimation error dynamics, following an approach suggested by Briat and Khammash (2016). An interval observer was also proposed by Bliman and D'Avila Barros (2016), which applies to SIR rather than SEIR models however and so does not consider the fourth compartment of the population corresponding to the incubation stage for diseases such as influenza. Furthermore, it assumes continuous-time dynamics, whereas we focus on discrete-time epidemic models, which have gained substantial importance during the last decade (Hu, Teng, & Jiang, 2012; Mickens, 2007). A more important difference is that Bliman and D'Avila Barros (2016) assumed perfect measurements of new infectives per unit of time βSI to be available, as well as lower and upper bounds on the transmission rate β. In contrast, we assume that PHS have only access to noisy measurements of the infectious population I, possibly to bounds on βSI, and that no bounds on the transmission rate β are given. Although the observer proposed by Bliman and D'Avila Barros (2016) provided accurate results in simulated models, in practice the transmission rate β is a highly uncertain parameter that cannot be obtained from biological considerations (Bichara, Cozic, & Iggidr, 2014; Hooker, Ellner, Roditi, & Earn, 2011) and its bounds are generally unknown in epidemiological models (Degue et al., 2016). Moreover, for SEIR models, the quantity βSI represents newly exposed individuals rather than new infectives, which can be difficult to measure since these individuals might not even feel symptoms yet. Furthermore, compared to the recent literature on interval observer design, such as Gucik-Derigny et al. (2015) and Robinson, Marzat, and Raïssi (2017), the matrix A governing the state dynamics is uncertain in this article. Only linear systems and unknown inputs that have no impact on the output are considered in Robinson et al. (2017). In contrast, we consider here a nonlinear system with unknown inputs that affect the output, leading us to design upper and lower bounds for the uncertain input before constructing an interval observer for the system. Finally, we use our interval observer to design a novel on-line outbreak detection algorithm. Namely, we leverage the bounds on the transmission rate β produced by our observer to decide if the disease-free equilibrium of the SEIR model becomes unstable.

In Section 2, we present the problem statement and some results on interval estimation and the stability of positive systems. Section 3 describes the application of these results to design an interval observer for a discrete-time SEIR epidemic model and discusses how to compute upper and lower bounds for the uncertain transmission rate β. Section 4 presents computational methods to obtain interval observer gains that minimise the L_∞-gain of the estimation error dynamics. The conditions obtained provide guarantees on the error bounds of the proposed interval observer. Section 5 describes an on-line outbreak detection algorithm based on the interval estimates provided in Section 3. Finally, numerical simulations presented in Section 6 illustrate the performance of the observer.

Notation. We denote the real numbers by $\mathbb{R}$, the integers by $\mathbb{Z}$, $\mathbb{R}_+ = \{\tau \in \mathbb{R} : \tau \geq 0\}$ and $\mathbb{Z}_+ = \mathbb{Z} \cap \mathbb{R}_+$. We denote the cones of vectors of dimension n with positive and nonnegative components by $\mathbb{R}^n_{>0}$ and $\mathbb{R}^n_+$ respectively. The standard simplex in $\mathbb{R}^n$ is $\Delta_n = \{x \in \mathbb{R}^n_+ \mid \sum_{i=1}^n x_i = 1\}$. We denote the p-norm of a vector $x \in \mathbb{R}^n$ by $|x|_p := (\sum_{i=1}^k |x_i|^p)^{1/p}$, for $p \in [1, \infty)$, and $|x|_\infty := \max_{i\in\{1,\dots,n\}} |x_i|$. For a vector-valued signal $u : \mathbb{Z}_+ \to \mathbb{R}^n$, we denote its L_∞-norm as $||u||_{L_\infty} := \sup_{t\geq 0} |u_t|_\infty$. We denote by $\mathcal{L}^n_\infty$ the set of signals u with the property $||u||_{L_\infty} < \infty$. The $n \times n$ identity matrix is denoted I_n and matrices with all elements equal to 1 and dimensions $n \times m$ and $p \times 1$ are denoted $\mathbb{1}_{n\times m}$ and $\mathbb{1}_p$, respectively. For two vectors $x_1, x_2 \in \mathbb{R}^n$ or matrices $A_1, A_2 \in \mathbb{R}^{n\times n}$, the relations $x_1 \leq x_2$ and $A_1 \leq A_2$ are understood element-wise. A matrix $A \in \mathbb{R}^{n\times n}$ is called Schur stable if all its eigenvalues have absolute value strictly less than one. It is called nonnegative if all its elements are nonnegative, i.e. if $A \geq 0$. A matrix $A \in \mathbb{R}^{n\times n}$ is Hurwitz if all its eigenvalues have negative real parts. It is called Metzler if all its elements outside of the main diagonal are nonnegative.

2. Problem statement

A discrete-time SEIR model obtained by discretizing a classical continuous-time model (Hethcote, 2000) illustrated on Figure 1, using a forward Euler discretization (Hu et al., 2012), reads

$$\begin{aligned} S_{t+1} &= (1-\mu)S_t - \beta S_t I_t + \mu, \\ E_{t+1} &= (1-\alpha-\mu)E_t + \beta S_t I_t, \\ I_{t+1} &= (1-\gamma-\mu)I_t + \alpha E_t, \\ R_{t+1} &= (1-\mu)R_t + \gamma I_t. \end{aligned} \tag{1}$$

In (1), $x_t := [S_t \;\; E_t \;\; I_t \;\; R_t]^T$ are state variables representing proportions of a population in each of four compartments. The (unitless) parameters α, β and γ stand for the uncertain transition rates from one disease stage to the next, while μ represents the natural birth and death rate. These parameters are assumed constant to simplify the discussion, but the extension of the observer design methodology in Section 3 to time-varying parameters is straightforward. We describe the disease transmissions that arise from contacts between susceptible and infectious people by the first equation of (1). At each time-period, the pathogen is transmitted by each infectious individual to β individuals, but a new disease case occurs only if the contact is made with a susceptible person, with probability S_t. Hence, at time t, a fraction βI_t of people in the compartment S migrate to

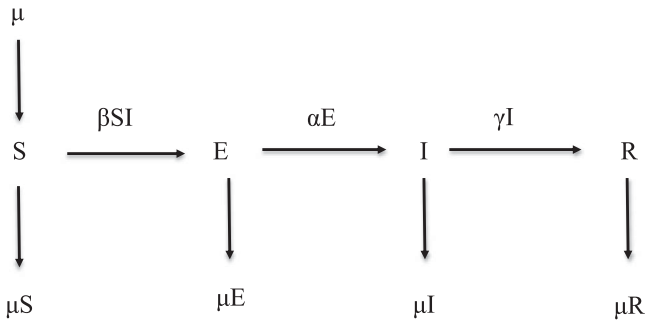

Figure 1. The Susceptible-Exposed-Infected-Recovered (SEIR) model.

the 'exposed but not yet infectious' compartment E. A fraction α of the people in compartment E move to the infectious compartment I while a fraction γ of infectious individuals migrate to the recovered compartment R, at which point they become immune.

The constants $\alpha \in [\underline{\alpha}, \bar{\alpha}]$, $\gamma \in [\underline{\gamma}, \bar{\gamma}]$ and $\mu \in [\underline{\mu}, \bar{\mu}]$ are unknown but taking values in given intervals of $\mathbb{R}_+$, i.e. the nonnegative parameters $\underline{\alpha}, \bar{\alpha}, \underline{\gamma}, \bar{\gamma}, \underline{\mu}, \bar{\mu} \in \mathbb{R}_+$ are known. The constant β is highly uncertain and no bounds on β are given a priori. The initial condition x_0 belongs to the standard simplex Δ_4, i.e. $x_0 \geq 0$ and $S_0 + E_0 + I_0 + R_0 = 1$. Although the exact value of x_0 is unknown, we assume that bounds $\underline{x}_0, \bar{x}_0 \in \mathbb{R}^4_+$ are given such that $\underline{x}_0 \leq x_0 \leq \bar{x}_0$. All compartments experience the same death rate equal to the birth rate μ at period t. Finally, we make the following assumption throughout the paper.

Assumption 2.1: *The parameters $\alpha, \beta, \gamma, \mu$ are nonnegative and satisfy the following constraints: $\mu + \alpha \leq 1$, $\mu + \gamma \leq 1$, $\mu + \beta \leq 1$.*

Assumption 2.1 is introduced to ensure nonnegativity of the state x of the system (1) and places an upper bound on the stepsize used for the Euler discretization. Although more refined numerical integration methods can be used to discretise the continuous-time SEIR model (Ibeas, de la Sen, Alonso-Quesada, & Zamani, 2015; Mickens, 2007) the model (1) can serve as a first step to apply the interval observer methodology.

Proposition 2.1: *Under Assumption* 2.1, *if $x_0 \in \Delta_4$, then $x_t \in \Delta_4$, for all $t \geq 0$. In particular, a state trajectory of the model* (1) *is nonnegative and in $\mathcal{L}^4_\infty$.*

Proof: By induction, suppose $x_t \in \Delta_4$. Then it is immediate from Assumption 2.1, $x_t \geq 0$, and the last three equations of (1) that $E_{t+1}, I_{t+1}, R_{t+1} \geq 0$. Moreover

$$S_{t+1} = (1 - \mu - \beta I_t) S_t + \mu,$$

and $I_t \leq 1$ because $x_t \in \Delta_4$. So

$$\mu + \beta I_t \leq \mu + \beta \leq 1,$$

by Assumption 2.1, and hence $S_{t+1} \geq 0$ as well. Finally,

$$\begin{aligned} S_{t+1} + E_{t+1} + I_{t+1} + R_{t+1} &= (1 - \mu)(S_t + E_t + I_t + R_t) + \mu \\ &= (1 - \mu) + \mu = 1, \end{aligned}$$

and so $x_{t+1} \in \Delta_4$. ■

The measured output consists of noisy counts of the infectious individuals (who typically present symptoms), which could be determined by PHS using data obtained from doctors and health centres for example Dukic et al. (2012),

$$y_t = I_t + v_t, \tag{2}$$

where $v \in \mathcal{L}_\infty$ is the measurement noise, with $\underline{v} \leq v_t \leq \bar{v}$, $\forall\, t \geq 0$, for some known constants $\underline{v}, \bar{v}$. The measurement noise \$v\$ can capture for instance the uncertain number of infectious individuals who do not go to a health centre to diagnose their disease.

We rewrite the system (1)–(2) as follows

$$\begin{aligned} x_{t+1} &= Ax_t + F\zeta_t + H\mu, \\ y_t &= Cx_t + v_t, \end{aligned} \tag{3}$$

where the incidence rate $\zeta_t := \beta S_t I_t$, i.e. the proportion of newly infected individuals in the population at each time period, is treated as an uncertain input. The uncertain matrix A and constant matrices C, F and H in (3) are defined as follows

$$C = [0\ \ 0\ \ 1\ \ 0], \quad F = [-1\ \ 1\ \ 0\ \ 0]^{\mathrm{T}}, \quad H = [1\ \ 0\ \ 0\ \ 0]^{\mathrm{T}},$$

$$A = \begin{bmatrix} 1-\mu & 0 & 0 & 0 \\ 0 & 1-\alpha-\mu & 0 & 0 \\ 0 & \alpha & 1-\mu-\gamma & 0 \\ 0 & 0 & \gamma & 1-\mu \end{bmatrix}.$$

Since the values of the parameters α, μ and γ are uncertain, the matrix A is unknown, but we have the bounds $\underline{A} \leq A \leq \bar{A}$, with

$$\underline{A} = \begin{bmatrix} 1-\bar{\mu} & 0 & 0 & 0 \\ 0 & 1-\bar{\alpha}-\bar{\mu} & 0 & 0 \\ 0 & \underline{\alpha} & 1-\bar{\gamma}-\bar{\mu} & 0 \\ 0 & 0 & \underline{\gamma} & 1-\bar{\mu} \end{bmatrix},$$

$$\bar{A} = \begin{bmatrix} 1-\underline{\mu} & 0 & 0 & 0 \\ 0 & 1-\underline{\alpha}-\underline{\mu} & 0 & 0 \\ 0 & \bar{\alpha} & 1-\underline{\gamma}-\underline{\mu} & 0 \\ 0 & 0 & \bar{\gamma} & 1-\underline{\mu} \end{bmatrix}.$$

In the sequel, we enforce nonnegativity and Schur stability of $\underline{A}$, $\bar{A}$ through the following assumptions, which strengthen the first two inequalities of Assumption 2.1.

Assumption 2.2: *The (nonnegative) upper bounds $\bar{\alpha}$, $\bar{\gamma}$, $\bar{\mu}$ are such that $\underline{A} \geq 0$, i.e.*

$$\bar{\alpha} + \bar{\mu} \leq 1 \quad \text{and} \quad \bar{\gamma} + \bar{\mu} \leq 1. \tag{4}$$

Furthermore, $\underline{\mu} > 0$.

Our goal in this paper consists in designing an interval observer, i.e. state signal bounds $0 \leq \underline{x}_t \leq x_t \leq \bar{x}_t$, for all $t \geq 0$, which can then be used to develop a decision rule for disease outbreak detection.

3. Interval observer design

In this section, we design an interval observer for the SEIR model (1)–(2). First, we review some basic facts about interval estimation and positive systems, which are needed in the following.

3.1 Preliminaries on positive systems

Given a matrix $A \in \mathbb{R}^{m\times n}$, define $A^+ = \max\{0, A\}$ applied element-wise, $A^- = A^+ - A$, and denote the matrix of absolute values of all elements by $|A| = A^+ + A^-$.

Lemma 3.1 (Efimov, Fridman, Raïssi, Zolghadri, & Seydou, 2012)**:** *Let $A \in \mathbb{R}^{m\times n}$ be a matrix and $x \in \mathbb{R}^n$ be a vector with $\underline{x} \le x \le \bar{x}$ for some $\underline{x}, \bar{x} \in \mathbb{R}^n$.*

Then

$$A^+\underline{x} - A^-\bar{x} \le Ax \le A^+\bar{x} - A^-\underline{x}. \tag{5}$$

Note in particular that if $A \ge 0$, then $A^+ = A$, $A^- = 0$, and (5) reads simply

$$A\underline{x} \le Ax \le A\bar{x}. \tag{6}$$

Next, consider the following discrete-time linear time-invariant (LTI) system

$$\begin{aligned} x_{t+1} &= Ax_t + B\omega_t, \quad \omega : \mathbb{Z}_+ \to \mathbb{R}^q_+, \\ y_t &= Cx_t + D\omega_t, \end{aligned} \tag{7}$$

where $x_t \in \mathbb{R}^n$, $y_t \in \mathbb{R}^p$ and the matrix $A \in \mathbb{R}^{n\times n}_+$. Any state trajectory of the LTI system (7) is element-wise nonnegative for all $t \ge 0$ provided that $x_0 \ge 0$, $B \in \mathbb{R}^{n\times q}_+$, and ω is nonnegative. In addition, the output signal y_t of such a system is nonnegative if $C \in \mathbb{R}^{p\times n}_+$ and $D \in \mathbb{R}^{p\times q}_+$. A dynamical system satisfying all these restrictions is called cooperative (monotone) or nonnegative (Farina & Rinaldi, 2000; Smith, 1995).

3.2 Interval observer design

Suppose for now that the following bounds on the incidence $\zeta_t = \beta S_t I_t$ are available

$$\underline{\zeta}_t \le \zeta_t \le \bar{\zeta}_t, \quad \forall\, t \ge 0, \tag{8}$$

where $\underline{\zeta}_t, \bar{\zeta}_t \ge 0$. For example, UNAIDS (2010) and Chowell, Sattenspiel, Bansal, and Viboud (2016) describe methods used for estimating the incidence of certain diseases. Moreover, the relation (8) generalises an assumption of Bliman and D'Avila Barros (2016), which considered that ζ_t could be measured perfectly. Then, the equations of our interval estimator for (3) take the following form

$$\begin{aligned} \underline{\chi}_{t+1} &= \underline{A}\underline{\chi}_t + F^+\underline{\zeta}_t - F^-\bar{\zeta}_t + H\underline{\mu} \\ &\quad + \underline{L}(y_t - C\underline{\chi}_t) - \underline{L}^+\bar{\nu} + \underline{L}^-\underline{\nu}, \\ \bar{\chi}_{t+1} &= \bar{A}\bar{\chi}_t + F^+\bar{\zeta}_t - F^-\underline{\zeta}_t + H\bar{\mu} \\ &\quad + \bar{L}(y_t - C\bar{\chi}_t) + \bar{L}^-\bar{\nu} - \bar{L}^+\underline{\nu}, \\ \underline{x}_t &= \max\{0, \underline{\chi}_t\}, \quad \bar{x}_t = \max\{0, \bar{\chi}_t\}, \\ \underline{\chi}_0 &= \underline{x}_0, \quad \bar{\chi}_0 = \bar{x}_0, \end{aligned} \tag{9}$$

where $\underline{x}_t$, $\bar{x}_t \in \mathbb{R}^4$ are respectively the lower and the upper interval estimates for the state x_t, and $\underline{\chi}_t$, $\bar{\chi}_t \in \mathbb{R}^4$ are the states of (9).

Define the interval observer's errors

$$\underline{e}_t = x_t - \underline{\chi}_t \quad \text{and} \quad \bar{e}_t = \bar{\chi}_t - x_t. \tag{10}$$

We select the interval observer gains $\bar{L} \in \mathbb{R}^{4\times 1}$, $\underline{L} \in \mathbb{R}^{4\times 1}$ such that the matrices $(\bar{A} - \bar{L}C)$ and $(\underline{A} - \underline{L}C)$ are Schur stable and nonnegative to enforce the positivity and the asymptotic stability of these errors. Observer gains that satisfy such conditions exist (for example $\underline{L} = \bar{L} = 0$).

Theorem 3.1: *Under Assumptions* 2.1 *and* 2.2*, if the matrices $(\bar{A} - \bar{L}C)$ and $(\underline{A} - \underline{L}C)$ are nonnegative, then the estimates $\underline{x}_t$ and $\bar{x}_t$ given by* (9) *yield the relations*

$$0 \le \underline{x}_t \le x_t \le \bar{x}_t, \quad \forall\, t \ge 0, \tag{11}$$

provided that $0 \le \underline{x}_0 \le x_0 \le \bar{x}_0$.

Proof: We can rewrite (3) as follows

$$x_{t+1} = (A' - LC)x_t + (A - A')x_t + F\zeta_t + H\mu + Ly_t - L\nu_t$$

for A' equal to $\underline{A}$ or $\bar{A}$ and L equal to $\underline{L}$ or $\bar{L}$. Therefore, the error dynamics satisfy the equations

$$\underline{e}_{t+1} = (\underline{A} - \underline{L}C)\underline{e}_t + \sum_{i=1}^{i=4}\underline{g}_i, \quad \bar{e}_{t+1} = (\bar{A} - \bar{L}C)\bar{e}_t + \sum_{i=1}^{i=4}\bar{g}_i, \tag{12}$$

where

$$\begin{aligned} \underline{g}_1 &= (A - \underline{A})x_t, \quad \bar{g}_1 = (\bar{A} - A)x_t, \\ \underline{g}_2 &= (\underline{L}^+\bar{\nu} - \underline{L}^-\underline{\nu}) - \underline{L}\nu_t, \quad \bar{g}_2 = \bar{L}\nu_t - (\bar{L}^+\underline{\nu} - \bar{L}^-\bar{\nu}), \\ \underline{g}_3 &= F\zeta_t - (F^+\underline{\zeta}_t - F^-\bar{\zeta}_t), \quad \bar{g}_3 = (F^+\bar{\zeta}_t - F^-\underline{\zeta}_t) - F\zeta_t, \\ \underline{g}_4 &= H\mu - H\underline{\mu}, \quad \bar{g}_4 = H\bar{\mu} - H\mu. \end{aligned}$$

When the Assumptions 2.1 and 2.2 are satisfied, we deduce from Proposition 2.1 and Lemma 3.1 that the signals $\{\underline{g}_i, \bar{g}_i, 1 \le i \le 4\}$ are nonnegative. Hence, we deduce from Section 3.1 that $\underline{e}_t \ge 0, \bar{e}_t \ge 0$ for all $t \ge 0$, since $\underline{e}_0 \ge 0$, $\bar{e}_0 \ge 0$ and the matrices $(\underline{A} - \underline{L}C)$ and $(\bar{A} - \bar{L}C)$ are nonnegative. Consequently, the order relation $\underline{\chi}_t \le x_t \le \bar{\chi}_t$ is satisfied for all $t \ge 0$. Therefore the inequality (11) is true by construction of $\underline{x}, \bar{x}$, using the fact that $x_t \ge 0$ from Proposition 2.1. ■

Remark 3.1: In general, when designing an interval observer, assuming that there exist gains $\underline{L}, \bar{L}$ such that the matrices $(\underline{A} - \underline{L}C)$ and $(\bar{A} - \bar{L}C)$ are Schur stable and nonnegative is restrictive since such gains may not exist. However, from the structure of the epidemic model (3) and the Assumptions 2.1 and 2.2, such gains $\underline{L}, \bar{L}$ exist for our problem (for example $\underline{L} = \bar{L} = 0$). Therefore, here one does not need to use transformation of coordinates methodologies such as those that proposed by Mazenc et al. (2013) and Raïssi, Efimov, and Zolghadri (2012).

To conclude this section, recall that our interval observer (9) design does not assume that lower and upper bounds on the transmission rate β were known a priori. We can then obtain lower and upper bounds on β from the observer. Indeed,

when $\underline{S}_t\underline{I}_t \neq 0$ for some t, (and hence $\bar{S}_t\bar{I}_t \neq 0$ also), we deduce from (8) the following bounds at time t

$$\underline{\beta}_t \leq \beta \leq \bar{\beta}_t, \tag{13}$$

with

$$\underline{\beta}_t = \max_{0\leq k\leq t}\{(\bar{S}_k\bar{I}_k)^{-1}\underline{\zeta}_k\}, \quad \bar{\beta}_t = \min_{0\leq k\leq t}\{(\underline{S}_k\underline{I}_k)^{-1}\bar{\zeta}_k\}. \tag{14}$$

Remark 3.2: In practice, the parameters of the epidemic model (1) may be time-varying, i.e. $\alpha_t, \mu_t, \gamma_t$ and the transmission rate β_t may vary with time. The observer design methodology proposed here still applies to such a case. However, the inequality (13) is then replaced by $\underline{\beta}_t \leq \beta_t \leq \bar{\beta}_t$, with $\underline{\beta}_t = (\bar{S}_t\bar{I}_t)^{-1}\underline{\zeta}_t$, $\bar{\beta}_t = (\underline{S}_t\underline{I}_t)^{-1}\bar{\zeta}_t, \forall\, t \geq 0$.

3.3 Bounding the incidence rate

In many cases, obtaining measurements or direct estimates of the incidence rate ζ_t, even in the form of reasonably accurate bounds of the form (8), might be difficult. For SEIR models in particular, this input corresponds to individuals moving to the exposed stage of the disease, where they might not yet experience symptoms, and hence are often not yet diagnosed. In this case, we propose a method for obtaining bounds (8) together with the state estimates. The drawback of this approach however is that it introduces a delay of two periods in the release of the state estimate.

From Equation (3), we get

$$y_{t+2} = Cx_{t+2} + v_{t+2}, \tag{15}$$

$$y_{t+2} = CA^2x_t + CAF\zeta_t + CF\zeta_{t+1} + CAH\mu + CH\mu + v_{t+2}. \tag{16}$$

The structure of the model (1)–(2) implies that $CF = 0$, $CH = 0$, $CAH = 0$ and $CAF = \alpha$. Hence, we obtain from (16)

$$\alpha\zeta_t = y_{t+2} - CA^2x_t - v_{t+2}.$$

Suppose now that we have the bounds $0 \leq \underline{x}_t \leq x_t \leq \bar{x}_t$ for some some $t \geq 0$ (for example $0 \leq \underline{x}_0 \leq x_0 \leq \bar{x}_0$). Notice that $\underline{A}^2 \leq A^2 \leq \bar{A}^2$, and $\underline{A}^2 \geq 0$ by Assumption 2.2. Hence, from (6) we get $\underline{A}^2\underline{x}_t \leq A^2x_t \leq \bar{A}^2\bar{x}_t$. Since the matrix C is also nonnegative, we then obtain the relations $\underline{\zeta}_t \leq \zeta_t \leq \bar{\zeta}_t$, for the same time period t, with

$$\begin{aligned}\underline{\zeta}_t &= \max\left\{0, \bar{\alpha}^{-1}\left(y_{t+2} - \bar{\nu} - C\bar{A}^2\bar{x}_t\right)\right\},\\ \bar{\zeta}_t &= \max\left\{0, \underline{\alpha}^{-1}\left(y_{t+2} - \underline{\nu} - C\underline{A}^2\underline{x}_t\right)\right\},\end{aligned} \tag{17}$$

where we also used the fact that $\zeta_t \geq 0$, by Proposition 2.1. The bounds (17) can then be used in the interval observer, as follows. Suppose that we have the state bounds $\underline{\chi}_t \leq x_t \leq \bar{\chi}_t$ for some time period t produced by the observer Equations (9), and hence $\underline{x}_t \leq x_t \leq \bar{x}_t$. This is true by hypothesis for $t = 0$, since $\underline{x}_0, \bar{x}_0$ are known. We then wait until period $t+2$ to obtain y_{t+2} and compute (17) to obtain $\underline{\zeta}_t, \bar{\zeta}_t$, which can now be used in the difference Equation (9) to produce $\underline{\chi}_{t+1}, \bar{\chi}_{t+1}, \underline{x}_{t+1}, \bar{x}_{t+1}$. Using the fact that $\underline{\zeta}_t \leq \zeta_t \leq \bar{\zeta}_t$, the argument of the proof of Theorem 3.1 then shows that $\underline{\chi}_{t+1} \leq x_{t+1} \leq \bar{\chi}_{t+1}$ and $\underline{x}_{t+1} \leq x_{t+1} \leq \bar{\chi}_{t+1}$. These state bounds therefore hold for all t by induction.

In conclusion, Theorem 3.1 remains valid when the bounds $\underline{\zeta}_t, \bar{\zeta}_t$ entering (9), instead of being known a priori, are obtained from (17) in parallel of the observer's iterations. The algorithm is then not causal since computing the state estimates for time $t+1$ requires the knowledge of y_{t+2}, introducing in practice a delay in the estimator. Note however that causality could be potentially recovered, at the price of a degradation in accuracy, by coupling the approach above with a method for predicting y_{t+2} from the measurements available up to time t, e.g. using a higher order sliding mode differentiator (Levant, Livne, & Yu, 2017). Details about the implementation of such schemes are beyond the scope of this paper and the characterisation of the resulting accuracy is left for future work.

We now turn to the problem of choosing appropriate gains $\underline{L}, \bar{L}$ for the interval observer. Theorem 3.1 guarantees that the errors (10) are nonnegative, in order to provide valid bounds on the state. In practice, we also want these errors to be bounded, and in fact as small as possible.

4. Selection of observer gains

In this section, we present a computational method to select the observer gains while minimising the errors $x - \underline{x}, \bar{x} - x$. The approach consists in computing the observer gains $\underline{L}$, $\bar{L}$ as solutions of an optimisation problem minimising the L_∞ gain from the disturbances to the estimation errors of interest (Briat & Khammash, 2016). Note that PHS design vaccination strategies to drive the total infected (exposed plus infectious) population asymptotically to zero (Alonso-Quesada et al., 2012; Alonso-Quesada, De la Sen, & Ibeas, 2017), and so for this reason and for concreteness we focus on estimating accurately the variable $s_t = x_{2,t} + x_{3,t} = E_t + I_t$. We define the upper $\bar{s}_t$ and lower $\underline{s}_t$ estimates as $\bar{s}_t = \bar{\chi}_{2,t} + \bar{\chi}_{3,t}$, $\underline{s}_t = \underline{\chi}_{2,t} + \underline{\chi}_{3,t}$. The corresponding estimation errors are $\underline{\xi}_t = s_t - \underline{s}_t = \underline{e}_{2,t} + \underline{e}_{3,t}$ and $\bar{\xi}_t = \bar{s}_t - s_t = \bar{e}_{2,t} + \bar{e}_{3,t}$. We then rewrite the error system (12) in the following form, considering $\underline{\xi}_t, \bar{\xi}_t$ as outputs

$$\begin{aligned}\underline{e}_{t+1} &= (\underline{A} - \underline{L}C)\underline{e}_t + \underline{\omega}_t + \underline{L}^+(\bar{\nu} - \nu_t) + \underline{L}^-(\nu_t - \underline{\nu})\\ \underline{\xi}_t &= \Phi\underline{e}_t,\end{aligned} \tag{18}$$

$$\begin{aligned}\bar{e}_{t+1} &= (\bar{A} - \bar{L}C)\bar{e}_t + \bar{\omega}_t + \bar{L}^-(\bar{\nu} - \nu_t) + \bar{L}^+(\nu_t - \underline{\nu}),\\ \bar{\xi}_t &= \Phi\bar{e}_t,\end{aligned} \tag{19}$$

for $\Phi = [0\ \ 1\ \ 1\ \ 0]$ and the following nonnegative signals

$$\begin{aligned}\underline{\omega}_t &= (A - \underline{A})x_t + F\zeta_t - F^+\underline{\zeta}_t + F^-\bar{\zeta}_t + H\mu - H\underline{\mu},\\ \bar{\omega}_t &= (\bar{A} - A)x_t + F^+\bar{\zeta}_t - F^-\underline{\zeta}_t - F\zeta_t + H\bar{\mu} - H\mu.\end{aligned}$$

We then aim to choose $\underline{L}$ minimising the L_∞-gain (peak-to-peak gain) from $[\underline{\omega}\ \ \bar{\nu} - \nu\ \ \nu - \underline{\nu}]^T$ to $\underline{\xi}$ in (18), and similarly for $\bar{L}$ and the L_∞-gain from $[\bar{\omega}\ \ \bar{\nu} - \nu\ \ \nu - \underline{\nu}]^T$ to $\bar{\xi}$ in (19). Note that these systems are nonnegative if the matrices $\underline{A} - \underline{L}C$ and $\bar{A} - \bar{L}C$ are nonnegative.

We start by recalling some definitions and general facts about the L_∞-gain of nonnegative systems, which has been studied in

Briat and Khammash (2016), Briat (2011) and Ebihara, Peaucelle, and Arzelier (2011). Denote $\mathcal{G}_0\omega := y$ the output signal of the system (7) when the initial condition is $x_0 = 0$ and the input is ω.

Definition 4.1: The L_∞-gain for the system (7) is defined as $\sup_{\|\omega\|_{L_\infty}=1} \|\mathcal{G}_0\omega\|_{L_\infty}$.

We then have the following theorem.

Theorem 4.1 (Briat & Khammash, 2016; Naghnaeian & Voulgaris, 2017)**:** *Let the matrix $A \in \mathbb{R}_+^{n\times n}$ and $B \in \mathbb{R}_+^{n\times q}$, $C \in \mathbb{R}_+^{p\times n}$, $D \in \mathbb{R}_+^{p\times q}$. For $\rho > 0$, the following statements are equivalent:*

(a) *The nonnegative LTI system* (7) *is asymptotically stable and its L_∞-gain is strictly less than ρ.*
(b) *The following Linear Programme (LP) is feasible:*

$$\text{There exists } \lambda \in \mathbb{R}^n_{>0} \quad \text{such that } \begin{bmatrix}(A-I_n)\lambda + B\mathbb{1}_q \\ C\lambda - \rho\mathbb{1}_p + D\mathbb{1}_q\end{bmatrix} < 0. \tag{20}$$

Theorem 4.1 forms the the basis for optimising the observer gains using linear programming, as shown in Proposition 4.1 below. Although this proposition can be obtained from the arguments presented by Briat and Khammash (2016), in particular their Proposition 19, we give below direct proofs, for completeness and clarity of exposition. First, we need the following result.

Theorem 4.2 (Farina & Rinaldi, 2000)**:** *Let the matrix $A \in \mathbb{R}^{n\times n}$ be Metzler. The following statements are equivalent:*

(a) *The matrix A is Hurwitz.*
(b) *There exists $h \in \mathbb{R}^n_{>0}$ such that $Ah < 0$.*
(c) *There exists $h \in \mathbb{R}^n_{>0}$ such that $h^T A < 0$.*

From this Theorem, we deduce a more convenient version of the LP (20) when the system (7) has a single output and $D = 0$.

Theorem 4.3: *Consider the system* (7) *and let the matrix $A \in \mathbb{R}_+^{n\times n}$ and $B \in \mathbb{R}_+^{n\times q}$, $C \in \mathbb{R}_+^{1\times n}$, $D = 0$. For $\rho > 0$, the following statements are equivalent:*

(a) *The nonnegative LTI system* (7) *is asymptotically stable and its L_∞-gain is strictly less than ρ.*
(b) *The following LP is feasible: there exists a diagonal matrix Ω with positive diagonal entries such that*

$$\mathbb{1}_{n+1}^T \begin{bmatrix}\Omega(A-I_n) & \Omega B\mathbb{1}_q \\ C & -\rho\end{bmatrix} < 0. \tag{21}$$

Proof: When $p = 1$ and $D = 0$, we can equivalently rewrite the condition (20) as

$$\text{There exists } \lambda \in \mathbb{R}^n_{>0} \quad \text{such that } \begin{bmatrix}A-I_n & B\mathbb{1}_q \\ C & -\rho\end{bmatrix}\begin{bmatrix}\lambda \\ 1\end{bmatrix} < 0. \tag{22}$$

In (22), the matrix in the left-hand side is Metzler since $A \in \mathbb{R}_+^{n\times n}$, $B \in \mathbb{R}_+^{n\times q}$ and $C \in \mathbb{R}_+^{1\times n}$. From Theorem 4.2, we can replace the LP (22) by

$$\text{There exists } \eta \in \mathbb{R}^{n+1}_{>0} \quad \text{such that } \eta^{\mathrm{T}}\begin{bmatrix}A-I_n & B\mathbb{1}_q \\ C & -\rho\end{bmatrix} < 0.$$

We can normalise the vector η in order to obtain the following LP

$$\text{There exists } \nu \in \mathbb{R}^n_{>0} \quad \text{such that } \begin{bmatrix}\nu \\ 1\end{bmatrix}^{\mathrm{T}}\begin{bmatrix}A-I_n & B\mathbb{1}_q \\ C & -\rho\end{bmatrix} < 0. \tag{23}$$

Then, we write $\nu = \Omega\mathbb{1}_n$ with $\Omega = \mathrm{diag}\{\nu\}$ and using the identity

$$\begin{bmatrix}\nu \\ 1\end{bmatrix}^T = \mathbb{1}_{n+1}^T\begin{bmatrix}\Omega & 0 \\ 0 & 1\end{bmatrix}$$

we immediately deduce (21) from (23). ■

We can now consider the problem of choosing the gain matrices $\bar{L}, \underline{L}$ to minimise the L_∞-gains of the error dynamics. First, we have the following proposition.

Proposition 4.1: *Let the Assumptions* 2.1 *and* 2.2 *be satisfied and let the matrices $\underline{A} - \underline{L}C$ and $\bar{A} - \bar{L}C$ be nonnegative. The L_∞-gain of the system* (18) *with inputs $[\underline{\omega}^{\mathrm{T}} \ \bar{\nu} - \nu \ \nu - \underline{\nu}]^{\mathrm{T}}$ and output $\underline{\xi}$ is smaller than $\underline{\rho} > 0$ if there exists a diagonal matrix $\underline{\Omega}$ with positive diagonal entries such that*

$$\mathbb{1}_5^{\mathrm{T}}\begin{bmatrix}\underline{\Omega}(\underline{A} - I_4 - (\underline{L}^+ - \underline{L}^-)C) & \underline{\Omega}(\mathbb{1}_4 + \underline{L}^+ + \underline{L}^-) \\ \Phi & -\underline{\rho}\end{bmatrix} < 0. \tag{24}$$

The L_∞-gain of the system (19) *with inputs $[\bar{\omega}^{\mathrm{T}} \ \bar{\nu} - \nu \ \nu - \underline{\nu}]^{\mathrm{T}}$ and output $\bar{\xi}$ is smaller than $\bar{\rho} > 0$ if there exists a diagonal matrix $\bar{\Omega}$ with positive diagonal entries such that*

$$\mathbb{1}_5^{\mathrm{T}}\begin{bmatrix}\bar{\Omega}(\bar{A} - I_4 - (\bar{L}^+ - \bar{L}^-)C) & \bar{\Omega}(\mathbb{1}_4 + \bar{L}^- + \bar{L}^+) \\ \Phi & -\bar{\rho}\end{bmatrix} < 0. \tag{25}$$

Furthermore, when the conditions (24)–(25) *hold, we get $\underline{\chi}, \bar{\chi} \in \mathcal{L}_\infty^4$ and so $\underline{x}, \bar{x} \in \mathcal{L}_\infty^4$.*

Proof: By definition, we have $\underline{L} = \underline{L}^+ - \underline{L}^-$ and $\bar{L} = \bar{L}^+ - \bar{L}^-$. Since the error systems (18)–(19) are nonnegative, we get immediately the LPs (24) and (25) from (21).

Moreover, when these conditions are satisfied, the error systems (18)–(19) are stable by Theorem 4.1, and this implies that $\underline{\chi}, \bar{\chi} \in \mathcal{L}_\infty^4$ since $x \in \mathcal{L}_\infty^4$ by Proposition 2.1. ■

Optimizing over $\underline{L}, \bar{L}$ can then be performed as follows.

Theorem 4.4: *Let the Assumption* 2.2 *be satisfied. Consider the following LPs with variables $\underline{\Omega}, \bar{\Omega} \in \mathbb{R}^{4\times 4}$ (diagonal matrices),*

$U_1, U_2, U_3, U_4 \in \mathbb{R}^4_+$, *and* $\underline{\rho}, \bar{\rho} \in \mathbb{R}_+$,

$$\inf_{\underline{\rho},\underline{\Omega},U_1,U_2} \quad \underline{\rho}, \tag{26}$$

$$s.t. \quad \mathbb{1}_5^{\mathrm{T}} \begin{bmatrix} \underline{\Omega}(\underline{A} - I_4) - (U_1 - U_2)C & \underline{\Omega}\mathbb{1}_4 + U_1 + U_2 \\ \Phi & -\underline{\rho} \end{bmatrix} < 0 \tag{27}$$

$$\underline{\Omega}\underline{A} - (U_1 - U_2)C > 0, \tag{28}$$

$$\underline{\Omega}\mathbb{1}_4 > 0, \tag{29}$$

$$U_1 \geq 0, \quad U_2 \geq 0, \quad \underline{\rho} > 0, \tag{30}$$

and

$$\inf_{\bar{\rho},\bar{\Omega},U_3,U_4} \quad \bar{\rho}, \tag{31}$$

$$s.t. \quad \mathbb{1}_5^{\mathrm{T}} \begin{bmatrix} \bar{\Omega}(\bar{A} - I_4) - (U_3 - U_4)C & \bar{\Omega}\mathbb{1}_4 + U_3 + U_4 \\ \Phi & -\bar{\rho} \end{bmatrix} < 0, \tag{32}$$

$$\bar{\Omega}\bar{A} - (U_3 - U_4)C > 0, \tag{33}$$

$$\bar{\Omega}\mathbb{1}_4 > 0, \tag{34}$$

$$U_3 \geq 0, \quad U_4 \geq 0, \quad \bar{\rho} > 0. \tag{35}$$

Then, we can compute nonnegative gains for the interval observer (9) *that minimise the* L_∞*-gains of the error systems* (18) *and* (19) *by taking*

$$\underline{L}^\star = (\underline{\Omega}^\star)^{-1}(U_1^\star - U_2^\star), \quad \bar{L}^\star = (\bar{\Omega}^\star)^{-1}(U_3^\star - U_4^\star),$$

where $\underline{\Omega}^\star, U_1^\star, U_2^\star$ *and* $\bar{\Omega}^\star, U_3^\star, U_4^\star$ *are respectively optimal solutions of the problems* (26)–(30) *and* (31)–(35).

Proof: The linear inequalities (27) and (32) are obtained by substituting $U_1 = \underline{\Omega}\underline{L}^+, U_2 = \underline{\Omega}\underline{L}^-$ and $U_3 = \bar{\Omega}\bar{L}^+, U_4 = \bar{\Omega}\bar{L}^-$ in (24)–(25). The constraints (28) and (33) are equivalent to saying that the matrices $(\bar{A} - \bar{L}C)$ and $(\underline{A} - \underline{L}C)$ are nonnegative. ■

Remark 4.1: Note that the LPs of Theorem 4.4 provide the observer matrices $\underline{L}, \bar{L}$ and the corresponding L_∞-gains at the same time, rather than following Remark 15 in Briat and Khammash (2016), which suggests to first solve the LPs for $\Phi = \mathbb{1}_n^T$ to obtain $\underline{L}, \bar{L}$ and then compute the L_∞-gain values from Theorem 4.1.

One can solve the optimisation problems (26)–(30) and (31)–(35) very efficiently with standard linear programming solvers, such as MOSEK (Andersen & Andersen, 2000), which uses interior-point methods (Nocedal & Wright, 2006), and Matlab's linprog or GLPK (GNU Linear Programming Kit Reference Manual, 2013), which use both interior-point methods and simplex algorithms (Nocedal & Wright, 2006). These solvers are commonly used with interfaces allowing users to enter the linear programmes in an intuitive form, such as AMPL (Fourer, Gay, & Kernighan, 2003), CVX (Grant & Boyd, 2014), or YALMIP (Löfberg, 2012).

5. On-line outbreak detection algorithm

In this section, we use the interval observer to design an on-line outbreak detection algorithm for the discrete-time SEIR model (1). We aim at computing a decision rule that determines whether a disease-free equilibrium of the discrete-time SEIR model (1) is locally asymptotically stable or not. An outbreak is detected when it can be concluded that the disease-free equilibrium is unstable.

First, we discuss the existence and stability of equilibrium points for the discrete-time SEIR model (1). The epidemic model (1) has two equilibrium points: a disease-free equilibrium point $P_1 = [1, 0, 0, 0]^{\mathrm{T}}$ and an endemic equilibrium point $P_2 = [S^\star, E^\star, I^\star, R^\star]^{\mathrm{T}}$ (see the Appendix for details about the computation of P_1 and P_2, as well as the formulas of $S^\star, E^\star, I^\star$ and $R^\star$). Define the following quantity

$$\mathcal{R}_0 := \frac{\alpha\beta}{(\mu + \gamma)(\mu + \alpha)}, \tag{36}$$

called the *basic reproduction ratio* (Alonso-Quesada et al., 2012, 2017).

Theorem 5.1 (Ibeas et al., 2015)**:** *Under Assumption* 2.1, *the disease-free equilibrium point* $P_1 = [1, 0, 0, 0]^{\mathrm{T}}$ *for the SEIR model* (1) *is locally asymptotically stable if* $\mathcal{R}_0 < 1$ *and unstable if* $\mathcal{R}_0 > 1$.

Theorem 5.1 states that $\mathcal{R}_0 = 1$ is a bifurcation value, with the stability properties of the disease-free equilibrium changing across $\mathcal{R}_0 = 1$. This can be used to derive conclusions about occurrence of an epidemic. Under Assumption 2.1, solutions of the discrete-time SEIR model (1) that start near the disease-free equilibrium P_1 tend towards P_1 as $t \to \infty$ if $\mathcal{R}_0 < 1$. On the other hand, if $\mathcal{R}_0 > 1$, either solutions of the discrete-time SEIR model (1) tend towards the endemic equilibrium point P_2 or some of the state variables oscillate (Ibeas et al., 2015, Theorem 3). Hence, if $\mathcal{R}_0 > 1$, the disease remains in the population in a constant or oscillatory way (Ibeas et al., 2015, Theorem 3) and the virus is able to invade the population (Rachah & Torres, 2017, Theorem 1).

We cannot use directly Theorem 5.1 to design a decision rule since the exact values of the parameters $\mu, \alpha, \gamma, \beta$ are not known and we have no information about the value of β. Instead, we use the following proposition.

Proposition 5.1: *Define the following quantities, at time* $t \geq 0$,

$$\begin{aligned} \mathcal{S}_t &:= \frac{\underline{\alpha}\underline{\beta}_t}{(\bar{\mu} + \bar{\gamma})(\bar{\mu} + \bar{\alpha})} - 1, \\ \mathcal{T}_t &:= 1 - \frac{\bar{\alpha}\bar{\beta}_t}{(\underline{\mu} + \underline{\gamma})(\underline{\mu} + \underline{\alpha})}, \end{aligned} \tag{37}$$

where the bounds $\underline{\beta}_t$ *and* $\bar{\beta}_t$ *are given by* (14).

- *If* $\mathcal{S}_t > 0$, *the disease-free equilibrium is unstable, the disease remains in the population.*
- *If* $\mathcal{T}_t > 0$, *solutions of the discrete-time SEIR model* (1) *that start near the disease-free equilibrium* P_1 *tend towards* P_1 *as* $t \to \infty$.

Proof: This result is an immediate consequence of Theorem 5.1 together with the bounds $\mathcal{S}_t \leq \mathcal{R}_0 - 1$ and $\mathcal{T}_t \leq 1 - \mathcal{R}_0$, which are deduced from (13). ■

We describe the final on-line outbreak detection decision rule in Algorithm 5. The main purpose of this decision rule is to provide a guarantee that $\mathcal{R}_0 > 1$ as soon as $\mathcal{S}_t > 0$. Note from (14) that $\underline{\beta}_t$ and hence $\mathcal{S}_t$ is non-decreasing (for the case where β is known to be constant), and so a decision reached at some time t cannot be contradicted at future times. The decision rule can provide confirmation of the occurrence of an outbreak, but since it can miss detections if the parameter bounds are conservative, it is not appropriate as an early warning system. However, the estimates provided by the interval observer (9) can still be useful for a variety of purposes, e.g. the design of vaccination campaigns.

Algorithm 1: On-line outbreak detection algorithm Given: 1. A nonlinear discrete-time SEIR epidemic model (1) where the transition rates α, γ, β and the natural birth rate μ are unknown time-invariant parameters and the bounds $\underline{\alpha}, \bar{\alpha}, \underline{\gamma}, \bar{\gamma}, \underline{\mu}, \bar{\mu}$ are given. 2. A set of measurement data $\{y_t\}$ corrupted by noise and the value of the bounds $\bar{\nu}, \underline{\nu}$. **At each time period t:** S1. Compute lower and upper bounds $\underline{\zeta}_t$ and $\bar{\zeta}_t$ for the time-varying unknown input ζ_t by using (8) or (17). S2. Determine interval estimates of the four compartment populations by using (9). S3. Compute the decision variables $\mathcal{S}_t$ and $\mathcal{T}_t$ with (37). S4. Take the decision d_t by using the following rule

$$d_t = \begin{cases} 0 & \text{if } \mathcal{T}_t > 0: \text{ solutions of the discrete-time SEIR} \\ & \quad \text{model (1) that start near} \\ & \quad \text{the disease-free equilibrium } P_1 \text{ tend towards } P_1 \\ & \quad \text{as } t \to \infty, \\ 1 & \text{if } \mathcal{S}_t > 0: \text{ the disease-free equilibrium is unstable,} \\ & \quad \text{the disease remains in the population,} \\ * & \text{no decision otherwise.} \end{cases}$$

Result: A sequence of decisions $\{d_t\}$. Stop as soon as $d_t \in \{0, 1\}$.

Remark 5.1: The interval estimation approach described in this paper can be extended to higher/lower order discrete-time epidemic models, when the model has more/less than 4 compartments, such as SEIR and SIR models with several parallel infective stages (Korobeinikov, 2009).

6. Simulations

We illustrate the performance of the proposed interval observer with a simulated example based on the 2014 outbreak of Ebola virus in West Africa (Rachah & Torres, 2016, 2017). The time period corresponds to one day and the following parameter values are considered for the SEIR model (1)–(2)

$$\beta = 0.4 \text{ per day}, \quad \alpha = 0.1887 \text{ per day},$$
$$\gamma = 0.1 \text{ per day}, \quad \mu = 0.0099 \text{ per day}.$$

Consider the case in which the parameters α, γ and μ deviate from the nominal values by $\sigma\%$, where σ is a given value.

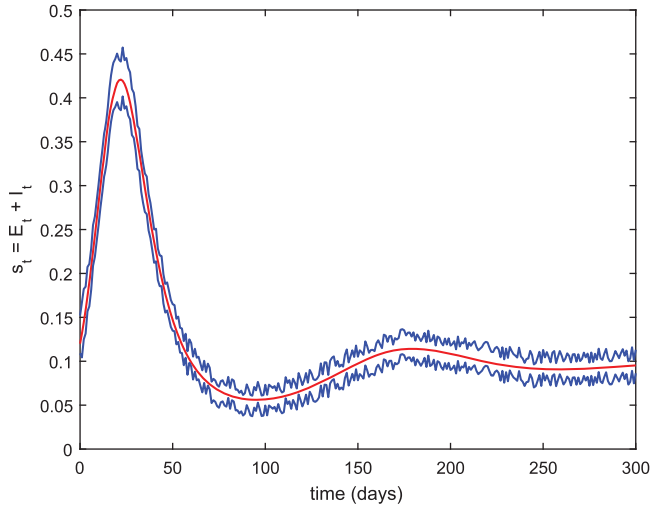

Figure 3. Evolution of the exposed plus infectious population s_t and the observed bounds when $\sigma = 7$.

We can then construct the matrices $\bar{A}$ and $\underline{A}$. The output measurements y_t are corrupted by a noise sequence ν_t consisting of independent and identically distributed random numbers sampled from a uniform distribution over the interval $[-V, V]$, with $V = 10^{-3}$. We assume here given bounds (8), with $\underline{\zeta}_t = \zeta_t - \varepsilon$ and $\bar{\zeta}_t = \zeta_t + \varepsilon$, where $\varepsilon = 10^{-4}$. The state's initial conditions are given by: $S_0 = 0.88$, $E_0 = 0.07$, $I_0 = 0.05$ and $R_0 = 0$. Let $\underline{x}_0 = x_0 - \theta_1$ and $\bar{x}_0 = x_0 + \theta_2$, with $\theta_1 = [0 \;\; 0.01 \;\; 0.001 \;\; 0]^{\mathrm{T}}$ and $\theta_2 = [0.05 \;\; 0.03 \;\; 0.002 \;\; 0.05]^{\mathrm{T}}$. To solve the optimisation problems of Theorem 4.4, we use the YALMIP toolbox for Matlab (Löfberg, 2012) together with the MOSEK solver.

When $\sigma = 7$, by using Theorem 4.4, we obtain the optimal interval observer gains

$$\underline{L}^\star = [0 \quad 0 \quad 0.8824 \quad 0.1213]^{\mathrm{T}},$$
$$\bar{L}^\star = [0 \quad 0 \quad 0.8978 \quad 0.1313]^{\mathrm{T}},$$

and we get the minimum L_∞ gains values $\underline{\rho}^\star = 7.4141$ and $\bar{\rho}^\star = 8.4052$. It can be seen onFigure 2, where the solid lines represent the true value of the states x_k, $1 \leq k \leq 4$, and the dashed lines are used for the interval estimates $\underline{x}_k$ and $\bar{x}_k$, that the interval estimates provided by (9) respect the ordering (11). Furthermore, we can deduce from Figure 2 that the disease is not eradicated from the population since $\underline{I}_t > 0$ at the end of the simulation.

We simulate now the case in which $V = 10^{-2}$ for the measurement noise, i.e. ν_t consists of independent and identically distributed random numbers sampled from a uniform distribution over the interval $[-10^{-2}, 10^{-2}]$. We see on Figure 3 that the maximum value of the exposed plus infectious population ($s_t = E_t + I_t$) is obtained at $t = 23$ days, time at which s_t, whose unknown but true value is 42.08%, is estimated by the interval observer to be between $\underline{s}_t = 40.3\%$ and $\bar{s}_t = 44.26\%$ of the total population. Hence, the time $t = 23$ days is critical.

By using Algorithm 5, we deduce from the results of simulations that $\mathcal{S}_t = 1.5413$, $\forall\, t \geq 0$, which implies that the disease-free equilibrium is unstable, and hence the disease remains in the population. The unknown true value of the basic reproduction ratio $\mathcal{R}_0$ is equal to $3.4582 > 1$, which implies also that

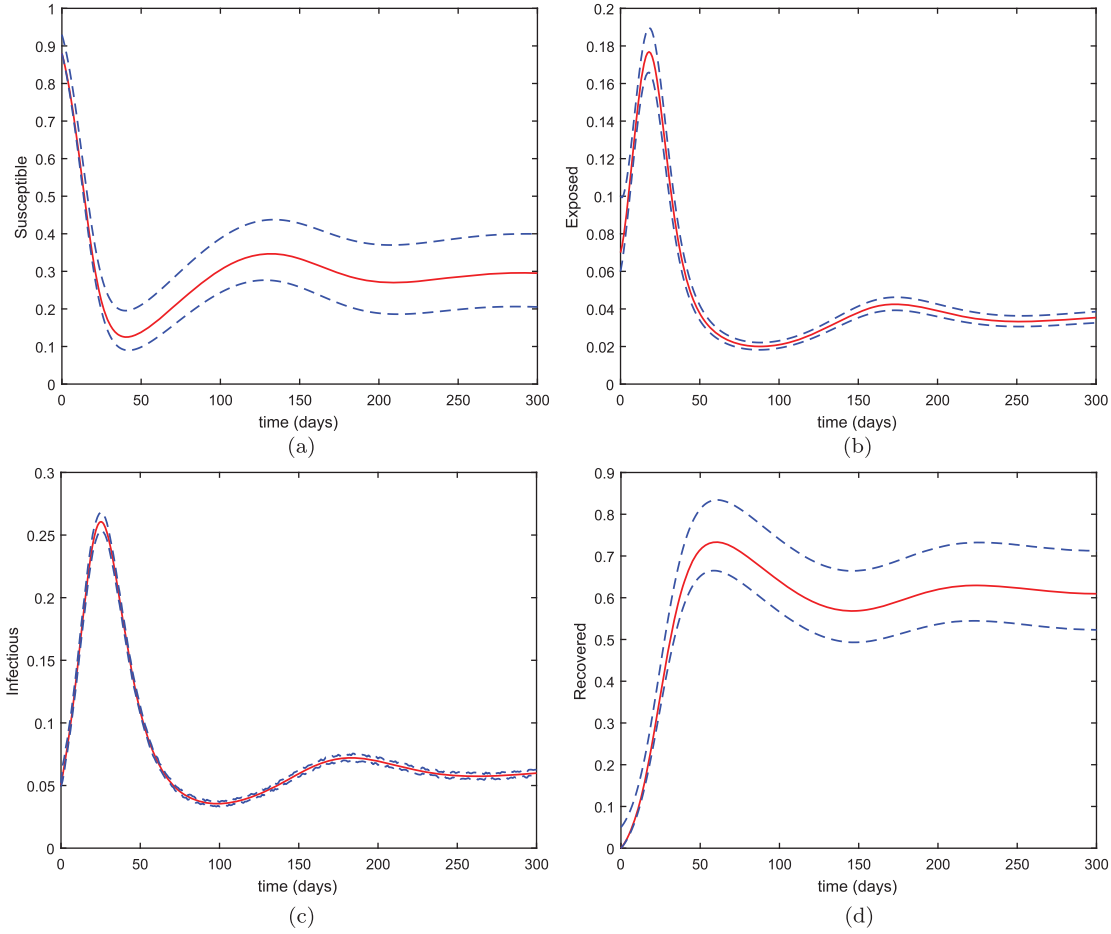

Figure 2. Evolution of the actual state and observed bounds when $\sigma = 7$. (a) Susceptible. (b) Exposed. (c) Infectious. (d) Recovered.

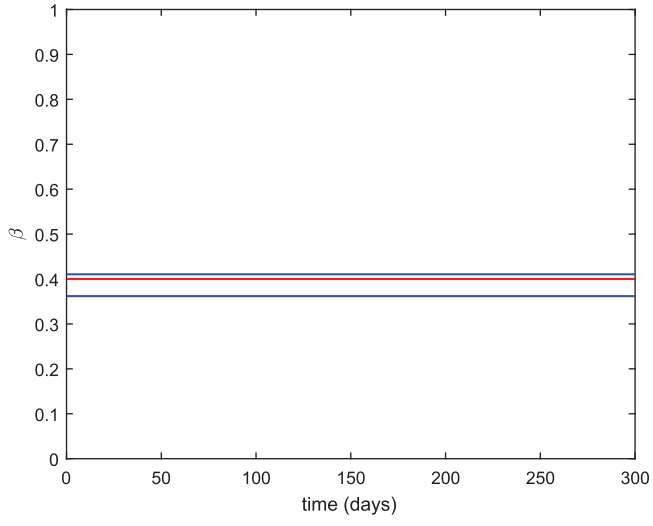

Figure 4. The unknown transmission rate β and the observed bounds when $\sigma = 7$.

the the disease-free equilibrium is unstable. Moreover, (14) provides bounds for the unknown transmission rate β shown on Figure 4.

For the rest of this section, we use the value $V = 10^{-2}$ for simulations. Let us consider now a situation in which the value of the parameter σ is 35. By using Theorem 4.4, we obtain the optimal interval observer gains

$$\underline{L}^{\star} = [0 \quad 0 \quad 0.8516 \quad 0.0795]^{\mathrm{T}},$$
$$\bar{L}^{\star} = [0 \quad 0 \quad 0.9286 \quad 0.1291]^{\mathrm{T}},$$

and we get the minimum L_∞ gains values $\underline{\rho}^{\star} = 6.0389$ and $\bar{\rho}^{\star} = 11.6485$. One can see on Figure 5, where the solid line represents the true value of the exposed plus infectious population $s_t = E_t + I_t$ and the dashed lines are used for the interval estimates $\underline{s}_t$ and $\bar{s}_t$, that the bounds respect the inclusion relation $\underline{s}_t \leq s_t \leq \bar{s}_t$, $\forall\, t \geq 0$.

By using Algorithm 5, we obtain that $\mathcal{S}_t = 0.1158$, $\forall\ t \geq 0$, which implies that the disease-free equilibrium is unstable. Consequently, the disease remains in the population. We conclude that the estimates of the observer for the Algorithm 5 are still useful when the parameters α, γ and μ deviate from the nominal values by 35%.

Consider finally a case in which the value of the parameter $\sigma = 70$. By using Theorem 4.4, we obtain the optimal interval observer gains

$$\underline{L}^{\star} = [0 \quad 0 \quad 0.8132 \quad 0.1076]^{\mathrm{T}},$$
$$\bar{L}^{\star} = [0 \quad 0 \quad 0.967 \quad 0.1977]^{\mathrm{T}},$$

and we get the minimum values $\underline{\rho}^{\star} = 4.9428$ and $\bar{\rho}^{\star} = 24.1354$. It can be inferred from Figure 6, that the bounds on the infected

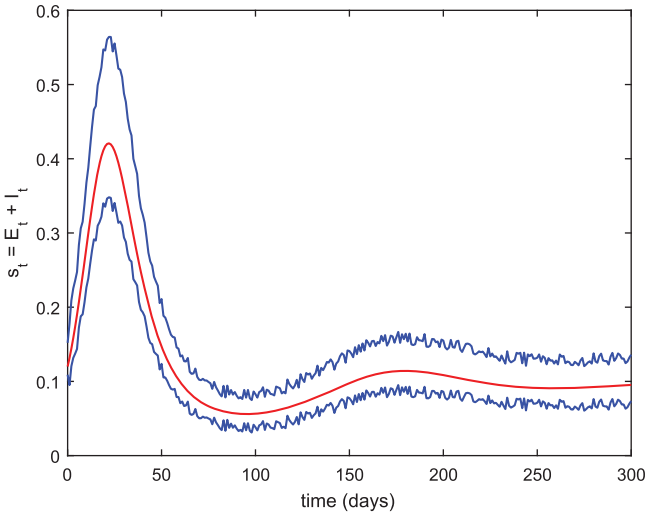

Figure 5. Evolution of the exposed plus infectious population s_t and the observed bounds when $\sigma = 35$.

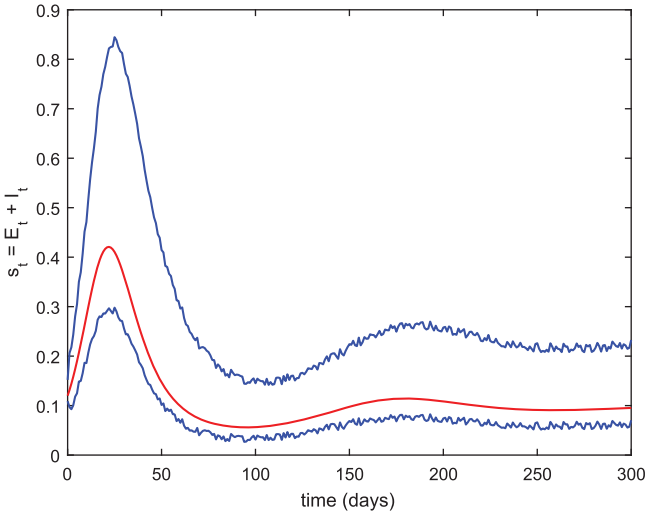

Figure 6. Evolution of the exposed plus infectious population s_t and the observed bounds when $\sigma = 70$.

population produced by the observer still respect the inclusion relation $\underline{s}_t \leq s_t \leq \bar{s}_t, \forall t \geq 0$. However, the accuracy of the estimates is worse than in the previous cases.Although the true value of $\mathcal{R}_0$ is greater than 1, Algorithm 5 does not allow us to detect the outbreak because $\mathcal{S}_t = -0.6752,\ \forall\ t \geq 0$ remains negative. Since the decision variable $\mathcal{T}_t = -66.0341,\ \forall\ t \geq 0$ remains negative, we cannot decide that no outbreak is present either, and hence our algorithm remains indecisive when the parameters α, γ and μ deviate from the nominal values by 70%. The Algorithm 5 is not appropriate as an early warning system when the deviation σ becomes too large. Nevertheless, the estimates provided by the interval observer (9) are still useful in this case.

7. Conclusion

We have considered the problem of state-observer design and on-line outbreak detection for a nonlinear discrete-time SEIR epidemic model in the presence of uncertainty. The proposed approach only requires sets of admissible values for the model's disturbances or uncertainties and parameters, and no information about the bounding values of the time-varying transmission rate from the 'susceptible' to the 'infected' stage. We have proposed a new approach for the estimation of the the four compartments' state, where an interval observer is used instead of a point-wise one. We have proposed an outbreak detection algorithm relying on the observer's estimates. In addition, we have computed optimal interval observer gains as solutions of linear programming problems. We have illustrated the performance of the proposed methodology in simulation. Future research can focus on performance evaluation using real data and interval observer design for more complex epidemiological models.

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ORCID

Kwassi H. Degue http://orcid.org/0000-0002-9745-8127
Jerome Le Ny http://orcid.org/0000-0002-3417-4135

References

Alonso-Quesada, S., De la Sen, M., Agarwal, R., & Ibeas, A. (2012, September). An observer-based vaccination control law for an SEIR epidemic model based on feedback linearization techniques for nonlinear systems. *Advances in Difference Equations*, *2012*(1), 191.

Alonso-Quesada, S., De la Sen, M., & Ibeas, A. (2017). On the discretization and control of an SEIR epidemic model with a periodic impulsive vaccination. *Communications in Nonlinear Science and Numerical Simulation*, *42*, 247–274.

Andersen, E. D., & Andersen, K. D. (2000). The Mosek interior point optimizer for linear programming: An implementation of the homogeneous algorithm. In H. Frenk, K. Roos, T. Terlaky, & S. Zhang (Eds.), *High performance optimization* (Vol. 33, pp. 197–232). Boston, MA: Springer.

Bichara, D., Cozic, N., & Iggidr, A. (2014, August). On the estimation of sequestered infected erythrocytes in plasmodium falciparum malaria patients. *Mathematical Biosciences and Engineering*, *11*(4), 741–759.

Bliman, P. A., & D'Avila Barros, B. (2016, September). Interval observer for SIR epidemic model subject to uncertain seasonality. *Proceedings of the 5th international symposium on positive systems theory and applications (POSTA 2016)*. Roma, Italy.

Briat, C. (2011, December). Robust stability analysis of uncertain linear positive systems via integral linear constraints: L_1- and L_∞-gain characterizations. *Proceedings of the 50th IEEE conference on decision and control (CDC)* (pp. 6337–6342). Orlando, Florida, USA.

Briat, C., & Khammash, M. (2016, December). Interval peak-to-peak observers for continuous- and discrete-time systems with persistent inputs and delays. *Automatica*, *74*(2016), 206–213.

Castillo-Chavez, C., Cooke, K., Huang, W., & Levin, S. A. (1989). The role of long incubation periods in the dynamics of HIV/AIDS. Part 1: Single populations models. *Journal of Mathematical Biology*, *27*, 373–398.

Chowell, G., Sattenspiel, L., Bansal, S., & Viboud, C. (2016, September). Mathematical models to characterize early epidemic growth: A review. *Physics of Life Reviews*, *18*, 66–97.

GNU Linear Programming Kit Reference Manual (2013, July). [Computer software manual].

Degue, K. H., Efimov, D., & Iggidr, A. (2016, June). Interval estimation of sequestered infected erythrocytes in malaria patients. *Proceedings of the 15th European control conference (ECC)*. Aalborg, Denmark.

Degue, K. H., Efimov, D., & Richard, J. P. (2018, July). Stabilization of linear impulsive systems under dwell-time constraints: Interval observer-based framework. *European Journal of Control*, *42*, 1–14.

Degue, K. H., & Le Ny, J. (2018, June). An interval observer for discrete-time SEIR epidemic models. *Proceedings of the American control conference (ACC)*. Milwaukee, WI, USA.

Diaby, M., Iggidr, A., & Sy, M. (2015, November). Observer design for a schistosomiasis model. *Mathematical Biosciences*, *269*, 17–29.

Dukic, V., Lopes, H. F., & Polson, N. G. (2012). Tracking epidemics with google flu trends data and a state-space SEIR model. *Journal of the American Statistical Association*, *107*(500), 1410–1426.

Ebihara, Y., Peaucelle, D., & Arzelier, D. (2011, December). L1 gain analysis of linear positive systems and its application. *Proceedings of the 50th IEEE conference on decision and control (CDC)* (pp. 4029–4035). Orlando, Florida, USA.

Efimov, D., Fridman, L., Raïssi, T., Zolghadri, A., & Seydou, R. (2012). Interval estimation for LPV systems applying high order sliding mode techniques. *Automatica*, *48*, 2365–2371. doi:10.1016/j.automatica.2012.06.073

Efimov, D., Perruquetti, W., Raïssi, T., & Zolghadri, A. (2013, July). On interval observer design for time-invariant discrete-time systems. *Proceedings of the 12th European control conference (ECC)*. Zurich, Switzerland.

Efimov, D., Polyakov, A., Fridman, E. M., Perruquetti, W., & Richard, J. P. (2015, July). Delay-dependent positivity: Application to interval observers. *Proceedings of the 14th European control conference (ECC)*. Linz, Austria.

Efimov, D., & Raïssi, T. (2015). Design of interval observers for uncertain dynamical systems. *Automation and Remote Control*, *76*, 1–29.

Efimov, D., Raïssi, T., & Zolghadri, A. (2013). Control of nonlinear and LPV systems: Interval observer-based framework. *IEEE Transactions on Automatic Control*, *58*(3), 773–778.

Fallas-Monge, J. J., Chavarría-Molina, J., & Alpízar-Brenes, G. (2016, November). Combinatorial metaheuristics applied to infectious disease models. Proceedings of the 36th IEEE central American and Panama convention (CONCAPAN XXXVI), San Jose, Costa Rica.

Farina, L., & Rinaldi, S. (2000). *Positive linear systems: Theory and applications*. New York: Wiley.

Feng, Z., Huang, W., & Castillo-Chavez, C. (2001, April). On the role of variable latent periods in mathematical models for Tuberculosis. *Journal of Dynamics and Differential Equations*, *13*(2), 425–452.

Fourer, R., Gay, D. M., & Kernighan, B. M. (2003). *AMPL: A modeling language for mathematical programming* (2nd ed.). Duxbury: The Scientific Press.

Gouzé, J., Rapaport, A., & Hadj-Sadok, M. (2000). Interval observers for uncertain biological systems. *Ecological Modelling*, *133*, 46–56.

Grant, M., & Boyd, S. (2014, March). *CVX: Matlab software for disciplined convex programming, version 2.1*. Retrieved from http://cvxr.com/cvx

Grassly, N. C., & Fraser, C. (2008, June). Mathematical models of infectious disease transmission. *Nature Reviews Microbiology*, *6*, 477–487.

Gucik-Derigny, D., Raïssi, T., & Zolghadri, A. (2015, June). A note on interval observer design for unknown input estimation. *International Journal of Control*, *89*(1), 25–37.

Hethcote, H. W. (2000). The mathematics of infectious diseases. *SIAM Review*, *42*(4), 599–653.

World Health Organization (2018, July). HIV/AIDS. *Global health observatory (GHO) data*. Retrieved from https://www.who.int/gho/hiv/en/

Hooker, G., Ellner, S. P., Roditi, L. D. V., & Earn, D. J. D. (2011, July). Parameterizing state-space models for infectious disease dynamics by generalized profiling: Measles in Ontario. *Journal of the Royal Society Interface*, *8*(60), 961–974.

Hu, Z., Teng, Z., & Jiang, H. (2012). Stability analysis in a class of discrete sirs epidemic models. *Nonlinear Analysis: Real World Applications*, *13*(5), 2017–2033.

Ibeas, A., de la Sen, M., Alonso-Quesada, S., & Zamani, I. (2015, April). Stability analysis and observer design for discrete-time SEIR epidemic models. *Advances in Difference Equations*, *2015*(1), 122.

Ibeas, A., de la Sen, M., Alonso-Quesada, S., Zamani, I., & Shafiee, M. (2014, December). Observer design for SEIR discrete-time epidemic models. *Proceedings of the 13th international conference on control automation robotics vision (ICARCV)* (pp. 1321–1326). Marina Bay Sands, Singapore.

Kaplan, E. H., Craft, D. L., & Wein, L. M. (2002, August). Emergency response to a smallpox attack: The case for mass vaccination. *Proceedings of the National Academy of Sciences of the United States of America*, *99*(16), 10935–10940.

Keeling, M. J., & Rohani, P. (2008). *Modeling infectious diseases in humans and animals*. Princeton and Oxford: Princeton University Press.

Kermack, W. O., & McKendrick, A. G. (1927). A contribution to the mathematical theory of epidemics. *Proceedings of the Royal Society of London A: Mathematical, Physical and Engineering Sciences*, *115*(772), 700–721.

Korobeinikov, A. (2009, January). Global properties of SIR and SEIR epidemic models with multiple parallel infectious stages. *Bulletin of Mathematical Biology*, *71*(1), 75–83.

Levant, A., Livne, M., & Yu, X. (2017). Sliding-mode-based differentiation and its application. *IFAC-PapersOnLine*, *50*(1), 1699–1704. (20th IFAC World Congress)

Löfberg, J. (2012). Automatic robust convex programming. *Optimization Methods and Software*, *27*(1), 115–129.

Mazenc, F., & Bernard, O. (2010). Asymptotically stable interval observers for planar systems with complex poles. *IEEE Transactions on Automatic Control*, *55*(2), 523–527.

Mazenc, F., & Bernard, O. (2011). Interval observers for linear time-invariant systems with disturbances. *Automatica*, *47*(1), 140–147.

Mazenc, F., Dinh, T. N., & Niculescu, S. I. (2012). Interval observers for discrete-time systems. *Proceedings of the 51th IEEE conference on decision and control (CDC)* (pp. 6755–6760). Hawaii.

Mazenc, F., Dinh, T. N., & Niculescu, S. I. (2013). Robust interval observers and stabilization design for discrete-time systems with input and output. *Automatica*, *49*, 3490–3497.

Mazenc, F., Dinh, T. N., & Niculescu, S. I. (2014). Interval observers for discrete-time systems. *International Journal of Robust and Nonlinear Control*, *24*, 2867–2890.

UNAIDS (2010). Methods for estimating HIV incidence. *UNAIDS quarterly update on HIV epidemiology / 1Q 2010*.

Mickens, R. E. (2007). Numerical integration of population models satisfying conservation laws: Nsfd methods. *Journal of Biological Dynamics*, *1*(4), 427–436.

Moisan, M., & Bernard, O. (2005, July). Interval observers for non monotone systems. application to bioprocess models. *Proceedings of the 16th IFAC triennal world congress*. Prague, Czech Republic.

Naghnaeian, M., & Voulgaris, P. G. (2017, June). Performance optimization over positive l_∞ cones. *Automatica*, *80*, 177–188.

Nocedal, J., & Wright, S. (2006). Numerical optimization (2nd ed., No. XXII). In P. Glynn & S. M. Robinson (Eds.) *Springer series in operations research*. New York: Springer-Verlag.

Rachah, A., & Torres, D. F. M. (2016, September). Dynamics and optimal control of Ebola transmission. *Mathematics in Computer Science*, *10*(3), 331–342.

Rachah, A., & Torres, D. F. M. (2017, May). *Analysis, simulation and optimal control of a SEIR model for Ebola virus with demographic effects*. arXiv preprint arXiv:1705.01079.

Raïssi, T., Efimov, D., & Zolghadri, A. (2012). Interval state estimation for a class of nonlinear systems. *IEEE Transactions on Automatic Control*, *57*(1), 260–265.

Robinson, E. I., Marzat, J., & Raïssi, T. (2017). Interval observer design for unknown input estimation of linear time-invariant discrete-time systems. *IFAC-PapersOnLine*, *50*(1), 4021–4026. (20th IFAC World Congress)

Rotondo, D., Cristofaro, A., Johansen, T. A., Nejjari, F., & Puig, V. (2017). State estimation and decoupling of unknown inputs in uncertain LPV systems using interval observers. *International Journal of Control*, *91*(8), 1–18.

Smith, H. (1995). *Monotone dynamical systems: An introduction to the theory of competitive and cooperative systems* (Vol. 41). Providence: AMS.

Vaillant, L., La Ruche, G., Tarantola, A., & Barboza, P. (2009, August). Epidemiology of fatal cases associated with pandemic H1N1 influenza 2009. *Eurosurveillance*, *14*(33), 1–6.

Yousfi, B., Raïssi, T., Amairi, M., Gucik-Derigny, D., & Aoun, M. (2017). Robust state estimation for singularly perturbed systems. *International Journal of Control*, *90*(3), 566–579.

Appendix. Determination of the equilibrium points of the epidemic model

We discuss here the existence and stability of equilibrium points for the discrete-time SEIR model (1). Recall that the model (3) is nonlinear since the unknown input ζ is the product of two state variables. We assume that the rates μ, α, β and γ are positive *constant* parameters. Any equilibrium point $[S, E, I, R]^{\mathrm{T}}$ is solution of the equations

$$-\beta SI + \mu - \mu S = 0, \tag{A1}$$

$$\beta SI - (\mu + \alpha)E = 0, \tag{A2}$$

$$\alpha E - (\mu + \gamma)I = 0, \tag{A3}$$

$$-\mu R + \gamma I = 0. \tag{A4}$$

By adding (A1) to (A2), we get

$$S = \frac{-(\mu + \alpha)E + \mu}{\mu}. \tag{A5}$$

From (A3), it follows that

$$I = \frac{\alpha E}{(\mu + \gamma)}, \tag{A6}$$

while from (A4), we get

$$R = \frac{\gamma I}{\mu}. \tag{A7}$$

It can now be inferred from (A5), (A6) and (A2) that

$$E\left(-(\mu + \alpha) + \frac{\beta\alpha(\mu - (\mu + \alpha)E)}{\mu(\mu + \gamma)}\right) = 0. \tag{A8}$$

Consequently, at an equilibrium either $E = 0$ or

$$E = E^* := \frac{\beta\alpha\mu - \mu(\mu + \gamma)(\mu + \alpha)}{\beta\alpha(\mu + \alpha)} = \frac{\mu}{(\mu + \alpha)} - \frac{\mu(\mu + \gamma)}{\beta\alpha}. \tag{A9}$$

For $E = 0$, it follows from (A5), (A6), (A7) that $S = 1$, $I = 0$ and $R = 0$, i.e. we obtain the disease-free equilibrium $P_1 = [1, 0, 0, 0]^{\mathrm{T}}$. For the other equilibrium with $E = E^*$, substituting (A9) in (A6), we get

$$I^\star = \frac{\alpha\mu}{(\mu + \gamma)(\mu + \alpha)} - \frac{\mu}{\beta}. \tag{A10}$$

It can be inferred from (A9) and (A5) that

$$S^\star = \frac{(\mu + \gamma)(\mu + \alpha)}{\beta\alpha}. \tag{A11}$$

Finally, substituting (A9) in (A6), we obtain

$$R^\star = \frac{\gamma}{\mu}\left(\frac{\alpha\mu}{(\mu + \gamma)(\mu + \alpha)} - \frac{\mu}{\beta}\right). \tag{A12}$$

The second equilibrium point is $P_2 = [S^\star, E^\star, I^\star, R^\star]^{\mathrm{T}}$.