



Published in final edited form as:

*J Differ Equ.* 2019 November ; 267(10): 5631–5661. doi:10.1016/j.jde.2019.06.002.

## Analysis of an epidemiological model structured by time-since-last-infection

Jorge A. Alfaro-Murillo<sup>a</sup>, Zhilan Feng<sup>b,\*</sup>, John W. Glasser<sup>c</sup>

<sup>a</sup>Center for Infectious Disease Modeling and Analysis, Yale School of Public Health, New Haven, CT, USA

<sup>b</sup>Department of Mathematics, Purdue University, West Lafayette, IN, USA

<sup>c</sup>National Center for Immunization and Respiratory Diseases, CDC, Atlanta, GA, USA

### Abstract

Modeling time-since-last-infection (TSLI) provides a means of formulating epidemiological models with fewer state variables (or epidemiological classes) and more flexible descriptions of infectivity after infection and susceptibility after recovery than usual. The model considered here has two time variables: chronological time ( $t$ ) and the TSLI ( $\tau$ ), and it has only two classes: never infected ( $\mathcal{N}$ ) and infected at least once ( $\mathcal{I}$ ). Unlike most age-structured epidemiological models, in which the  $i$  equation is formulated using  $\left(\frac{\partial}{\partial \tau} + \frac{\partial}{\partial t}\right)i(\tau, t)$ , ours uses a more general differential operator. This allows weaker conditions for the infectivity and susceptibility functions, and thus, is more generally applicable. We reformulate the model as an age dependent population problem for analysis, so that published results for these types of problems can be applied, including the existence and regularity of model solutions. We also show how other coupled models having two types of time variables can be stated as age dependent population problems.

### Keywords

Epidemiological model; Age-since-last-infection; Existence and uniqueness of solutions; Stability

## 1. Introduction

In many diseases with temporary immunity to reinfection, the infectivity of infected individuals and the susceptibility of recovered ones depends on their times since last infection. Ordinary differential equation systems can model such diseases by adding multiple state variables. Models structured by time-since-last-infection, considered in [1,2], can instead reduce the number of variables (or compartments) by using a single time variable for everyone who has been infected at least once. This approach differs from models structured by age or age-of-infection (see, e.g., [3–14]. See also the review in [2]).

\*Corresponding author. zfeng@math.purdue.edu (Z. Feng).

**Publisher's Disclaimer:** Disclaimer

**Publisher's Disclaimer:** The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention or other institutions with which they are affiliated.

The TSLI model considered by Alfaro-Murillo, et al. [2] is a two-dimensional system including only two variables:  $\mathcal{N}(t)$  for the number of never infected people at time  $t$ , and  $i(\tau, t)$  for the density of those who have been infected at least once, with  $\tau$  representing their times since last infection. Let  $D$  denote the differentiation operator defined as:

$$D \ell(\tau, t) = \lim_{h \rightarrow 0^+} \frac{\ell(\tau + h, t + h) - \ell(\tau, t)}{h}, \quad (1)$$

for any function  $\ell$  that is defined on a subset of  $\mathbb{R}_+ \times \mathbb{R}_+$  (where  $\mathbb{R}_+$  is the set of non-negative real numbers) and has its range defined in a Banach space. We show in Section 2.1 how the operator  $D\ell(\tau, t)$  is a generalization of the partial derivatives  $(\frac{\partial}{\partial \tau} + \frac{\partial}{\partial t})\ell(\tau, t)$ . The model reads:

$$\begin{aligned} \frac{d}{dt} \mathcal{N}(t) &= - \left[ \int_0^\infty T(v) \frac{i(v, t)}{\mathcal{P}(t)} dv \right] \mathcal{N}(t) - \mu \mathcal{N}(t) + \mu \mathcal{P}(t), \\ D i(\tau, t) &= - \left[ \int_0^\infty T(v) \frac{i(v, t)}{\mathcal{P}(t)} dv \right] k(\tau) i(\tau, t) - \mu i(\tau, t), \\ i(0, t) &= \left[ \int_0^\infty T(v) \frac{i(v, t)}{\mathcal{P}(t)} dv \right] \left[ \mathcal{N}(t) + \int_0^\infty k(\tau) i(\tau, t) d\tau \right], \\ \mathcal{N}(0) &= N_0, \quad i(\tau, 0) = i_0(\tau), \quad \mathcal{P}(t) = \mathcal{N}(t) + \int_0^\infty i(\tau, t) d\tau. \end{aligned} \quad (2)$$

There are two time variables in System (2). The first is  $t$ , representing chronological time (or simply time), whereas the second is  $\tau$ , representing the amount of time that has elapsed since a person's most recent infection, referred to as time since last infection (TSLI).  $\mathcal{N}(t)$  denotes the total number of individuals in the never-infected class at time  $t$  and  $i(\tau, t)$  denotes the density of individuals who have been infected at least once and have TSLI  $\tau$  at time  $t$ .

Thus, the quantity  $\int_{u_1}^{u_2} i(\tau, t) d\tau$  is the number of individuals at time  $t$  whose last infection was between  $u_1$  and  $u_2$  units of time ago, and  $\mathcal{P}(t)$  denotes the total population at time  $t$ . The only parameters considered in the model are the *per capita* natural death rate ( $\mu$ ) and those for the transmission rate ( $T(\tau)$ ) and infectivity ( $k(\tau)$ ) functions, the latter of which represents a factor of reduction in the probability of being infected as a function of TSLI.

A solution: of System (2) is a pair of function,  $(\mathcal{N}, i)$  with  $\mathcal{N}: \mathbb{R}_+ \rightarrow \mathbb{R}_+$  being differentiable and  $i: \mathbb{R}_+ \rightarrow L_+^1(\mathbb{R})$  being continuous (where  $L_+^1$  is the space of non-negative Lebesgue integrable functions, see Definition 3), that solve the equations in System (2) for all  $t \geq 0$  and almost everywhere (a.e.) for  $\tau \in (0, \infty)$ .

The analysis presented in [2] is for the case when the parameter functions  $T(\tau)$  and  $k(\tau)$  satisfy stronger conditions than here so that  $i(\tau, t)$  has continuous partial derivatives and

satisfies a partial differential equation. Specifically, the following system is considered in [2]:

$$\begin{aligned} \frac{d}{dt}\mathcal{N}(t) &= - \left[ \int_0^\infty T(u) \frac{i(u,t)}{P} du \right] \mathcal{N}(t) - \mu \mathcal{N}(t) + \mu P, \\ \left( \frac{\partial}{\partial \tau} + \frac{\partial}{\partial t} \right) i(\tau, t) &= - \left[ \int_0^\infty T(u) \frac{i(u,t)}{P} du \right] k(\tau) i(\tau, t) - \mu i(\tau, t), \end{aligned} \quad (3a)$$

with conditions:

$$\begin{aligned} i(0, t) &= \left[ \int_0^\infty T(u) \frac{i(u,t)}{P} du \right] \left[ \mathcal{N}(t) + \int_0^\infty k(\tau) i(\tau, t) d\tau \right], \\ \mathcal{N}(0) = N_0, \quad i(\tau, 0) = i_0(\tau), \quad \text{where } P &= \mathcal{N}(t) + \int_0^\infty i(\tau, t) d\tau. \end{aligned} \quad (3b)$$

In this paper, we present an analysis of the general model (System (2)) with weaker conditions on  $T$  and  $k$ , under which the solution  $i(\tau, t)$  may not have continuous partial derivatives (see Theorem 4). This may allow the model to have broader applications. The approach used to study the general model is to formulate the system as an age dependent population (ADP) problem. We use the term ‘‘ADP problem’’ to refer to a particular model formulation for age-dependent populations (specified in Section 2), for which theoretical results are available, including the existence, uniqueness, positivity, and regularity of solutions. We first introduce another formulation of general model, termed a *coupled model*, or a model with two time variables (see Section 2.2). We illustrate how coupled models can be stated as ADP problems in general, so that all theory developed for ADP problems can be applied to coupled models.

The paper is organized as follows. In Section 2, we demonstrate the link between ADP problems and models with two time variables (or coupled models). Properties of solutions to the generic ADP problem are also discussed in this section, and the results are applied to the reformulation of the general model as a coupled model. Example reformulations of other models as coupled models, as well as the relation between  $D_{\ell}(\tau, t)$  and  $\left( \frac{\partial}{\partial \tau} + \frac{\partial}{\partial t} \right) \ell(\tau, t)$ , are also presented. Application of results in Section 2 to the general model is presented in Section 3, including the existence and regularity of model solutions. Section 4 includes a discussion of the results.

## 2. Links between ADP problems and coupled models

In this section, we present solutions to a generic ADP problem and formulate a coupled model as an ADP problem. Then solution properties of the coupled model are discussed by applying results for ADP problems. Example reformulations of other models as coupled models are also presented.

## 2.1. The operator D and its relation to a transport equation

Many age-structured epidemic models are stated in terms of a transport partial differential equation of the form

$$\left(\frac{\partial}{\partial \tau} + \frac{\partial}{\partial t}\right) \ell(\tau, t) = f(\ell), \quad (4)$$

where  $f$  is a given function. The  $i$  equation in System (3) is also in this form. Next we explain why we state the coupled problem in Section 2.3 with the operator D instead.

Classical solutions of a partial differential equation such as Equation (4) are  $C^1$  functions (i.e., have continuous partial derivatives). If  $\ell \in C^1$ , we can show that  $D\ell(\tau, t)$  exists and satisfies

$$D\ell(\tau, t) = \left(\frac{\partial}{\partial \tau} + \frac{\partial}{\partial t}\right) \ell(\tau, t).$$

Indeed, suppose that  $\ell : \mathbb{R}_+ \times [0, \bar{t}) \rightarrow \mathbb{R}^2$  is a  $C^1$  function in a neighborhood of  $(\tau, t)$ . Let  $\epsilon > 0$ . There exists  $\delta > 0$  such that if  $0 < h < \delta$  then

$$\left| \frac{\partial}{\partial \tau} \ell(\tau, t+h) - \frac{\partial}{\partial \tau} \ell(\tau, t) \right| < \frac{\epsilon}{5},$$

$$\left| \frac{\ell(\tau, t+h) - \ell(\tau, t)}{h} - \frac{\partial}{\partial t} \ell(\tau, t) \right| < \frac{\epsilon}{5},$$

and  $\frac{\partial}{\partial \tau} \ell(\tau, t+h)$  exists. Given any such  $h > 0$ , there exists  $h' > 0$  such that

$$\left| \frac{\ell(\tau+h, t+h) - \ell(\tau+h', t+h)}{h} \right| < \frac{\epsilon}{5},$$

$$\left| \frac{\ell(\tau+h', t+h) - \ell(\tau, t+h)}{h'} - \frac{\partial}{\partial \tau} \ell(\tau, t+h) \right| < \frac{\epsilon}{5},$$

$$\left| \frac{\ell(\tau, t+h)}{h'} - \frac{\ell(\tau, t+h)}{h} \right| < \frac{\epsilon}{5}.$$

Therefore,

$$\begin{aligned}
 & \left| \frac{\ell(\tau+h, t+h) - \ell(\tau, t)}{h} - \left( \frac{\partial}{\partial \tau} \ell(\tau, t) + \frac{\partial}{\partial t} \ell(\tau, t) \right) \right| \\
 & \leq \left| \frac{\ell(\tau+h, t+h) - \ell(\tau+h', t+h)}{h} - \frac{\ell(\tau+h', t+h) - \ell(\tau, t)}{h'} \right| + \left| \frac{\ell(\tau, t+h) - \ell(\tau, t)}{h} - \frac{\partial}{\partial t} \ell(\tau, t) \right| \\
 & + \left| \frac{\ell(\tau+h', t+h) - \ell(\tau, t+h)}{h'} - \frac{\partial}{\partial \tau} \ell(\tau, t+h) \right| + \left| \frac{\ell(\tau, t+h) - \ell(\tau, t)}{h} - \frac{\partial}{\partial t} \ell(\tau, t) \right| \\
 & + \left| \frac{\partial}{\partial \tau} \ell(\tau, t+h) - \frac{\partial}{\partial \tau} \ell(\tau, t) \right| \\
 & < \epsilon,
 \end{aligned}$$

for any  $0 < h < \delta$ . It follows that  $D\ell(\tau, t)$  exists and is equal to  $\left(\frac{\partial}{\partial \tau} + \frac{\partial}{\partial t}\right)\ell(\tau, t)$ . Therefore, any solution to a transport equation such as Equation (4) will also be a solution to the same equation with the operator  $D$ .

The solution function  $i(\tau, t)$  can be  $C^1$  if adequate conditions are imposed on  $T$  and  $k$  (see Theorem 4). However under weaker conditions on  $T$  and  $k$  we can obtain solutions for  $i$  that are not  $C^1$  and still get information about the number of infected individuals with TSLI between  $u_1$  and  $u_2$  as  $\int_{u_1}^{u_2} i(\tau, t) d\tau$  does not change if the  $i$  function has different values on a set with measure zero in  $\tau$ . As we do not want to impose extra conditions for  $T$  and  $k$  to leave the application of the general model as broad as possible, we will consider the general operator  $D$  and solution functions  $i$  to be a continuous  $L^1$ -valued function with domain in  $[0, \infty)$ , that is, for each non-negative  $t$  the function  $i(\cdot, t)$  defined as  $\tau \mapsto i(\tau, t)$  is  $L^1$ .

### 2.2. The generic ADP problem

We define an ADP problem as described in [15, Chapter 1]. An ADP problem is described by the following three equations:

$$D \ell(\tau, t) = G(\ell(\cdot, t))(\tau), \tag{5a}$$

$$\ell(0, t) = F(\ell(\cdot, t)), \tag{5b}$$

$$\ell(\tau, 0) = \phi(\tau), \tag{5c}$$

with  $G: L^1 \rightarrow L^1$ ,  $F: L^1 \rightarrow \mathbb{R}^n$ , and  $\phi \in L^1$ . In ADP problems Equations (5a), (5b) and (5c) are termed the Balance Law, the Birth Law, and the initial condition, respectively.

For ease of presentation, we introduce the following definition:

**Definition 1.** For  $\bar{t} > 0$ , let  $L_{\bar{t}} = \mathcal{C}([0, \bar{t}]; L^1)$  be the Banach space of continuous  $L^1$ -valued functions on  $[0, \bar{t}]$  with the norm:

$$\| \ell \|_{L_{\bar{t}}} = \sup_{0 \leq t \leq \bar{t}} \| \ell(t) \|,$$

where  $\ell \in L_{\bar{t}}$ .

In a natural way, an element of  $L_{\bar{t}}$  can be identified with an element of  $L^1((0, \infty) \times (0, \bar{t}); \mathbb{R}^n)$  [15, Lemma 2.1], which allows us to use the same symbol for both; i.e.,

$$\ell(t)(\tau) = \ell(\cdot, t)\tau = \ell(\tau, t),$$

where  $0 \leq t \leq \bar{t}$ , and a.e.  $\tau > 0$ .

**Definition 2.** Let  $\bar{t} > 0$ . Let  $F: L^1 \rightarrow \mathbb{R}^n$ ,  $G: L^1 \rightarrow L^1$ , and  $\phi \in L^1$ . We say that a function  $\ell \in L_{\bar{t}}$  is a solution of the ADP problem for the initial distribution  $\phi$  on  $[0, \bar{t}]$  provided that  $\ell$  satisfies the equations in System (5) for all  $t \in [0, \bar{t}]$  and a.e. for  $\tau \in (0, \infty)$ .

If we assume that  $\ell$  is a solution of the ADP problem on  $[0, \bar{t}]$  and  $c \in \mathbb{R}$ , then we can define a “cohort function”:

$$w_c(t) = \ell(t + c, t)$$

for every  $t_c \leq t \leq \bar{t}$ , where  $t_c = \max\{-c, 0\}$ . Using Equation (5a), we can show that the right derivative of this function exists and satisfies

$$w'_c(t+) = \lim_{h \rightarrow 0^+} \frac{w_c(t+h) - w_c(t)}{h} = G(\ell(\cdot, t))(t+c) \tag{6}$$

a.e. for  $t \in (t_c, \bar{t})$ . If  $G$  is Lipschitz on norm-balls of  $L^1$ , the function  $G(\ell(\cdot, t))(\tau)$  is integrable as a function from  $(0, \infty) \times (0, \bar{t})$  to  $\mathbb{R}^n$  [15, Lemma 2.2], and so  $w'_c(t+)$  is also integrable in  $[0, \bar{t}]$ . Therefore, we have that any function of the form,

$$t \mapsto C + \int_{t_c}^t w'_c(s+) ds,$$

has a derivative equal to  $w'_c(t+)$  a.e.  $t \in (t_c, \bar{t})$  [16, Chapter 5, Theorem 10]. So, we can integrate Equation (6) and obtain

$$w_c(t) = \begin{cases} w_c(t-\tau) + \int_{t-\tau}^t G(\ell(\cdot, s))(s+c) ds & \text{a. e. } \tau \in (0, t), \\ w_c(0) + \int_0^t G(\ell(\cdot, s))(s+c) ds & \text{a. e. } \tau \in (t, \infty). \end{cases}$$

Substituting  $c = \tau - t$ , and using Equation (5b), we obtain the integral equation:

$$\ell(\tau, t) = \begin{cases} F(\ell(\cdot, t - \tau)) + \int_{t-\tau}^t G(\ell(\cdot, s))(s + \tau - t) ds & \text{a. e. } \tau \in (0, t), \\ \phi(\tau - t) + \int_0^t G(\ell(\cdot, s))(s + \tau - t) ds & \text{a. e. } \tau \in (t, \infty). \end{cases} \quad (7)$$

In conclusion, if  $G$  is Lipschitz on norm-balls of  $L^1$ , every solution of the ADP problem satisfies Equation (7). Clearly, not every solution of Equation (7) is a solution of the ADP problem, because the function  $\ell$  in Equation (7) need not be differentiable in the sense of the operator  $D$ . The converse is true under certain conditions (see Theorem 2.9 in [15] and Theorem 2.3 in [17]), a fact that we will use later.

If both functions  $F$  and  $G$  are Lipschitz on norm-balls of  $L^1$ , then a function  $\ell$  satisfies Equation (7), for  $t \in [0, \bar{t}]$ , if and only if  $\ell$  is a *mild solution* of the ADP problem (See Theorem 2.2 in [15]) according to Definitions 4–6 in the Appendix.

We define an *equilibrium solution* for the ADP problem in Definition 7 of the Appendix. A very important result in the theory of ADP problems is that, if  $F: L^1_+ \rightarrow \mathbb{R}^n_+$  and  $G: L^1_+ \rightarrow L^1$  are Lipschitz on norm-balls of  $L^1$  and there exists a function  $c_3$  that satisfies (ii) in the proof of part (c) for Proposition 2, then  $\phi$  is an equilibrium solution of the ADP problem if and only if  $\phi$  is absolutely continuous with the properties that  $\phi' \in L^1$ ,  $\phi' = G(\phi)$ , and  $\phi(0) = F(\phi)$  [15, Proposition 4.1]. We will make use of this result later.

### 2.3. General formulation of coupled models

In this section, we focus on models consisting of both equations that depend only on time  $t$  and variables that depend on both time  $t$  and  $\tau$  (System (2) is an example). For ease of reference, we refer to this type of model as a coupled model. Several other examples are provided in Section 2.6. A general formulation for such a system is given below.

Let  $X(t)$  denote the vector of functions that depend only on  $t$ , and let  $y(\tau, t)$  denote the vector of functions that depend on both  $t$  and  $\tau$ . The general coupled model has the following form:

$$\begin{aligned} \frac{dX(t)}{dt} &= F_x(X(t), y(\cdot, t)) + M_x(X(t), y(\cdot, t))X(t), \\ Dy(\tau, t) &= G_y(X(t), y(\cdot, t))(\tau), \end{aligned} \quad (8a)$$

with boundary and initial conditions

$$y(0, t) = F_y(X(t), y(\cdot, t)), \quad X(0) = X_0, \quad y(\cdot, 0) = \phi_y, \quad (8b)$$

where  $F_x: \mathbb{R}^m \times L^1(\mathbb{R}^k) \rightarrow \mathbb{R}^m$ ,  $M_x: \mathbb{R}^m \times L^1(\mathbb{R}^k) \rightarrow \mathcal{B}(\mathbb{R}^m, \mathbb{R}^m)$ ,  $G_y: \mathbb{R}^m \times L^1(\mathbb{R}^k) \rightarrow L^1(\mathbb{R}^k)$ ,  $F_y: \mathbb{R}^m \times L^1(\mathbb{R}^k) \rightarrow \mathbb{R}^k$ ,  $X_0 \in \mathbb{R}^m$  and  $\phi_y \in L^1(\mathbb{R}^k)$ . The operator  $D$  is defined in Equation (1).

A solution to System (8) is a set of functions  $X(t)$  and  $y(\tau, t)$  that satisfy the equations for time  $t \in [0, \bar{t}]$  for some  $\bar{t} > 0$  and a.e. for  $\tau \in (0, \infty)$ . An equilibrium of the system is a solution that is constant on time  $t$ .

**2.4. From coupled models to ADP problems and solution properties**

We can reformulate the coupled model (System (8)) as an ADP problem described in System (5) by defining the functions  $F: L^1(\mathbb{R}^{m+k}) \rightarrow \mathbb{R}^{m+k}$  and  $G: L^1(\mathbb{R}^{m+k}) \rightarrow L^1(\mathbb{R}^{m+k})$  as

$$F \begin{pmatrix} \phi_x \\ \phi_y \end{pmatrix} = \begin{pmatrix} F_x \left( \int_0^\infty \phi_x(\tau) d\tau, \phi_y \right) \\ F_y \left( \int_0^\infty \phi_x(\tau) d\tau, \phi_y \right) \end{pmatrix}, \tag{9a}$$

$$G \begin{pmatrix} \phi_x \\ \phi_y \end{pmatrix}(\tau) = \begin{pmatrix} M_x \left( \int_0^\infty \phi_x(v) dv, \phi_y \right) \phi_x(\tau) \\ G_y \left( \int_0^\infty \phi_x(v) dv, \phi_y \right)(\tau) \end{pmatrix}, \tag{9b}$$

where  $\phi = \begin{pmatrix} \phi_x \\ \phi_y \end{pmatrix}$  with  $\phi_x \in L^1(\mathbb{R}^m)$  and  $\int_0^\infty \phi_x(\tau) d\tau = X_0$ .

Let  $\pi^{(m)}$  and  $\pi^{(-k)}$  denote the projection functions in Definition 8 of the Appendix. Then the following result holds:

**Theorem 1.** *Consider System (8) as an ADP problem (System (5)) with  $F$  and  $G$  being defined as in System (9). Assume that  $F$  and  $G$  are Lipschitz on norm-balls of  $L^1$ . If the ADP problem has a solution  $\ell \in L_{\bar{t}}$  for the functions  $F$  and  $G$  and the initial condition  $\phi$ , then System (8) has a solution  $X(t), y(\tau, t)$  for  $t \in [0, \bar{t}]$  and a.e. for  $\tau \in (0, \infty)$ , given by*

$$X(t) = \pi^{(m)} \left( \int_0^\infty \ell(\tau, t) d\tau \right) \quad \text{and} \quad y(\cdot, t) = \pi^{(-k)}(\ell(\cdot, t)).$$

**Proof.** Let  $\bar{t} > 0$  such that  $\ell \in L_{\bar{t}}$  is a solution of the ADP problem on  $[0, \bar{t}]$  for the functions  $F, G$  and the initial condition  $\phi$ . Define

$$X(t) = \pi^{(m)} \left( \int_0^\infty \ell(\tau, t) d\tau \right) \quad \text{and} \quad y(\cdot, t) = \pi^{(-k)}(\ell(\cdot, t)).$$

Applying  $\pi^{(m)}$  to Equation (5c), we have

$$\pi^{(m)}(\ell(\tau, 0)) = \phi_x(\tau);$$



integrating, we obtain Equation (8b). Applying  $\pi^{(-k)}$  to Equation (5a) and using the definition of  $G$  in Equation (9b), we obtain the  $y(\tau, t)$  in Equation (8a). In the same way, from Equation (5b) and the definition of  $F$  in Equation (9a), we obtain the  $y(0, t)$  in Equation (8b). Also, applying  $\pi^{(-k)}$  to Equation (5c) yields the  $y(\cdot, 0)$  in Equation (8b).

It remains to show that  $X$  satisfies Equation (8a). Notice that

$$\pi^{(m)}\left(F(\ell(\cdot, t)) + \int_0^\infty G(\ell(\cdot, t))(\tau) d\tau\right) = F_X(X(t), y(\cdot, t)) + M_X(X(t), y(\cdot, t))X(t).$$

Thus, it suffices to show that

$$\frac{d}{dt}X(t) = \pi^{(m)}\left(F(\ell(\cdot, t)) + \int_0^\infty G(\ell(\cdot, t))(\tau) d\tau\right).$$

Recall from Section 2.2 that, if  $F$  and  $G$  are Lipschitz on norm-balls of  $L^1$ , a solution of the ADP problem is also a mild solution of the ADP problem. Hence, if  $h > 0$ , then

$$\begin{aligned} & \left| h^{-1}[X(t+h) - X(t)] - \pi^{(m)}\left(F(\ell(\cdot, t)) + \int_0^\infty G(\ell(\cdot, t))(\tau) d\tau\right) \right| \\ &= \left| h^{-1}\pi^{(m)}\left(\int_0^\infty \ell(\tau, t+h) d\tau - \int_0^\infty \ell(\tau, t) d\tau\right) - \pi^{(m)}\left(F(\ell(\cdot, t)) - \int_0^\infty G(\ell(\cdot, t))(\tau) d\tau\right) \right| \\ &\leq \left| h^{-1}\pi^{(m)}\left(\int_0^h \ell(\tau, t+h) - F(\ell(\cdot, t)) d\tau\right) \right| \\ &+ \left| \pi^{(m)}\left(\int_0^\infty h^{-1}[\ell(\tau+h, t+h) - \ell(\tau, t)] - G(\ell(\cdot, t))(\tau) d\tau\right) \right| \\ &\leq h^{-1} \int_0^h |\ell(\tau, t+h) - F(\ell(\cdot, t))| d\tau + \int_0^\infty |h^{-1}[\ell(\tau+h, t+h) - \ell(\tau, t)] - G(\ell(\cdot, t))(\tau)| d\tau, \end{aligned}$$

which tends to zero as  $h \rightarrow 0^+$  by the limit equations in Definition 4 of the Appendix. This shows that the right derivative of  $X$  exists and is equal to

$$\pi^{(m)}\left(F(\ell(\cdot, t)) + \int_0^\infty G(\ell(\cdot, t))(\tau) d\tau\right) \text{ for } t \in [0, \bar{t}].$$

For the left derivative, let  $h > 0$ . Using similar estimates as for the right derivative, we obtain

$$\begin{aligned} & \left| h^{-1}[X(t) - X(t-h)] - \pi^{(m)} \left( F(\ell(\cdot, t)) + \int_0^\infty G(\ell(\cdot, t))(\tau) d\tau \right) \right| \\ & \leq \left| h^{-1} \int_0^h \ell(\tau, t) d\tau - F(\ell(\cdot, t)) \right| \\ & + \left| h^{-1} \left[ \int_h^\infty \ell(\tau, t) d\tau - \int_0^\infty \ell(\tau, t-h) d\tau \right] - \int_0^\infty G(\ell(\cdot, t))(\tau) d\tau \right|. \end{aligned}$$

The first factor in the last sum goes to zero as  $h \rightarrow 0^+$  by the Fundamental Theorem of Calculus and the fact that  $\ell$  is a solution of the ADP problem (in particular Equation (5b)):

$$\lim_{h \rightarrow 0^+} h^{-1} \int_0^h \ell(\tau, t) d\tau = \ell(0, t) = F(\ell(\cdot, t)).$$

For the second factor, recall that, if  $F$  and  $G$  are Lipschitz on norm-balls of  $L^1$ , then  $\ell$  is a mild solution of the ADP problem if and only if it satisfies the integral equation of the problem, Equation (7) [15, Theorem 2.2]. Using Equation (7), for any  $0 < h < \min \{ \tau, t \}$ , we have

$$\ell(\tau, t) - \ell(\tau-h, t-h) = \int_{t-h}^t G(\ell(\cdot, s))(s + \tau - t) ds,$$

and for  $h < t$ ,

$$\begin{aligned}
 & \left| h^{-1} \left[ \int_h^\infty \ell(\tau, t) d\tau - \int_0^\infty \ell(\tau, t-h) d\tau \right] - \int_0^\infty G(\ell(\cdot, t))(\tau) d\tau \right| \\
 &= \left| h^{-1} \left[ \int_h^\infty \ell(\tau, t) - \ell(\tau-h, t-h) d\tau \right] - \int_0^\infty G(\ell(\cdot, t))(\tau) d\tau \right| \\
 &= \left| h^{-1} \left[ \int_h^\infty \int_{t-h}^t G(\ell(\cdot, s))(s+\tau-t) ds d\tau \right] - \int_0^\infty G(\ell(\cdot, t))(\tau) d\tau \right| \\
 &= \left| \int_0^\infty h^{-1} \left[ \int_{t-h}^t G(\ell(\cdot, s))(s+\tau+h-t) - G(\ell(\cdot, t))(\tau) ds \right] d\tau \right| \\
 &\leq \int_0^\infty \left| h^{-1} \left[ \int_{t-h}^t (G(\ell(\cdot, s))(s+\tau+h-t) - G(\ell(\cdot, t))(\tau)) ds \right] \right| d\tau \\
 &\leq h^{-1} \int_{t-h}^t \int_0^\infty |G(\ell(\cdot, s))(s+\tau+h-t) - G(\ell(\cdot, t))(s+\tau+h-t)| d\tau ds \\
 &\quad + h^{-1} \int_{t-h}^t \int_0^\infty |G(\ell(\cdot, t))(s+\tau+h-t) - G(\ell(\cdot, t))(\tau)| d\tau ds \\
 &\leq \sup_{t-h \leq s \leq t} \|G(\ell(\cdot, s)) - G(\ell(\cdot, t))\| + \sup_{t-h \leq s \leq t} \int_0^\infty |G(\ell(\cdot, t))(s+\tau+h-t) - G(\ell(\cdot, t))(\tau)| d\tau
 \end{aligned}$$

In the last inequality, the first factor in the sum tends to zero as  $h \rightarrow 0^+$  because the function  $t \mapsto G(\ell(\cdot, t))$  is continuous [15, Lemma 2.2]. The second factor tends to zero by the continuity of the translation in  $L^1$ .  $\square$

### 2.5. Equilibrium solutions of the coupled model and ADP problem

For any coupled model where Theorem 1 can be applied, an equilibrium solution of the respective ADP problem translates into an equilibrium solution of the coupled model by applying the projection  $\pi^{(m)}$  and integrating to obtain the equilibrium for  $X$  or applying the projection  $\pi^{(-k)}$  to obtain the equilibrium for  $y$ . In some cases, those are the only equilibrium solutions of the coupled model, as stated in the following theorem.

**Theorem 2.** *Consider System (8) as an ADP problem (System (5)) by letting  $F$  and  $G$  be as defined in System (9). Assume that  $F$  and  $G$  are Lipschitz on norm-balls of  $L^1$ . If the ADP problem has an equilibrium solution  $\phi$ , then*

$$X_0 = \pi^{(m)} \left( \int_0^\infty \phi(\tau) d\tau \right), \quad \phi_y(\tau) = \pi^{(-k)}(\phi(\tau))$$

is an equilibrium solution of the System (8).

Conversely, suppose that  $X_0, \phi_y$  is an equilibrium solution of System (8) such that

- i.  $\phi_y$  is absolutely continuous,
- ii.  $\phi'_y \in L^1$ , and
- iii. all eigenvalues of  $M_x(X_0, \phi_y)$  have negative real parts.

Then,

$$\phi(\tau) = \begin{pmatrix} e^{M_x(X_0, \phi_y)\tau} F_x(X_0, \phi_y) \\ \phi_y(\tau) \end{pmatrix}$$

is an equilibrium solution of the ADP problem.

**Proof.** Under the assumptions of the theorem, if the ADP problem has an equilibrium solution  $\phi$ , then we can apply Theorem 1 to obtain a solution of the coupled model (System (8)). Because the equilibrium solution of the ADP problem does not depend on  $t$ , neither will the solution of the coupled model.

On the other hand, let  $(X_0, \phi_y)$  be an equilibrium solution of the coupled model (System (8)) that satisfies (i), (ii) and (iii). Define

$$\phi(\tau) = \begin{pmatrix} \phi_x(\tau) \\ \phi_y(\tau) \end{pmatrix} = \begin{pmatrix} e^{M_x(X_0, \phi_y)\tau} F_x(X_0, \phi_y) \\ \phi_y(\tau) \end{pmatrix}.$$

Then

$$\int_0^{\bar{\tau}} \phi_x(\tau) d\tau = (M_x(X_0, \phi_y))^{-1} e^{M_x(X_0, \phi_y)\bar{\tau}} F_x(X_0, \phi_y) - (M_x(X_0, \phi_y))^{-1} F_x(X_0, \phi_y).$$

The inverse  $(M_x(X_0, \phi_y))^{-1}$  exists because we are assuming that all eigenvalues of the matrix  $M_x(X_0, \phi_y)$  have negative real parts. Moreover, if all eigenvalues of a square matrix  $A$  have negative real parts, then  $\lim_{\tau \rightarrow \infty} e^{A\tau} x_0 = 0$  for any vector  $x_0$  of the same dimension as  $A$  [18, Chapter 1, Theorem 2]. Thus,

$$\int_0^{\infty} \phi_x(\tau) d\tau = -(M_x(X_0, \phi_y))^{-1} F_x(X_0, \phi_y).$$

By Equation (8a) and the fact that, if  $(X_0, \phi_y)$  is an equilibrium solution of the coupled model, then it satisfies  $X'(t) = 0$ , we have

$$-(M_x(X_0, \phi_y))^{-1} F_x(X_0, \phi_y) = X_0.$$

Hence,  $\int_0^{\infty} \phi_x(\tau) d\tau = X_0$ .

From the definition of  $\phi_x$  and the fact that  $\phi_y$  is absolutely continuous,  $\phi$  is absolutely continuous. Moreover,

$$\phi'_x(x) = M_x(X_0, \phi_y)\phi_x(\tau),$$

so  $\phi'_x \in L^1$ . Also, from the assumption that  $\phi_y \in L^1$ , we have that  $\phi' \in L^1$ .

Now we can show that  $\phi$  is indeed a solution of the ADP problem:

$$\phi(0) = \begin{pmatrix} F_x(X_0, \phi_y) \\ \phi_y(0) \end{pmatrix} = \begin{pmatrix} F_x(X_0, \phi_y) \\ F_y(X_0, \phi_y) \end{pmatrix} = F(\phi)$$

and

$$D\phi(\tau) = \phi'(\tau) = \begin{pmatrix} M_x(X_0, \phi_y)\phi_x(\tau) \\ \phi'_y(\tau) \end{pmatrix} = G(\phi)(\tau),$$

where  $F$  and  $G$  are as in System (9).  $\square$

## 2.6. Other examples of coupled models

**Example 1.** Brauer, et al. [4] studied a model of cholera that has three epidemiological classes: susceptible individuals ( $S(t)$ , only dependent on time), infected individuals ( $i(t, \cdot)$ , structured by time since infection), and contaminated water ( $p(t, \cdot)$ , structured by the time that the pathogen has been in the water). Let

$$X(t) = S(t), \quad y(\cdot, t) = \begin{pmatrix} i(\cdot, t) \\ p(\cdot, t) \end{pmatrix}.$$

Then the functions corresponding to those in System (8) are:

$$F_x(X(t), y(\cdot, t)) = A,$$

$$M_x(X(t), y(\cdot, t)) = -\mu - \int_0^\infty (\beta_d k(\tau) \beta_i q(\tau)) y(\cdot, t) d\tau,$$

$$G_y(X(t), y(\cdot, t))(\tau) = - \begin{pmatrix} \theta(\tau) & 0 \\ 0 & \delta(\tau) \end{pmatrix} y(\cdot, t),$$

$$F_y(X(t), y(\cdot, t)) = X(t) \int_0^\infty \begin{pmatrix} \beta_d k(\tau) & \beta_i q(\tau) \\ \xi(\tau) & 0 \end{pmatrix} y(\tau, t) d\tau,$$

with the initial conditions:

$$X_0 = S_0, \quad \phi_y = \begin{pmatrix} i_0 \\ p_0 \end{pmatrix}.$$

**Example 2.** Bhattacharya and Adler [19] describe an SIRS model in which the susceptible  $S(t)$  and infected  $I(t)$  classes depend only on time, whereas the recovered class  $R(\cdot, t)$  is structured by time since recovery. Their model can be formulated in the form of System (8). Let

$$X(t) = \begin{pmatrix} S(t) \\ I(t) \end{pmatrix}, \quad y(\cdot, t) = R(\cdot, t).$$

The corresponding functions are

$$F_x(X(t), y(\cdot, t)) = \begin{pmatrix} \int_0^\infty \rho(\tau) y(\tau, t) d\tau \\ 0 \end{pmatrix},$$

$$M_x(X(t), y(\cdot, t)) = \begin{pmatrix} -\beta \pi_2(X(t)) & 0 \\ \beta \pi_2(X(t)) & -\gamma \end{pmatrix},$$

$$G_y(X(t), y(\cdot, t))(\tau) = -\rho(\tau) y(\tau, t),$$

$$F_y(X(t), y(\cdot, t)) = \gamma \pi_2(X(t)),$$

where  $\pi_2$  is the projection defined as  $\pi_2(x_1, x_2, \dots, x_n) = x_i$  with the initial conditions

$$X_0 = \begin{pmatrix} S_0 \\ I_0 \end{pmatrix}, \quad \phi_y = 0.$$

**Example 3.** Magal and McCluskey [20] describe a two-group SIR model in which there are two susceptible classes ( $S_1$  and  $S_2$ ) and two recovered classes ( $R_1$  and  $R_2$ ) that depend only on time, and two infected classes ( $i_1(\cdot, t)$  and  $i_2(\cdot, t)$ ) that are structured by the time since infection. Their model can be formulated in the form of System (8) by letting

$$X(t) = \begin{pmatrix} S_1(t) \\ S_2(t) \\ R_1(t) \\ R_2(t) \end{pmatrix}, \quad y(\cdot, t) = \begin{pmatrix} i_1(\cdot, t) \\ i_2(\cdot, t) \end{pmatrix}.$$

The corresponding functions are

$$F_x(X(t), y(\cdot, t)) = \begin{pmatrix} \Lambda - \pi^{(2)}(X(t)) \bullet \int_0^\infty B(\tau)y(\tau, t)d\tau \\ \int_0^\infty M(\tau)y(\tau, t)d\tau \end{pmatrix},$$

$$M_x(X(t), y(\cdot, t)) = - \begin{pmatrix} D & 0 \\ 0 & D \end{pmatrix},$$

$$G_y(X(t), y(\cdot, t))(\tau) = -(M(\tau) + D)y(\tau, t),$$

$$F_y(X(t), y(\cdot, t)) = \pi^{(2)}(X(t)) \bullet \int_0^\infty B(\tau)y(\tau, t)d\tau \int_0^\infty M(\tau)y(\tau, t)d\tau,$$

where  $\bullet$  represents the dot product of vectors,  $\pi^{(2)}$  is the projection defined as

$$\pi^{(m)}(x_1, x_2, \dots, x_n) = (x_1, x_2, \dots, x_m),$$

with  $0 < m < n$ , and with the notation

$$\Lambda = \begin{pmatrix} \lambda_1 \\ \lambda_2 \end{pmatrix}, \quad B(\tau) = \begin{pmatrix} 0 & \beta_2(\tau) \\ \beta_1(\tau) & 0 \end{pmatrix},$$

$$M(\tau) = \begin{pmatrix} m_1(\tau) & 0 \\ 0 & m_2(\tau) \end{pmatrix}, \quad D = \begin{pmatrix} d_1 & 0 \\ 0 & d_2 \end{pmatrix}.$$

The initial conditions are

$$X_0 = \begin{pmatrix} S_0 \\ R_0 \end{pmatrix}, \quad \phi_y = i_0.$$

### 3. Solution properties of the general model

We first simplify the general model (System (2)) by showing that the total population size  $\mathcal{P}(t)$  remains constant for all  $t \geq 0$  and then analyze it by reformulating it as a coupled model.

#### 3.1. Simplification of the general model

Let  $N_0 \in \mathbb{R}_+$  and  $i_0 \in L^1_+(\mathbb{R})$  be such that  $N_0 + \int_0^\infty i_0(\tau) d\tau > 0$ . A solution of the general model (System (2)) is a pair of functions,  $\mathcal{N}(t): \mathbb{R}_+ \rightarrow \mathbb{R}_+$  differentiable and  $i(\cdot, t): \mathbb{R}_+ \rightarrow L^1_+(\mathbb{R})$  continuous, that solve the equations in System (8a) for all  $t \geq 0$  and a.e. for  $\tau \in (0, \infty)$ .

**Assumption 1.** Let  $T, k: \mathbb{R}_+ \rightarrow \mathbb{R}_+$  be bounded functions such that  $\int_0^\infty T(\tau) d\tau > 0$  and

$$\begin{aligned} & \left( i \right) \int_0^\infty T(\tau) d\tau < \infty \text{ or} \\ & \left( ii \right) k(\tau) = 0 \text{ a. e. for } \tau > 0. \end{aligned} \tag{10}$$

**Proposition 1.** Let  $T, k$  satisfy Assumption 1. For any solution  $(\mathcal{N}(t), i(\tau, t))$  of System (2), the total population remains constant; i.e.,  $\mathcal{P}(t) = P$ , where

$$P = N_0 + \int_0^\infty i_0(\tau) d\tau. \tag{11}$$

**Proof.** Suppose that  $(\mathcal{N}, i)$  is a solution of System (2). To simplify the notation, define

$$\mathcal{B}(t) = \int_0^\infty T(v) \frac{i(v, t)}{\mathcal{P}(t)} dv$$

and  $w_c(t) = i(t + c, t)$  for any  $c \in \mathbb{R}$  and  $t \geq t_c$ , where  $t_c = \max\{-c, 0\}$ . Note that

$$\begin{aligned} \lim_{h \rightarrow 0^+} \frac{w_c(t+h) - w_c(t)}{h} &= \lim_{h \rightarrow 0^+} \frac{i(t+c+h, t+h) - i(t+c, t)}{h} \\ &= \text{Di}(t+c, t) \\ &= -\mathcal{B}(t)k(t+c)w_c(t) - \mu w_c(t). \end{aligned}$$



Thus, the right derivative of  $w'_c(t+)$  exists a.e. From Assumption 1, we know that

$\mathcal{B}(t)k(t+c)$  is either bounded by  $\int_0^\infty T(\tau)d\tau \times \sup_\tau\{k(\tau)\}$  or is zero a.e. Therefore,  $w'_c(t+)$  is integrable in  $[0, \bar{t}]$  for any  $\bar{t} > 0$ , whenever  $w_c(t)$  is integral in  $[0, \bar{t}]$ . Because  $i: \mathbb{R}_+ \rightarrow L^1_+(\mathbb{R})$  is continuous, this is the case for any  $\bar{t} > 0$ . so, we can integrate  $w'_c(t+)$  to obtain that  $w_c$  satisfies a.e. the integral equation:

$$w_c(t) = - \int_{t_c}^t [\mathcal{B}(s)k(s+c)w_c(s) + \mu w_c(s)]ds + w_c(t_c);$$

that is,

$$w_c(t) = \begin{cases} w_c(0) - \int_0^t [\mathcal{B}(s)k(s+c)w_c(s) + \mu w_c(s)]ds & \text{if } c > 0, \\ w_c(-c) - \int_0^t [\mathcal{B}(s)k(s+c)w_c(s) + \mu w_c(s)]ds & \text{if } c < 0. \end{cases}$$

Letting  $\tau = t + c$  and using the  $i(0, t)$  and  $i(\tau, 0)$  equations in System (2), we obtain:

$$i(\tau, t) = i_0(\tau - t) - \int_0^t [\mathcal{B}(s)k(\tau - t + s)i(\tau - t + s, s) + \mu i(\tau - t + s, s)]ds,$$

a.e. for  $\tau < t$ , and

$$i(\tau, t) = \mathcal{B}(t - \tau) \left[ \mathcal{N}(t - \tau) + \int_0^\infty k(v)i(v, t - \tau)dv \right] - \int_{t - \tau}^t [\mathcal{B}(s)k(\tau - t + s)i(\tau - t + s, s) + \mu i(\tau - t + s, s)]ds,$$

a.e. for  $\tau > t$ . Integrating, we have

$$\begin{aligned}
 \int_0^\infty i(\tau, t) d\tau &= \int_0^t \mathcal{B}(t-\tau) \left[ \mathcal{N}(t-\tau) + \int_0^\infty k(v) i(v, t-\tau) dv \right] d\tau \\
 &- \int_0^t \int_{t-\tau}^t [\mathcal{B}(s) k(\tau-t+s) i(\tau-t+s, s) + \mu i(\tau-t+s, s)] ds d\tau \\
 &+ \int_t^\infty i_0(\tau-t) d\tau \\
 &- \int_t^\infty \int_0^t [\mathcal{B}(s) k(\tau-t+s) i(\tau-t+s, s) + \mu i(\tau-t+s, s)] ds d\tau.
 \end{aligned} \tag{12}$$

Changing the limits of integration and making the change of variable  $v = \tau - t + s$  yields

$$\begin{aligned}
 &\int_0^t \int_{t-\tau}^t [\mathcal{B}(s) k(\tau-t+s) i(\tau-t+s, s) + \mu i(\tau-t+s, s)] ds d\tau \\
 &= \int_0^t \int_0^s [\mathcal{B}(v) k(v) i(v, s) + \mu i(v, s)] dv ds,
 \end{aligned}$$

and

$$\begin{aligned}
 &\int_t^\infty \int_0^t [\mathcal{B}(s) k(\tau-t+s) i(\tau-t+s, s) + \mu i(\tau-t+s, s)] ds d\tau \\
 &= \int_0^t \int_s^\infty [\mathcal{B}(v) k(v) i(v, s) + \mu i(v, s)] dv ds.
 \end{aligned}$$

Using  $s = t - \tau$  and  $v = \tau - t$  in the other two integrals of Equation (12), we get

$$\int_0^\infty i(\tau, t) d\tau = \int_0^t \mathcal{B}(s) \mathcal{N}(s) ds - \mu \int_0^t \|i(\cdot, s)\| ds + \int_0^\infty i_0(v) dv. \tag{13}$$

Integrating the  $\mathcal{N}$  equation in System (2), we obtain

$$\mathcal{N}(t) = - \int_0^t \mathcal{B}(s) \mathcal{N}(s) ds + \mu \int_0^t \|i(\cdot, s)\| ds + N_0. \tag{14}$$

Finally, adding Equation (13) and Equation (14), we complete the proof.  $\square$

### 3.2. The general model as an ADP problem

Proposition 1 allows us to reduce System (2) to the following simpler system (i.e., replacing the function  $\mathcal{P}(t)$  by the constant  $P$ ):

$$\begin{aligned}
 \frac{d}{dt}\mathcal{N}(t) &= - \left[ \int_0^\infty T(v) \frac{i(v,t)}{P} dv \right] \mathcal{N}(t) - \mu \mathcal{N}(t) + \mu P, \\
 Di(\tau, t) &= - \left[ \int_0^\infty T(v) \frac{i(v,t)}{P} dv \right] k(\tau) i(\tau, t) - \mu i(\tau, t), \\
 i(0, t) &= \left[ \int_0^\infty T(v) \frac{i(v,t)}{P} dv \right] \left[ \mathcal{N}(t) + \int_0^\infty k(\tau) i(\tau, t) d\tau \right], \\
 \mathcal{N}(0) &= N_0, \quad i(\tau, 0) = i_0(\tau), \\
 P &= N_0 + \int_0^\infty i_0(\tau) d\tau.
 \end{aligned} \tag{15}$$

We can then rewrite System (15) as a coupled model as in System (8), which can be studied as an ADP problem. Let

$$\begin{aligned}
 F_x(X, \phi_y) &= \mu X + \mu \int_0^\infty \phi_y(\tau) d\tau, \\
 M_x(X, \phi_y) &= - \int_0^\infty T(\tau) \frac{\phi_y(\tau)}{P} d\tau - \mu, \\
 G_y(X, \phi_y) &= - \left[ \int_0^\infty T(\tau) \frac{\phi_y(\tau, t)}{P} d\tau \right] k(\tau) \phi_y(\tau, t) - \mu \phi_y(\tau), \\
 F_y(X, \phi_y) &= \left[ \int_0^\infty T(\tau) \frac{\phi_y(\tau)}{P} d\tau \right] \left[ X + \int_0^\infty k(\tau) \phi_y(\tau) d\tau \right],
 \end{aligned} \tag{16}$$

with  $X_0 = N_0$ ,  $\phi_y = i_0$ .

For ease of presentation, we introduce the following notation and functions:

- i.** For  $0 < \bar{t} \leq \infty$  and  $\phi \in L^1((0, \bar{t}), \mathbb{R}^2)$ , let

$$\phi^n = \pi_1 \circ \phi, \quad \phi^i = \pi_2 \circ \phi,$$

where  $\pi_1$ ,  $\pi_2$  are the projections to the first and second entries as in Definition 8. Thus,  $\phi^n$  and  $\phi^i$  are the never-infected part of  $\phi$  and the infected-at-least-once part of  $\phi$ , respectively.

- ii.** Let  $\mathcal{F}: L^1 \rightarrow \mathbb{R}$  denote the function

$$\mathcal{F}(\phi) = \int_0^\infty T(\tau) \frac{\phi^i(\tau)}{P} d\tau. \tag{17}$$

iii. Let  $\mathcal{W}: L^1 \rightarrow \mathbb{R}$  denote the weighted function

$$\mathcal{W}(\phi) = \int_0^\infty [\phi^n(\tau) + k(\tau)\phi^i(\tau)] d\tau. \tag{18}$$

iv. Let  $\underline{\mathcal{W}}: L^1 \rightarrow \mathbb{R}$  denote the non-weighted function

$$\underline{\mathcal{W}}(\phi) = \int_0^\infty [\phi^n(\tau) + \phi^i(\tau)] d\tau. \tag{19}$$

Notice that  $\underline{\mathcal{W}}(\phi) = \|\phi\|$  if  $\phi \in L^1_+$ .

Let

$$F \begin{pmatrix} \phi^n \\ \phi^i \end{pmatrix} = \begin{pmatrix} \mu \int_0^\infty [\phi^n(\tau) + \phi^i(\tau)] d\tau \\ \int_0^\infty T(v) \frac{\phi^i(v)}{P} dv \int_0^\infty [\phi^n(\tau) + k(\tau)\phi^i(\tau)] d\tau \end{pmatrix} \tag{20a}$$

$$= \begin{pmatrix} \mu \underline{\mathcal{W}}(\phi) \\ \mathcal{F}(\phi) \mathcal{W}(\phi) \end{pmatrix},$$

$$G \begin{pmatrix} \phi^n \\ \phi^i \end{pmatrix}(\tau) = \begin{pmatrix} - \left[ \int_0^\infty T(v) \frac{\phi^i(v)}{P} dv \right] \phi^n(\tau) - \mu \phi^n(\tau) \\ - \left[ \int_0^\infty T(v) \frac{\phi^i(v)}{P} dv \right] k(\tau) \phi^i(\tau) - \mu \phi^i(\tau) \end{pmatrix} \tag{20b}$$

$$= \begin{pmatrix} -\mathcal{F}(\phi) \phi^n(\tau) - \mu \phi^n(\tau) \\ -\mathcal{F}(\phi) S(\tau) \phi^i(\tau) - \mu \phi^i(\tau) \end{pmatrix}.$$

Using the  $F$  and  $G$  functions defined in System (20), we can translate System (15) into an ADP problem (see System (5) and System (9)). Thus, to apply the results in Section 2 to describe solution properties of System (15), we focus in the following section on the properties of the functions  $F$  and  $G$  given in System (20).

### 3.3. Basic results for the ADP version of the general model

For ease of presentation, we state in this section some preliminary results that we will use in the next section to obtain our main results.

**Proposition 2.** *Let  $P > 0$ ,  $\mu = 0$ , and  $T, k: \mathbb{R}_+ \rightarrow \mathbb{R}_+$  be bounded. The following results hold:*

- a. *The functions  $\mathcal{F}$ ,  $\mathcal{W}$  and  $\mathcal{U}$  defined in Equations (17)–(19) are bounded linear operators. Moreover,*

$$\|\mathcal{F}\|_{\text{op}} \leq \frac{\sup_{\tau} T(\tau)}{P}, \quad \|\mathcal{W}\|_{\text{op}} \leq \sup_{\tau} \left\{ k(\tau) \right\}, \quad \|\mathcal{U}\|_{\text{op}} = 1.$$

- b. *If  $\phi \in L^1$ , then there exists  $0 < \bar{t} \leq \infty$  and  $\ell \in L^1_{\bar{t}}$  such that  $\ell$  is the unique mild solution of the ADP problem on  $[0, \bar{t}]$  for the functions  $F, G$  given in System (20) and the initial distribution  $\phi$ .*
- c. *If  $\phi \in L^1_+$  then the mild solution  $\ell$  of the ADP problem on  $[0, \bar{t}_{\phi}]$  for the function  $F, G$  given in System(20), the initial distribution  $\phi$  and  $\bar{t}_{\phi}$  is as in Definition 5, has the property that  $\ell(\cdot, t) \in L^1_+$  for  $0 \leq t < \bar{t}_{\phi}$ .*

The proof can be found in Appendix B.1.

**Proposition 3.** *Let  $P > 0$ ,  $\mu = 0$ , and let  $T, k: \mathbb{R}_+ \rightarrow \mathbb{R}_+$  be bounded, and  $\phi \in L^1$ . Let  $\ell$  be the mild solution of the ADP problem on  $[0, \bar{t}_{\phi}]$  for the functions  $F, G$  given in System (20) and the initial condition  $\phi$ , where  $\bar{t}_{\phi}$  is as in Definition 5. Then  $\mathcal{U}(\ell(\cdot, t))$  is constant for all  $0 \leq t < \bar{t}_{\phi}$ . Additionally, if  $\phi \in L^1_+$ , then  $\|\ell(\cdot, t)\| = \|\phi\|$  for all  $0 \leq t < \bar{t}_{\phi}$ .*

The proof can be found in Appendix B.2.

**Proposition 4.** *Let  $P > 0$ ,  $\mu = 0$ ,  $T, k: \mathbb{R}_+ \rightarrow \mathbb{R}_+$  be bounded, and  $\phi \in L^1_+$ . Let  $\ell$  be the mild solution of the ADP problem on  $[0, \bar{t}_{\phi}]$  for the functions  $F, G$  given in System (20) and the initial condition  $\phi$ , where  $\bar{t}_{\phi}$  is as in Definition 5. Then  $\bar{t}_{\phi} = \infty$ .*

The proof can be found in Appendix B.3.

### 3.4. Existence and regularity of the model solution

Based on the results stated in the previous section, we describe the properties of the solutions to the general model (System (15)). Definitions for some of the terms can be found in Appendix A. For example, a function being *globally Lipschitz* (Definition 9) and *F-differentiable* (Definition 10).

**Proposition 5.** *Let  $P > 0$ ,  $\mu = 0$ . Let  $T: \mathbb{R}_+ \rightarrow \mathbb{R}_+$  be a bounded function, and let  $k: \mathbb{R}_+ \rightarrow \mathbb{R}_+$  be a bounded globally Lipschitz function. Let  $\phi \in L^1_+$  be a continuous function such that  $\phi(0) = F(\phi)$ . Then there exists a unique continuous function  $\ell: \mathbb{R}_+ \rightarrow L^1_+$  that is the solution*

of the ADP problem for the functions  $F$  and  $G$  given in System (20) and the initial condition  $\phi$ .

The proof can be found in Appendix B.4.

The results described in Proposition 5 can be translated back to our original problem to obtain the first theorem of existence (and regularity) of solutions:

**Theorem 3.** Let  $\mu > 0$ . Let  $T: \mathbb{R}_+ \rightarrow \mathbb{R}_+$  be a function and  $k: \mathbb{R}_+ \rightarrow \mathbb{R}_+$  a globally Lipschitz function satisfying Assumption 1. Let  $N_0 > 0$  and let  $i_0: \mathbb{R}_+ \rightarrow \mathbb{R}_+$  be a continuous function such that  $i_0 \in L^1_+$  and

$$i_0(0) = \left[ \int_0^\infty T(v) \frac{i_0(v)}{N_0 + \int_0^\infty i_0(\tau) d\tau} dv \right] \left[ N_0 + \int_0^\infty k(\tau) i_0(\tau) d\tau \right]. \quad (21)$$

Then there exists a differentiable function  $\mathcal{N}: \mathbb{R}_+ \rightarrow \mathbb{R}_+$  and a continuous function  $i: \mathbb{R}_+ \rightarrow L^1_+(\mathbb{R})$  that solve System (15).

**Proof.** Let  $\phi^n$  be any continuous function from  $\mathbb{R}_+$  to  $\mathbb{R}_+$  such that

$$\phi^n(0) = \mu P, \quad \int_0^\infty \phi^n(\tau) d\tau = N_0.$$

Because we showed in Proposition 2 that  $F$  and  $G$  given in System (20) are Lipschitz on norm-balls of  $L^1$ , we can use Theorem 1 to translate results of a solution of the ADP problem for the functions  $F$  and  $G$  and initial condition

$$\phi = \begin{pmatrix} \phi^n \\ i_0 \end{pmatrix}$$

to results for solutions of the System (15), and by Proposition 1, of the general model (System (2)).

The first result is existence of a solution. We know that  $\phi \in L^1_+$  is continuous, and by the definition of  $\phi$  and Equation (21), we have

$$\phi(0) = \begin{pmatrix} \phi^n(0) \\ i_0(0) \end{pmatrix} = \begin{pmatrix} \mu P \\ \mathcal{F}(\phi) \left[ N_0 + \int_0^\infty k(\tau) i_0(\tau) d\tau \right] \end{pmatrix} = F(\phi).$$

So, given the hypothesis of Proposition 5, we can conclude that there is a solution for System (15). Moreover, this solution is defined for all  $t \in \mathbb{R}_+$ , and satisfies

$$\begin{aligned} \mathcal{N}(t) &= \pi_1 \left( \int_0^\infty \ell(\tau, t) d\tau \right), \\ i(\tau, t) &= \pi_2(\ell(\tau, t)) \end{aligned}$$

where  $\ell$  is the solution of the ADP problem.  $\square$

By Part (c) of Proposition 2,  $\ell(\cdot, t) \in L^1_+$  for all  $t \in \mathbb{R}_+$ , so  $\mathcal{N}(t) \geq 0$  and  $i(\cdot, t) \in L^1_+$  as required.  $\square$

This result is not very restrictive in the conditions imposed on the initial distribution. We only require it to be continuous,  $L^1$  and to satisfy the non-local boundary condition. However, we are imposing an additional restriction on the susceptibility function,  $k$ , namely for it to be globally Lipschitz. We can dispense with this so long as we impose a stronger condition on the initial distribution. Our regularity results will then be stronger for the solution of the ADP problem. For this, we first need to show that our functions  $F$  and  $G$  are continuously F-differentiable.

**Proposition 6.** *Let  $P > 0, \mu \geq 0$ . Let  $T, k: \mathbb{R}_+ \rightarrow \mathbb{R}_+$  be bounded functions. Then*

1. *The function  $F: L^1 \rightarrow \mathbb{R}^2$  defined by Equation (20a) is a continuously F-differentiable function relative to  $L^1$ . Its F-derivative is given by*

$$F'(\phi_0)(\phi) = \begin{pmatrix} \mu \mathcal{W}(\phi) \\ \mathcal{F}(\phi_0) \mathcal{W}(\phi) + \mathcal{F}(\phi) \mathcal{W}(\phi_0) \end{pmatrix}.$$

2. *The function  $G: L^1 \rightarrow L^1$  defined by Equation (20b) is a continuously F-differentiable function relative to  $L^1$ . Its F-derivative is given by*

$$G'(\phi_0)(\phi)(\tau) = - \begin{pmatrix} \mathcal{F}(\phi_0) \phi^n(\tau) + \mathcal{F}(\phi) \phi_0^n(\tau) + \mu \phi^n(\tau) \\ \mathcal{F}(\phi_0) k(\tau) \phi^i(\tau) + \mathcal{F}(\phi) k(\tau) \phi_0^i(\tau) + \mu \phi^i(\tau) \end{pmatrix}.$$

The proof can be found in Appendix B.5.

**Proposition 7.** *Let  $P > 0, \mu \geq 0$ , and let  $T, k: \mathbb{R}_+ \rightarrow \mathbb{R}_+$  be bounded. Let  $\phi \in L^1_+$  be absolutely continuous such that  $\phi' \in L^1$  and  $\phi(0) = F(\phi)$ . Then there exists a unique solution,  $\ell$  of the ADP problem for the  $F, G$  given in System (20) and the initial condition  $\phi$ , such that*

- a.  *$\ell(\cdot, t)$  is absolutely continuous for any  $t \in \mathbb{R}_+$*
- b. *For every  $t \in \mathbb{R}_+$  the function  $\tau \mapsto \ell(\tau, t)$  is differentiable and its derivative is in  $L^1$ .*
- c. *The function  $t \mapsto \ell(\cdot, t)$  is continuously differentiable from  $\mathbb{R}_+$  to  $L^1$ .*

- d. *also satisfies*  $\left(\frac{\partial}{\partial \tau} + \frac{\partial}{\partial t}\right) \ell(\tau, t) = G(\ell(\cdot, t))(\tau)$  for every  $t \in \mathbb{R}_+$  and a.e. for  $\tau \in (0, \infty)$ .

The proof can be found in Appendix B.6.

Finally, we can translate this into a result for the general model (System (2)), as stated below:

**Theorem 4.** Let  $\mu > 0$ . Let  $T, k: \mathbb{R}_+ \rightarrow \mathbb{R}_+$  be functions that satisfy Assumption 1. Let  $N_0 > 0$ , and let  $i_0: \mathbb{R}_+ \rightarrow \mathbb{R}_+$  an absolutely continuous function such that  $i_0 \in L^1_+$ ,  $i'_0 \in L^1$  and

$$i_0(0) = \left\| \int_0^\infty T(v) \frac{i_0(v)}{N_0 + \int_0^\infty i_0(\tau) d\tau} dv \right\| \left\| N_0 + \int_0^\infty k(\tau) i_0(\tau) d\tau \right\|.$$

Then there exist a continuously differentiable function  $\mathcal{N}: \mathbb{R}_+ \rightarrow \mathbb{R}_+$  and a continuous function  $i: \mathbb{R}_+ \rightarrow L^1_+(\mathbb{R})$  that solve System (2). Moreover,  $i(\cdot, t)$  is absolutely continuous for any  $t \in \mathbb{R}_+$  and

$$D(i(\tau, t)) = \left(\frac{\partial}{\partial \tau} + \frac{\partial}{\partial t}\right) i(\tau, t)$$

for every  $t \in \mathbb{R}_+$  and a.e. for  $\tau \in (0, \infty)$

**Proof.** Let  $\phi_x \in L^1_+$  be any the absolutely continuous function such that  $\phi'_x \in L^1$ ,  $\phi_x(0) = \mu P$  and  $\int_0^\infty \phi_x(\tau) d\tau = N_0$ . As in the proof of Theorem 3, the result follows by applying Theorem 1 and Proposition 7.  $\square$

## 4. Discussion

We present a novel approach for epidemiological models by using two time variables, chronological time  $t$  and time-since-last infection (TSLI). One advantage of this approach is that fewer state variables are needed; in the general model (System (2)) considered, there are only two:  $\mathcal{N}(t)$ , the number of never infected people at time  $t$ , and  $i(\tau, t)$ , the density of people at time  $t$  who were infected at least once with their last infections occurring  $\tau$  units of time ago.

In most models with age-of-infection  $\tau$ , the infected state variable, such as  $i(\tau, t)$ , denotes the density of those who are either latently infected or infectious, and the equation is written using partial derivatives,  $\left(\frac{\partial}{\partial \tau} + \frac{\partial}{\partial t}\right) i(\tau, t)$ . This requires stronger conditions on the model parameter functions (e.g.,  $T(\tau)$ ,  $k(\tau)$  and  $i_0(\tau)$ ) for the solution  $i(\tau, t)$  to be in  $C^1$ . In our model, individuals in the  $i(\tau, t)$  class include not only latently infected and infectious, but also recovered, who may or may not have immunity; i.e., everyone except those who have never been infected. In addition, the equation for  $i(\tau, t)$  is described using the differential



operator  $D$ , which allows weaker conditions on the parameter functions. We show that if  $i \in C^1$  then  $Di(\tau, t) = \left(\frac{\partial}{\partial \tau} + \frac{\partial}{\partial t}\right)i(\tau, t)$ .

To analyze the existence and regularity of solutions to the general model (System (2)), we apply published results for ADP problems, a term that refers to age-dependent populations as specified in Section 2.2 (see, e.g., [15,17]). For ease of framing the general model (System (2)) as an ADP problem, we first reformulate it as a coupled model as shown in Section 2.3. We also reformulate several published models to illustrate how readily age-structured models can be formulated as coupled models (see Section 2.6). In turn, coupled models can be formulated as ADP problems (System (5)), in which case results for those problems can be applied.

The general model (System (2)) can be used to study the dynamics of transmission and control of many infectious diseases. The special feature of the class  $\mathcal{X}(\tau, t)$ , together with the parameter functions  $T(\tau)$  and  $k(\tau)$  for infectivity and susceptibility based on TSLI, permits multiple scenarios, including: (i) complete immunity from natural infections ( $k(\tau) = 0$ ); (ii) partial or temporary immunity from infections ( $0 < k(\tau) < 1$ ); and (iii) enhanced susceptibility due to infections ( $\sup k(\tau) > 1$ ). For example, one might make the following assumptions on  $T$  and  $k$ : (i) there exists a finite period during which individuals are infectious; (ii) immunity eventually wanes (i.e.,  $k$  increases); and (iii) once-infected individuals become as susceptible as they ever would be. In other words, there exists  $\tau_0$  and  $\tau_1$  with  $0 < \tau_0 < \tau_1$  such that  $T(\tau) = 0$  for  $\tau > \tau_0$ ,  $k(\tau) = 0$  for  $\tau < \tau_0$ , and  $k(\tau) = \sup k$  for  $\tau > \tau_1$ . Applications of the general model (System (2)) under these conditions to study diseases such as tuberculosis and influenza will be presented elsewhere.

### Acknowledgment

ZF's research is partially supported by NSF grant DMS-1814545.

### Appendix A.: Definitions

This appendix includes definitions and terminology mentioned in the main text.

**Definition 3.**  $L^1_+ = L^1_+(\mathbb{R}^n) = \{\phi \in L^1 : \phi(\tau) \in \mathbb{R}^n_+ \text{ a. e. } \tau > 0\}$ .

**Definition 4.** Let  $\bar{t} > 0$ ,  $\ell \in L^1_{\bar{t}}$ ,  $F: L^1 \rightarrow \mathbb{R}^n$ ,  $G: L^1 \rightarrow L^1$ , and  $\phi \in L^1$ . We say that  $\ell$  is a mild solution of the ADP problem on  $[0, \bar{t}]$  for the initial distribution  $\phi$  provided that  $\ell$  satisfies:

$$\lim_{h \rightarrow 0^+} \int_0^{\infty} \left| h^{-1} [\ell(\tau + h, t + h) - \ell(\tau, t)] - G(\ell(\cdot, t))(\tau) \right| d\tau = 0, \tag{A.1}$$

$$\lim_{h \rightarrow 0^+} h^{-1} \int_0^h \left| \ell(\tau, t + h) - F(\ell(\cdot, t)) \right| d\tau = 0, \tag{A.2}$$

and

$$\ell(\cdot, 0) = \phi, \quad 0 \leq t \leq \bar{t}. \quad (\text{A.3})$$

**Definition 5.** For  $0 < \bar{t} \leq \infty$ , we say that  $\hat{A}$  is the solution (respectively mild solution) of the ADP problem on  $[0, \bar{t})$  for the initial distribution  $\phi$ , provided that, for all  $\bar{t} < \hat{t}$ ,  $\hat{A}$  restricted to  $[0, \bar{t}]$  is the solution (respectively mild solution) of the ADP problem on  $[0, \bar{t}]$  for the initial condition  $\phi$  restricted to  $[0, \bar{t}]$ .

**Definition 6.** If there exists a mild solution of the ADP problem on  $[0, \bar{t}]$  for some  $\bar{t} > 0$ , we denote by  $\bar{t}_\phi$ , the maximal  $\hat{t} > 0$ , such that there exists a mild solution of the ADP problem in  $[0, \hat{t})$ .

**Definition 7.** Given  $\phi \in L^1$ ,  $F: L^1(\mathbb{R}^n) \rightarrow \mathbb{R}^n$  and  $G: L^1(\mathbb{R}^n) \rightarrow L^1(\mathbb{R}^n)$ , we define an *equilibrium solution* of the ADP problem for the functions  $F$ ,  $G$  and initial condition  $\phi$  as a solution of the ADP problem for the same functions on  $[0, \infty)$  such that  $\ell(\cdot, t) = \phi$  for all  $t \geq 0$ .

**Definition 8.** We define the projection function to the  $i$ -th entry  $\pi_i: \mathbb{R}^n \rightarrow \mathbb{R}$  as

$$\pi_i(x_1, \dots, x_n) = x_i;$$

for  $m \in \mathbb{N}$ ,  $0 < m < n$ , the projection to the first  $m$  entries  $\pi^{(m)}: \mathbb{R}^n \rightarrow \mathbb{R}^m$  as

$$\pi^{(m)}(x_1, \dots, x_n) = (x_1, \dots, x_m);$$

and, for  $k \in \mathbb{N}$ ,  $0 < k < n$ , the projection to the last  $k$  entries  $\pi^{(-k)}: \mathbb{R}^n \rightarrow \mathbb{R}^k$  as

$$\pi^{(-k)}(x_1, \dots, x_n) = (x_{n-k+1}, \dots, x_n).$$

**Definition 9.** Let  $X$  and  $Y$  be normed spaces with norms  $\|\cdot\|_X$  and  $\|\cdot\|_Y$ , respectively, and let  $\mathcal{H}: X \rightarrow Y$ . We say that  $\mathcal{H}$  is Lipschitz on norm-balls of  $X$  if, for all  $r > 0$ , there exists  $c(r) > 0$  such that

$$\|\mathcal{H}(x_1) - \mathcal{H}(x_2)\|_Y \leq c(r)\|x_1 - x_2\|_X$$

for all  $x_1, x_2 \in X$  such that  $\|x_1\|_X, \|x_2\|_X \leq r$ . If  $c(r)$  can be chosen to be the same constant for all  $r > 0$ , then  $\mathcal{H}$  is said to be globally Lipschitz.

**Definition 10.** Let  $X$  and  $Y$  be normed spaces with norms  $\|\cdot\|_X$  and  $\|\cdot\|_Y$ , respectively, and let  $D \subset X$ . We say that  $\mathcal{H}: D \rightarrow Y$  is F-differentiable relative to  $D$  at  $x_0 \in D$  if there exists  $\mathcal{H}'(x_0) \in B(X, Y)$ , such that, given any  $\epsilon > 0$ , there exists  $\delta > 0$  such that, if  $x \in D$  and  $\|x - x_0\|_X < \delta$ , then

$$\|\mathcal{H}(x) - \mathcal{H}(x_0) - \mathcal{H}'(x_0)(x - x_0)\|_Y \leq \epsilon \|x - x_0\|_X.$$

$\mathcal{H}$  is said to be continuously F-differentiable relative to  $D$  on  $A \subset D$  if it is F-differentiable relative to  $D$  at each  $x \in A$  and if the map  $x \mapsto \mathcal{H}'(x)$  is continuous from  $A$  to  $B(X, Y)$ .  $\mathcal{H}'(x)$  is called the F-derivative of  $\mathcal{H}$  at  $x$ .

## Appendix B.: Proofs

### B.1. Proof of Proposition 2

**Proof.** To simplify notation, let  $\hat{T} = \sup_{\tau} \{T(\tau)\}$  and  $\hat{k} = \sup_{\tau} \{k(\tau)\}$

Part (a). The linearity follows by the definition of the functions and fact that integration is a linear operator.

For  $\phi \in L^1$ , we have  $|\mathcal{F}(\phi)| \leq \int_0^\infty T(\tau) |\phi^o(\tau)| / P \, d\tau \leq \hat{T} \|\phi\| / P$ ,  
 $|\mathcal{W}(\phi)| \leq \int_0^\infty [|\phi^n(\tau)| + k(\tau) |\phi^i(\tau)|] d\tau \leq \hat{k} \|\phi\|$ , and  $|\mathcal{Z}(\phi)| \leq \int_0^\infty [|\phi^n(\tau)| + |\phi^i(\tau)|] \tau = \|\phi\|$ . In addition,  $|\mathcal{Z}(\phi)| = \|\phi\|$  if  $\phi \in L^1_+$ .

Part (b). Existence and uniqueness of the mild solution of the ADP problem is guaranteed if  $F$  and  $G$  are Lipschitz on norm-balls of  $L^1$  [15, Theorem 2.1]. In other words, we need to show that there exist functions  $c_1, c_2: \mathbb{R}_+ \rightarrow \mathbb{R}_+$  such that  $|F(\phi_1) - F(\phi_2)| \leq c_1(r) \|\phi_1 - \phi_2\|$  and  $\|G(\phi_1) - G(\phi_2)\| \leq c_2(r) \|\phi_1 - \phi_2\|$  for all  $\phi_1, \phi_2 \in L^1$  with  $\|\phi_1\|, \|\phi_2\| \leq r$ .

If  $\|\phi_1\|, \|\phi_2\| \leq r$ , using Part (a), we have

$$\begin{aligned} |F(\phi_1) - F(\phi_2)| &= |\mu \mathcal{Z}(\phi_1) - \mu \mathcal{Z}(\phi_2)| + |\mathcal{F}(\phi_1) \mathcal{W}(\phi_1) - \mathcal{F}(\phi_2) \mathcal{W}(\phi_2)| \\ &= \mu |\mathcal{Z}(\phi_1 - \phi_2)| + |\mathcal{F}(\phi_1) \mathcal{W}(\phi_1) - \mathcal{F}(\phi_1) \mathcal{W}(\phi_2) + \mathcal{F}(\phi_1) \mathcal{W}(\phi_2) - \mathcal{F}(\phi_2) \mathcal{W}(\phi_2)| \\ &\leq \mu \|\phi_1 - \phi_2\| + |\mathcal{F}(\phi_1)| \|\mathcal{W}(\phi_1 - \phi_2)\| + |\mathcal{W}(\phi_2)| |\mathcal{F}(\phi_1 - \phi_2)| \\ &\leq \mu \|\phi_1 - \phi_2\| + \frac{\hat{T}}{P} \|\phi_1\| \|\mathcal{W}(\phi_1 - \phi_2)\| + \hat{k} \|\phi_2\| |\mathcal{F}(\phi_1 - \phi_2)| \\ &\leq \mu \|\phi_1 - \phi_2\| + \frac{\hat{T}}{P} \|\phi_1\| \hat{k} \|\phi_1 - \phi_2\| + \hat{k} \|\phi_2\| \frac{\hat{T}}{P} \|\phi_1 - \phi_2\| \\ &\leq \mu \|\phi_1 - \phi_2\| + 2r \frac{\hat{T}}{P} \hat{k} \|\phi_1 - \phi_2\|. \end{aligned}$$

Thus, we can choose

$$c_1(r) = \frac{2\hat{k}\hat{T}r}{P} + \mu.$$

Similarly, if  $\|\phi_1\|, \|\phi_2\| \leq r$ , then

$$\begin{aligned}
 \|G(\phi_1) - G(\phi_2)\| &= \int_0^\infty \left| -\mathcal{F}(\phi_1)\phi_1^n(\tau) + \mathcal{F}(\phi_2)\phi_1^n(\tau) - \mu\phi_1^n(\tau) + \mu\phi_2^n(\tau) \right| d\tau \\
 &+ \int_0^\infty \left| -\mathcal{F}(\phi_1)S(\tau)\phi_1^i(\tau) + \mathcal{F}(\phi_2)k(\tau)\phi_1^i(\tau) - \mu\phi_1^i(\tau) + \mu\phi_2^i(\tau) \right| d\tau \\
 &\leq \int_0^\infty \left| \mathcal{F}(\phi_1)\phi_1^n(\tau) - \mathcal{F}(\phi_2)\phi_2^n(\tau) \right| d\tau + \mu \int_0^\infty \left| \phi_1^n(\tau) - \phi_2^n(\tau) \right| d\tau \\
 &+ \int_0^\infty \left| \mathcal{F}(\phi_1)k(\tau)\phi_1^i(\tau) - \mathcal{F}(\phi_2)k(\tau)\phi_2^i(\tau) \right| d\tau + \mu \int_0^\infty \left| \phi_1^i(\tau) - \phi_2^i(\tau) \right| d\tau \\
 &\leq \int_0^\infty \left| \mathcal{F}(\phi_1)\phi_1^n(\tau) - \mathcal{F}(\phi_1)\phi_2^n(\tau) \right| + \left| \mathcal{F}(\phi_1)\phi_2^n(\tau) - \mathcal{F}(\phi_2)\phi_2^n(\tau) \right| d\tau \\
 &+ \int_0^\infty \left| \mathcal{F}(\phi_1)k(\tau)\phi_1^i(\tau) - \mathcal{F}(\phi_1)k(\tau)\phi_2^i(\tau) \right| + \left| \mathcal{F}(\phi_1)k(\tau)\phi_2^i(\tau) \right. \\
 &\quad \left. - \mathcal{F}(\phi_2)k(\tau)\phi_2^i(\tau) \right| d\tau + \mu \left\| \phi_1 - \phi_2 \right\| \\
 &\leq |\mathcal{F}(\phi_1)|\hat{k} \|\phi_1 - \phi_2\| + |\mathcal{F}(\phi_1 - \phi_2)|\hat{k} \|\phi_2\| + \mu \|\phi_1 - \phi_2\| \\
 &\leq 2\frac{\hat{T}}{P}\hat{k}r \|\phi_1 - \phi_2\| + \mu \|\phi_1 - \phi_2\|.
 \end{aligned}$$

Thus, we can also take

$$c_2(r) = \frac{2\hat{k}\hat{T}r}{P} + \mu.$$

Part (c). We can guarantee that  $\ell(\cdot, t) \in L^1_+$  if we have the following two conditions [15, Theorem 2.4]:

- i.**  $F(L^1_+) \subseteq \mathbb{R}^2_+$ , and
- ii.** there exists an increasing function  $c_3: \mathbb{R}_+ \rightarrow \mathbb{R}_+$  such that

$$G(\phi) + c_3(r)\phi \in L^1_+$$

whenever  $r > 0$ ,  $\phi \in L^1_+$ , and  $\|\phi\| \leq r$ .

Clearly  $F(L^1_+) \subseteq \mathbb{R}^2_+$ , so we only need to show that there exists a suitable function  $c_3$ .

If  $\|\phi\| \leq r$ , using Part (a), we have

$$\begin{aligned}
 -G(\phi)(\tau) &= \begin{pmatrix} \mathcal{F}(\phi)\phi^n(\tau) + \mu\phi^n(\tau) \\ \mathcal{F}(\phi)k(\tau)\phi^i(\tau) + \mu\phi^i(\tau) \end{pmatrix} \leq (\hat{k}\mathcal{F}(\phi) + \mu)\phi(\tau) \\
 &\leq \left( \hat{k}\frac{\hat{T}}{P} \|\phi\| + \mu \right) \phi(\tau) \leq \left( \hat{k}\frac{\hat{T}}{P}r + \mu \right) \phi(\tau).
 \end{aligned}$$

Therefore, we can take

$$c_3(r) = \frac{\widehat{k}\widehat{T}r}{P} + \mu.$$

□

## B.2. Proof of Proposition 3

**Proof.** For  $0 < t < \bar{t}_\phi$  and  $h > 0$ , we have

$$\begin{aligned} & h^{-1} \int_0^\infty [\ell(\tau, t+h) - \ell(\tau, t)] d\tau \\ &= h^{-1} \int_0^h \ell(\tau, t+h) d\tau + h^{-1} \int_h^\infty \ell(\tau, t+h) d\tau - h^{-1} \int_0^\infty \ell(\tau, t) d\tau \\ &= h^{-1} \int_0^h \ell(\tau, t+h) d\tau + \int_0^\infty h^{-1} [\ell(\tau+h, t+h) - \ell(\tau, t)] d\tau, \end{aligned}$$

which converges  $F(\ell(\cdot, t)) + \int_0^\infty G(\ell(\cdot, t))(\tau) d\tau$  as  $h \rightarrow 0^+$  because of Equations (A.1) and (A.2).

Adding the entries of vectors  $h^{-1} \int_0^\infty \ell(\tau, t+h) - \ell(\tau, t) d\tau$  and  $F(\ell(\cdot, t)) + \int_0^\infty G(\ell(\cdot, t))(\tau) d\tau$ , we obtain

$$\frac{\underline{\mathcal{W}}(\ell(\cdot, t+h)) - \underline{\mathcal{W}}(\ell(\cdot, t))}{h} \rightarrow 0$$

as  $h \rightarrow 0^+$ . In other words,  $t \mapsto \underline{\mathcal{W}}(\ell(\cdot, t))$  is differentiable from the right in  $(0, \bar{t}_\phi)$ , and its right derivative is 0.

Given  $0 < \bar{t} < \bar{t}_\phi$ ,  $\ell \in L_{\bar{t}}$  so the restriction of the solution is a continuous  $\mathcal{A}$  on  $[0, \bar{t}]$  is a continuous function of  $t$  from  $[0, \bar{t}]$  to  $L^1$ ; therefore,  $\underline{\mathcal{W}}(\ell(\cdot, t))$  is also continuous in  $[0, \bar{t}]$ . Any continuous function in  $[0, \bar{t}]$  that has non-negative right derivative everywhere in  $(0, \bar{t})$  is non-decreasing in  $[0, \bar{t}]$  [16, Chapter 5, Proposition 2]. Because both  $\underline{\mathcal{W}}(\ell(\cdot, t))$  and  $-\underline{\mathcal{W}}(\ell(\cdot, t))$  have non-negative right derivatives, we can conclude that  $\underline{\mathcal{W}}(\ell(\cdot, t))$  is constant in  $[0, \bar{t}]$  for any  $0 < \bar{t} < \bar{t}_\phi$ .

Finally, if  $\phi \in L_+^1$ , because of Equation(A.3),

$$\underline{\mathcal{W}}(\ell(\cdot, 0)) = \underline{\mathcal{W}}(\phi) = \int_0^\infty [\phi^n(\tau) + \phi^t(\tau)] d\tau = \|\phi\|,$$

so  $\mathcal{U}(\ell(\cdot, t)) = \|\phi\|$  for all  $0 \leq t < \bar{t}_\phi$ . Additionally, from Part (c) of Proposition 2, we know that, if  $\phi \in L^1_+$ ,  $\ell(\cdot, t) \in L^1_+$ , then  $\mathcal{U}(\ell(\cdot, t)) = \|\ell(\cdot, t)\|$  for all  $0 \leq t < \bar{t}_\phi$ .  $\square$

### B.3. Proof of Proposition 4

**Proof.** If  $\bar{t}_\phi < \infty$ , then  $\limsup_{t \rightarrow 0} \|\ell(\cdot, t)\| = \infty$  [Theorem 2.3]. By Proposition 3, we know that  $\|\ell(\cdot, t)\|$  remains bounded (actually it is constant) for all  $t \in [0, \bar{t}_\phi)$  if  $\phi \in L^1_+$ . So, we can conclude that  $\bar{t}_\phi = \infty$ .  $\square$

### B.4. Proof of Proposition 5

**Proof.** The existence and uniqueness of a mild solution  $\ell$  of the ADP problem is guaranteed by Part (b) of Proposition 2. Also  $t_\phi = \infty$  because of Proposition 4 and  $\ell(\cdot, t) \in L^1_+$  for every  $t \in \mathbb{R}_+$  because of Part (c) of Proposition 2.

Note that

$$G(\phi)(\tau) = -M(\tau, \phi)\phi$$

for all  $\tau > 0$ , where  $M: \mathbb{R}_+ \times L^1 \rightarrow \mathcal{B}(\mathbb{R}^2, \mathbb{R}^2)$  is defined as

$$M(\tau, \phi) = \begin{pmatrix} \mathcal{F}(\phi) + \mu & 0 \\ 0 & k(\tau)\mathcal{F}(\phi) + \mu \end{pmatrix}.$$

For  $G$  of this form, the mild solution of the ADP problem in  $[0, \bar{t}_\phi)$  is a continuous solution of the ADP problem in  $[0, \bar{t}_\phi)$  [15, Theorem 2.9] if

- i.  $\phi \in L^1$  is continuous and  $\phi(0) = F(\phi)$ ,
- ii.  $F$  is Lipschitz on norm-balls of  $L^1$ , and
- iii. there exist increasing functions  $c_4, c_5, c_6: \mathbb{R}_+ \rightarrow \mathbb{R}_+$  such that, for all  $\phi_1, \phi_2 \in L^1$ ,  $\tau_1, \tau_2 \geq 0$ :
  - a.  $\|M(\tau_1, \phi_1) - M(\tau_2, \phi_1)\|_{\text{op}} \leq c_4(\|\phi_1\|)|\tau_1 - \tau_2|$
  - b.  $\|M(\tau_1, \phi_1)\|_{\text{op}} \leq c_5(\|\phi_1\|)$
  - c.  $\|M(\tau_1, \phi_1) - M(\tau_1, \phi_2)\|_{\text{op}} \leq c_6(\tau_1)\|\phi_1 - \phi_2\|$  if  $\|\phi_1\|, \|\phi_2\| \leq r$ .

(i) is part of the hypothesis and we already showed (ii) in the proof of Proposition 2, so we proceed to prove (iii).

Define  $\hat{T} = \sup_{\tau} \{T(\tau)\}$  and  $\hat{k} = \sup_{\tau} \{k(\tau)\}$ . Let  $\phi_1, \phi_2 \in L^1$ ,  $\tau_1, \tau_2 \geq 0$ . Using the fact that  $k$  is globally Lipschitz, let  $K$  be a constant such that

$$|k(\tau) - k(\tau')| \leq K|\tau - \tau'|$$

for all  $\tau, \tau' \geq 0$ . We have

$$\begin{aligned} \|M(\tau_1, \phi_1) - M(\tau_2, \phi_1)\|_{\text{op}} &= |k(\tau_1) - k(\tau_2)| \|\mathcal{F}(\phi_1)\| \\ &\leq \frac{\widehat{K}\widehat{T}}{P} \|\phi_1\| |\tau_1 - \tau_2|. \end{aligned}$$

and can take  $c_4(r) = \frac{\widehat{K}\widehat{T}r}{P}$

On the other hand,

$$\begin{aligned} \|M(\tau_1, \phi_1)\|_{\text{op}} &= \sup_{|x_1| + |x_2| = 1} \{|\mathcal{F}(\phi_1)x_1 + \mu x_1| + |k(\tau_1)\mathcal{F}(\phi_1)x_2 + \mu x_2|\} \\ &\leq \sup_{|x_1| + |x_2| = 1} \{|\mathcal{F}(\phi_1)x_1| + \mu|x_1| + |k(\tau_1)\mathcal{F}(\phi_1)x_2| + \mu|x_2|\} \\ &\leq \sup_{|x_1| + |x_2| = 1} \{\widehat{k}|\mathcal{F}(\phi_1)| + \mu\} \\ &\leq \frac{\widehat{k}\widehat{T}}{P} \|\phi_1\| + \mu, \end{aligned}$$

and we can take  $c_5(r) = \frac{\widehat{k}\widehat{T}r}{P} + \mu$ .

Finally,

$$\begin{aligned} \|M(\tau_1, \phi_1) - M(\tau_1, \phi_2)\|_{\text{op}} &= \sup_{|x_1| + |x_2| = 1} \{|\mathcal{F}(\phi_1 - \phi_2)x_1| + |k(\tau_1)\mathcal{F}(\phi_1 - \phi_2)x_2|\} \\ &\leq \sup_{|x_1| + |x_2| = 1} \{\widehat{k}|\mathcal{F}(\phi_1 - \phi_2)|(|x_1| + |x_2|)\} \\ &\leq \frac{\widehat{k}\widehat{T}}{P} \|\phi_1 - \phi_2\|, \end{aligned}$$

and we can take  $c_6(r) = \frac{\widehat{k}\widehat{T}}{P}$ .  $\square$

### B.5. Proof of Proposition 6

**Proof.** Let  $\phi_0 \in L^1$ . Define  $\widehat{T} = \sup_{\tau} \{T(\tau)\}$  and  $\widehat{k} = \sup_{\tau} \{k(\tau)\}$ . Note that both  $F'(\phi_0)$  and  $G'(\phi_0)$  defined above are linear operators from  $L^1$  to  $\mathbb{R}^2$  and from  $L^1$  to  $L^1$ , respectively. They are bounded linear operators because

$$\begin{aligned} |F'(\phi_0)(\phi)| &= \left| \mu \underline{\mathcal{W}}(\phi) \right| + |\mathcal{F}(\phi_0)\mathcal{W}(\phi) + \mathcal{F}(\phi)\mathcal{W}'(\phi_0)| \\ &\leq \left( \mu + |\mathcal{F}(\phi_0)|\widehat{k} + \frac{\widehat{T}}{P} |\mathcal{W}'(\phi_0)| \right) \|\phi\|, \end{aligned}$$

and

$$\begin{aligned}
\|G'(\phi_0)(\phi)\| &= \int_0^\infty |\mathcal{F}(\phi_0)\phi^n(\tau) + \mathcal{F}(\phi)\phi_0^n(\tau) + \mu\phi^n(\tau)|d\tau \\
&+ \int_0^\infty |\mathcal{F}(\phi_0)k(\tau)\phi^i(\tau) + \mathcal{F}(\phi)k(\tau)\phi_0^i(\tau) + \mu\phi^i(\tau)|d\tau \\
&\leq \left( |\mathcal{F}(\phi_0)|\hat{k} + \frac{\hat{T}}{P}\hat{k}\|\phi_0\| + \mu \right) \|\phi\|,
\end{aligned}$$

for any  $\phi \in L^1$ .

Now, let  $\epsilon > 0$  and  $\phi \in L^1$ . We have

$$\begin{aligned}
&|F(\phi) - F(\phi_0) - F'(\phi_0)(\phi - \phi_0)| \\
&= |\mathcal{F}(\phi)\mathcal{W}(\phi) - \mathcal{F}(\phi_0)\mathcal{W}(\phi_0) - \mathcal{F}(\phi_0)\mathcal{W}(\phi - \phi_0) - \mathcal{F}(\phi - \phi_0)\mathcal{W}(\phi_0)| \\
&= |\mathcal{F}(\phi)\mathcal{W}(\phi - \phi_0) - \mathcal{F}(\phi_0)\mathcal{W}(\phi - \phi_0)| \\
&= |\mathcal{F}(\phi - \phi_0)\mathcal{W}(\phi - \phi_0)| \\
&\leq \frac{\hat{T}}{P}\hat{k}\|\phi - \phi_0\|^2 \\
&\leq \epsilon\|\phi - \phi_0\|,
\end{aligned}$$

if  $\hat{T} = 0$ ,  $\hat{k} = 0$ , or if  $\|\phi - \phi_0\| < \delta = \min\left\{1, \frac{P\epsilon}{\hat{T}\hat{k}}\right\}$  when  $\hat{T} \neq 0$  and  $\hat{k} \neq 0$ .

Likewise, we have

$$\begin{aligned}
&\|G(\phi) - G(\phi_0) - G'(\phi_0)(\phi - \phi_0)\| \\
&= \int_0^\infty |\mathcal{F}(\phi - \phi_0)\phi^n(\tau) - \mathcal{F}(\phi - \phi_0)\phi_0^n(\tau)|d\tau \\
&+ \int_0^\infty |\mathcal{F}(\phi - \phi_0)k(\tau)\phi^i(\tau) - \mathcal{F}(\phi - \phi_0)k(\tau)\phi_0^i(\tau)|d\tau \\
&\leq \hat{k}|\mathcal{F}(\phi - \phi_0)| \int_0^\infty |\phi^n(\tau) - \phi_0^n(\tau) + \phi^0(\tau) - \phi_0^0(\tau)|d\tau \\
&= \hat{k}|\mathcal{F}(\phi - \phi_0)|\|\phi - \phi_0\| \\
&\leq \hat{k}\frac{\hat{T}}{P}\|\phi - \phi_0\|^2,
\end{aligned}$$

which again is smaller than  $\epsilon$  if  $\hat{T} = 0$ ,  $\hat{k} = 0$ , or if  $\|\phi - \phi_0\| < \delta = \min\left\{1, \frac{P\epsilon}{\hat{T}\hat{k}}\right\}$  when  $\hat{T} \neq 0$  and  $\hat{k} \neq 0$ .

Now, let  $\phi_1, \phi_2 \in L^1$ . We have



$$\begin{aligned} \|F'(\phi_1) - F'(\phi_2)\|_{\text{op}} &= \sup_{\|\phi\|=1} |\mathcal{F}(\phi_1 - \phi_2)\mathcal{W}'(\phi) + \mathcal{F}(\phi)\mathcal{W}'(\phi_1 - \phi_2)| \\ &\leq \sup_{\|\phi\|=1} \left\{ \frac{\hat{T}}{P} \|\phi_1 - \phi_2\| \hat{k} \|\phi\| + \frac{\hat{T}}{P} \|\phi\| \hat{k} \|\phi_1 - \phi_2\| \right\} \\ &= 2 \frac{\hat{T}}{P} \hat{k} \|\phi_1 - \phi_2\|. \end{aligned}$$

Thus,  $\phi \mapsto F'(\phi)$  is a continuous function from  $L^1$  to  $B(L^1, \mathbb{R}^2)$ .

On the other hand,

$$\begin{aligned} \|G'(\phi_1) - G'(\phi_2)\|_{\text{op}} &= \sup_{\|\phi\|=1} \left\{ \int_0^\infty |\mathcal{F}(\phi_1 - \phi_2)\phi^n(\tau) + \mathcal{F}(\phi)(\phi_1^n(\tau) - \phi_2^n(\tau))| d\tau \right. \\ &\quad \left. + \int_0^\infty |\mathcal{F}(\phi_1 - \phi_2)k(\tau)\phi^i(\tau) + \mathcal{F}(\phi)k(\tau)(\phi_1^i(\tau) - \phi_2^i(\tau))| d\tau \right\} \\ &\leq \sup_{\|\phi\|=1} \left\{ \|\mathcal{F}(\phi_1 - \phi_2)\| \hat{k} \|\phi\| + \mathcal{F}(\phi)\hat{k} \|\phi_1 - \phi_2\| \right\} \\ &\leq 2 \frac{\hat{T}}{P} \hat{k} \|\phi_1 - \phi_2\|. \end{aligned}$$

Thus,  $\phi \mapsto G'(\phi)$  is also continuous as a function from  $L^1$  to  $B(L^1, L^1)$ .  $\square$

### B.6. Proof of Proposition 7

**Proof.** A mild solution of the ADP problem on  $[0, \bar{t}_\phi)$  is a solution of the ADP problem and satisfies conditions (a)–(d) for any  $t \in [0, \bar{t}_\phi)$  as long as the following conditions hold [17, Theorem 2.3]:

- i. The functions  $F$  and  $G$  are Lipschitz on norm-balls of  $L^1_+$ ,
- ii. There exists a function  $c_3$  that satisfies (ii) in the proof of Proposition 2, Part (c).
- iii. The functions  $F$  and  $G$  are continuously F-differentiable relative to  $L^1_+$
- iv. The initial condition  $\phi$  has the properties:  $\phi \in L^1_+$  and is absolutely continuous,  $\phi' \in L^1$ , and  $\phi(0) = F(\phi)$ .

The existence and uniqueness of the mild solution of the ADP problem can be guaranteed by Proposition 2. Conditions (i) and (ii) are shown in the proofs of Parts (b) and (c) of Proposition 2, respectively. Condition (iii) is Proposition 6, whereas (iv) is part of the hypothesis. Finally, the fact that  $\bar{t}_\phi = \infty$  was the result of Proposition 4.  $\square$

### References

[1]. Alfaro-Murillo JA, An Epidemic Model Structured by the Time Since Last Infection, Ph.D. thesis, Purdue University, 2013.  
 [2]. Alfaro-Murillo JA, Feng Z, Glasser JW, A review and extension of time-since-infection models in epidemiology, submitted for publication.

- [3]. Brauer F, The Kermack-McKendrick epidemic model revisited, *Mathematical Biosciences* 198 (2) (2005) 119–131. [PubMed: 16135371]
- [4]. Brauer F, Shuai Z, van den Driessche P, Dynamics of an age-of-infection cholera model, *Mathematical Biosciences and Engineering* 10 (5 & 6) (2013) 1335–1349. [PubMed: 24245619]
- [5]. Breda D, Diekmann O, de Graaf WF, Pugliese A, Vermiglio R, On the formulation of epidemic models (an appraisal of Kermack and McKendrick), *Journal of Biological Dynamics* 6 (sup2) (2012) 103–117. [PubMed: 22897721]
- [6]. Diekmann O, Montijn R, Prelude to Hopf bifurcation in an epidemic model: analysis of a characteristic equation associated with a nonlinear Volterra integral equation, *Journal of Mathematical Biology* 14 (1) (1982) 117–127. [PubMed: 7077184]
- [7]. Feng Z, Iannelli M, Milner FA, A two-strain tuberculosis model with age of infection, *SIAM Journal on Applied Mathematics* 62 (5) (2002) 1634–1656.
- [8]. Feng Z, Thieme H, Endemic models with arbitrarily distributed periods of infection I: fundamental properties of the model, *SIAM Journal on Applied Mathematics* 61 (3) (2000) 803–833.
- [9]. Feng Z, Thieme HR, Endemic models with arbitrarily distributed periods of infection II: fast disease dynamics and permanent recovery, *SIAM Journal on Applied Mathematics* 61 (3) (2000) 983–1012.
- [10]. Hethcote HW, Thieme HR, Stability of the endemic equilibrium in epidemic models with subpopulations, *Mathematical Biosciences* 75 (2) (1985) 205–227.
- [11]. Inaba H, Kermack and McKendrick revisited: the variable susceptibility model for infectious diseases, *Japan Journal of Industrial and Applied Mathematics* 18 (2) (2001) 273–292.
- [12]. Kermack WO, McKendrick AG, A contribution to the mathematical theory of epidemics, *Proceedings of the Royal Society of London. Series A* 115 (772) (1927) 700–721.
- [13]. Thieme HR, Castillo-Chavez C, How may infection-age-dependent infectivity affect the dynamics of HIV/AIDS?, *SIAM Journal on Applied Mathematics* 53 (5) (1993) 1447–1479.
- [14]. Webb GF, D'Agata EMC, Magal P, Ruan S, Falkow S, A model of antibiotic-resistant bacterial epidemics in hospitals, *Proceedings of the National Academy of Sciences of the United States of America* 102 (37) (2005) 13343–13348. [PubMed: 16141326]
- [15]. Webb GF, *Theory of Nonlinear Age-Dependent Population Dynamics*, Monographs and Textbooks in Pure and Applied Mathematics, vol. 89, Marcel Dekker, New York, 1985.
- [16]. Royden HL, *Real Analysis*, 3rd edition, Macmillan, New York, 1988.
- [17]. Ruess WM, Linearized stability and regularity for nonlinear age-dependent population models, in: *Functional Analysis and Evolution Equations*, 2007, pp. 561–576, 10.1007/978-3-7643-7794-6\_34.
- [18]. Perko L, *Differential Equations and Dynamical Systems*, 3rd edition, Springer, 2001.
- [19]. Bhattacharya S, Adler FR, A time since recovery model with varying rates of loss of immunity, *Bulletin of Mathematical Biology* 74 (12) (2012) 2810–2819. [PubMed: 23097124]
- [20]. Magal P, McCluskey C, Two-group infection age model including an application to nosocomial infection, *SIAM Journal on Applied Mathematics* 73 (2) (2013) 1058–1095, 10.1137/120882056, <http://epubs.siam.org/doi/abs/10.1137/120882056>.