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M. Lazarova; S. Markov; A. Vassilev

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Reaction Networks with Application to Epidemiological Outbreaks and Biological Growth

M. Lazarova,[1, a)] S. Markov,[2, b)] and A. Vassilev[3, c)]

[1]*Faculty of Applied Mathematics and Informatics, Technical University of Sofia, Sofia, Bulgaria*
[2]*Institute of Mathematics and Informatics, Bulgarian Academy of Sciences, Sofia, Bulgaria*
[3]*Faculty of Economics and Business Administration, St. Kliment Ohridski University of Sofia, Sofia, Bulgaria*

[a)]meglena.laz@tu-sofia.bg
[b)]smarkov@bio.bas.bg
[c)]Corresponding author: a.vassilev@feb.uni-sofia.bg

Abstract. Several classes of reaction networks possessing clear physical and biological interpretation together with the induced dynamical systems are discussed and analyzed. The studied reaction networks include basic reactions such as versions of exponential radioactive decay growth and SIS epidemiological models. We analyze the solutions of the generated systems of ordinary differential equations and define different summary measures of their speed of development. We then graphically present the obtained solutions and study the possibility of introducing exogenous catalytic species that enrich the dynamic behavior of the system considered.

INTRODUCTION

Systems of reactions – chemical, biological or social – can be formalized as *reaction networks*. The study of the reaction networks is referred to as *reaction network theory* (RNT) or traditionally *chemical reaction network theory* (CRNT). Reaction networks are useful tool for modeling and simulation of epidemiological outbreaks and biological growth processes, see [1], [2], [3], [4]. The main purpose of our joint work is to study certain characteristics of some dynamical systems' solutions induced by chemical reaction networks. The studied dynamical systems are close to Gompertzian and logistic type growth models [2], [5], [6].

A reaction network can be presented symbolically as a system of elementary reactions. An illustrative example is given by:

$$S+Q \xrightarrow{k} P+R. \tag{1}$$

The interpretation of this expression is that two or more species on the left side of the arrow, called *reactants* or *reagents* (in this example species S and Q) react and as a result of the reaction one or more species, named *products* (here P and R) are produced.

All species (reactants and products) partaking in a reaction are denoted by uppercase letters. A positive number called "rate parameter" is written over the reaction arrow. It indicates the velocity of the reaction. The reactants on the left side of the reaction arrow either decay or remain constant, whereas the product species on the right side of the arrow grow. In some cases species may appear two or more times at one side of the arrow, such as $A+A$, briefly denoted as $2A$. The sign "+" has different meaning when it is placed on the left or on the right side of the reaction arrow. On the left side the "+" means reaction between the enlisted reactants. On the right no reaction is assumed between the product species but the "+" sign is used to separate the different products.The masses of the species are taken as functions of time t and are denoted by corresponding lowercase letters, such as $s = s(t), p = p(t), \ldots$ The species are assumed to be involved in a reaction network which is governed by mass action kinetics (see, *e.g.*, [7]). Therefore the reaction network induces an unique dynamical system of reaction equations for the rates $s' = ds(t)/dt, p' = dp(t)/dt, \ldots$ of the concentrations.

The elementary reaction (1) is an example of a reaction network written in *canonical form*. For the reactions in canonical form the arrow should point to the right. If a process is bidirectional, then each direction should be described by a separate elementary reaction.

THE ONE-STEP EXPONENTIAL GROWTH-DECAY MODEL

In this work the growth-decay models are introduced with their reaction networks presentation and the solutions of the induced systems of differential equations. The dynamical system suggests some insight for the "inner mechanism"

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that controls the behavior of the solutions and the physical meaning of the parameters involved in the system.

The one-step exponential growth-decay model is defined by the reaction network:

$$S \xrightarrow{k} P$$

The dynamical system generated by this reaction network is:

$$s' = -ks,\ p' = +ks. \tag{2}$$

The system is coupled with the initial conditions:

$$s(0) = s_0 > 0,\ p(0) = p_0 \geq 0, \tag{3}$$

where the the conservation relation is represented by:

$$s' + p' = 0 \quad \Rightarrow \quad s + p = c = const,\ s_0 + p_0 = c.$$

Then the solution to the model is the following:

$$s(t) = s_0 e^{-kt},\ p(t) = c - s_0 e^{-kt},\ c = s_0 + p_0.$$

Special characteristics of growth and decay models

Different parametrizations of a growth or a decay curve may be inspected and compared graphically but it is often convenient to rely on summary numerical measures that characterize the speed of development of the respective phenomenon. Below we review the concept of half-life, which is useful in characterizing the speed of decay of a species. We also propose measures that can be applied to gauge the rate of growth of a species. These measures, in a sense, mirror the idea of half-life in the case of a growing species.

Consider a monotonically decreasing function $x(t)$. **Half-life** is defined as the time t_h such that

$$x(t_h) = \frac{x(0)}{2},$$

i.e. the moment when a mass or concentration is reduced to half its initial level.

We can define a counterpart concept in the case of a monotonically increasing function $x(t)$. Assuming that the function satisfies $x(0) > 0$, **doubling time** is the time t_d such that

$$x(t_d) = 2x(0),$$

i.e. the time when twice the initial mass is reached.

For increasing functions that eventually reach a horizontal asymptote (saturation level), say $x(\infty)$, one can also be interested in the time when the function reaches the midpoint between the initial condition and equilibrium. Formally, **half-convergence time** is the time t_c which satisfies

$$x(t_c) = \frac{x(0) + x(\infty)}{2}.$$

We apply these concepts to alternative parametrizations of the models discussed below. As an illustration, Figure 1 shows different versions of the one-step exponential growth-decay model together with the numerical characteristics defined above, i.e. half-life, doubling time and half-convergence time.

TWO-STEP EXPONENTIAL GROWTH-DECAY MODEL

The two-step exponential growth decay model (see [1], [3] or, for a historical reference, [8]) is defined by the following reaction network:

$$S \xrightarrow{k_1} P \xrightarrow{k_2} Q$$

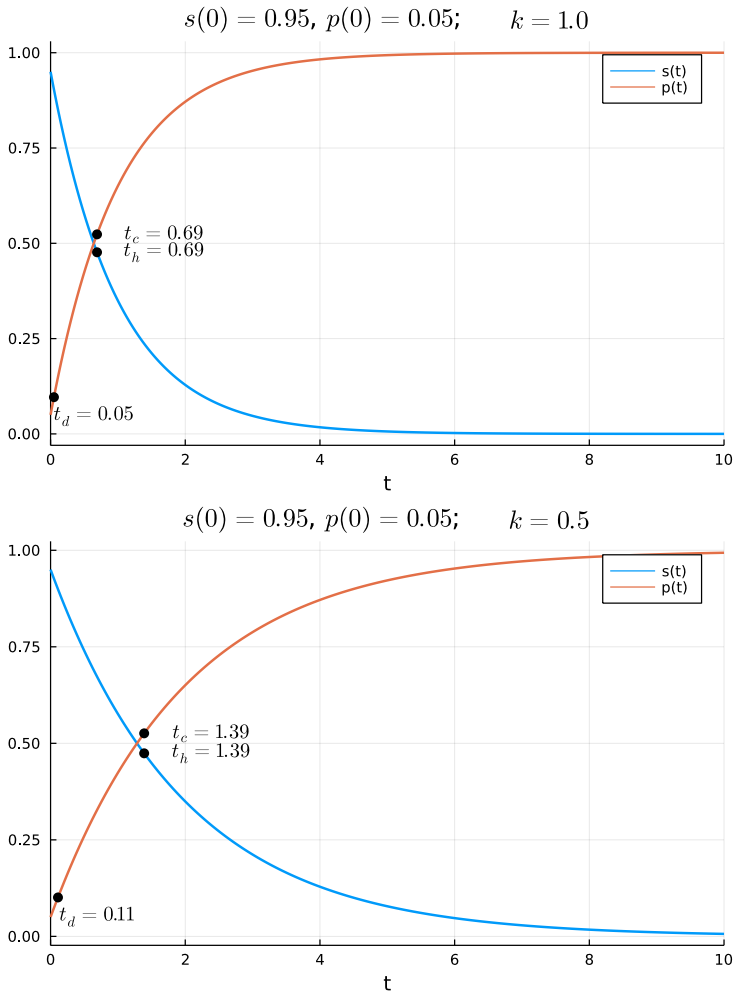

FIGURE 1. The solution of (2) and (3) for different values of k

The dynamical system associated with the reaction network above is given by:

$$s' = -k_1 s,\ p' = k_1 s - k_2 p,\ q' = k_2 p, \tag{4}$$

with the following initial conditions:

$$s(0) = s_0 > 0,\ p(0) = p_0 \geq 0,\ q(0) = q_0 \geq 0. \tag{5}$$

The conservation relation that is valid for this model is the following:

$$s' + p' + q' = 0 \quad \Rightarrow \quad s + p + q = c = const,\ s_0 + p_0 + q_0 = c.$$

Here the functions $s(t)$ and $q(t)$ are the *decay* and *growth* components of the network, similarly to the 1-step exponential growth decay model. We refer to the function $p(t)$ as the *outbreak function* (also *population outbreak, PO function*).

The solution components of (4) and (5) are shown in Figure 2. Figure 3 presents the respective growth and decay components along with their half-life, doubling time and half-convergence time.

A notable feature of the two-step exponential growth decay model is the existence of the so-called lag time. Briefly, if the growth component $q(t)$ of the model has an inflection point at t^*, one can construct a line with slope equal to $q'(t^*)$ passing through the point $(t^*, q(t^*))$. Let this line intersect the abscissa at t_a. Then the lag time for the growth function $q(t)$ is defined as $t^* - t_a$. More details can be found in [9].

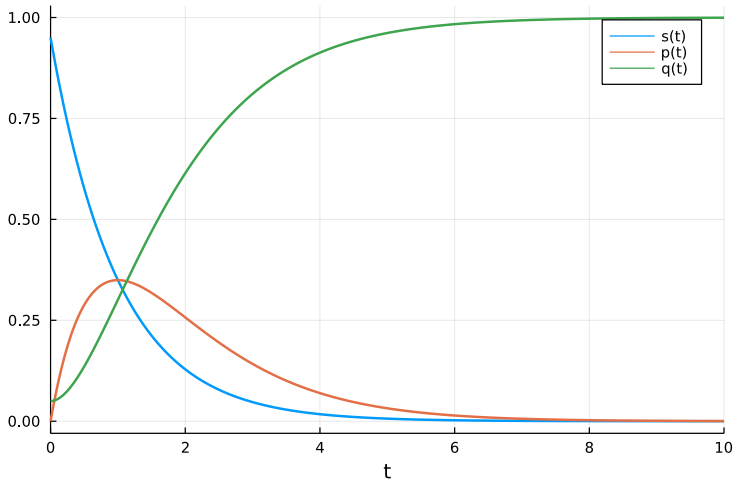

FIGURE 2. The solution of (4) and (5) for $s_0 = 0.95$, $p_0 = 0.0$, $q_0 = 0.05$ and $k_1 = 1.0$, $k_2 = 1.0$

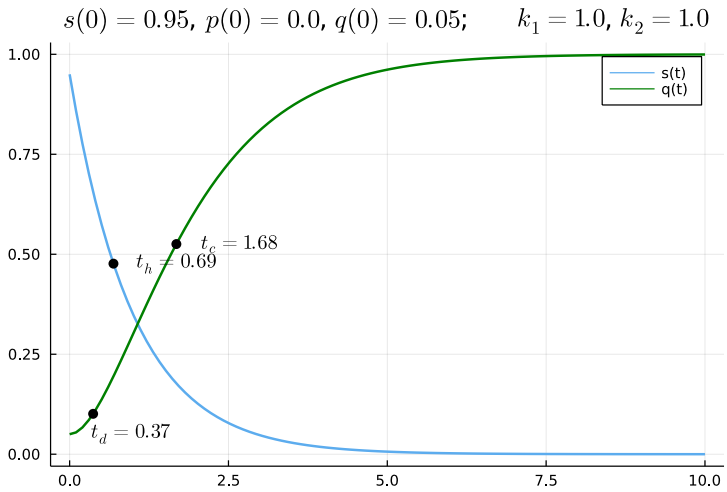

FIGURE 3. The growth and decay components from Figure 2

In contrast to the two-step exponential growth-decay model, the one-step exponential growth-decay model does not have a lag time. While technically this is due to the absence of inflection points for the one-step model, the existence of a lag time for the two-step model can be interpreted as reflecting the properties of the outbreak function, which peaks and then starts declining, thus limiting the growth of $q(t)$.

EPIDEMIOLOGICAL MODELS AND APPLICATIONS

Epidemiological SIS model

The SIS model (see [10] for a basic introduction and motivation) is one of the fundamental epidemiological models that may be applied to the study of recurrent epidemics. Different versions of this model can be developed, *e.g.*, featuring stochastic dynamics as in [11], impulsive dynamics as in [12] or various social phases ([13]).

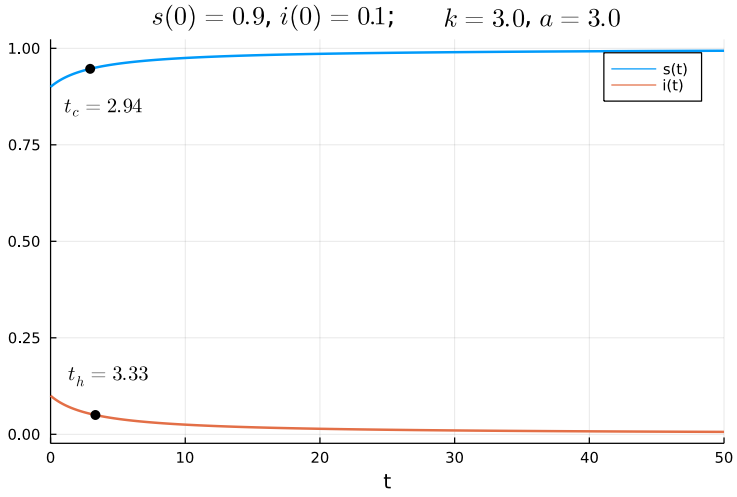

FIGURE 4. Epidemiological SIS model in the case of no disease outbreak

The epidemiological SIS model is given by a reaction network of the following form:

$$S + I \xrightarrow{k} 2I$$
$$I \xrightarrow{a} S.$$

Here S denotes the susceptible individuals, who become infected (I) upon contact with an infected person. Infected members of the population return to susceptible status upon recovering from the disease.

The dynamical system generated by this reaction network is:

$$\begin{aligned} s' &= ai - kis \\ i' &= -ai + kis, \end{aligned} \tag{6}$$

with the following initial conditions:

$$s(0) = s_0 > 0, i(0) = i_0 > 0. \tag{7}$$

The conservation relation for this model is:

$$s' + i' = 0 \quad \Rightarrow \quad s + i = s_0 + i_0 = const.$$

Depending on the initial conditions and parameter values a disease can die out, resulting in a disease-free equilibrium (Figure 4), or get a hold in a population, leading to an endemic equilibrium (Figure 5).

More precisely, the type of equilibrium that obtains can be inferred through the basic reproduction number $\mathscr{R}_0$ (see [14], ch. 2). Summarizing this discussion, we can formulate the following

Proposition 1 *The basic reproduction number $\mathscr{R}_0$ for the SIS model is equal to $\frac{k}{a}(s_0 + i_0)$. For $\mathscr{R}_0 > 1$, the endemic equilibrium obtains, and for $\mathscr{R}_0 < 1$ the disease-free equilibrium obtains.*

Epidemiological SIS model with exogenous catalytic species

The epidemiological SIS model with exogenous catalytic species has the following reaction network:

$$C + S + I \xrightarrow{k} C + 2I$$
$$I \xrightarrow{a} S$$

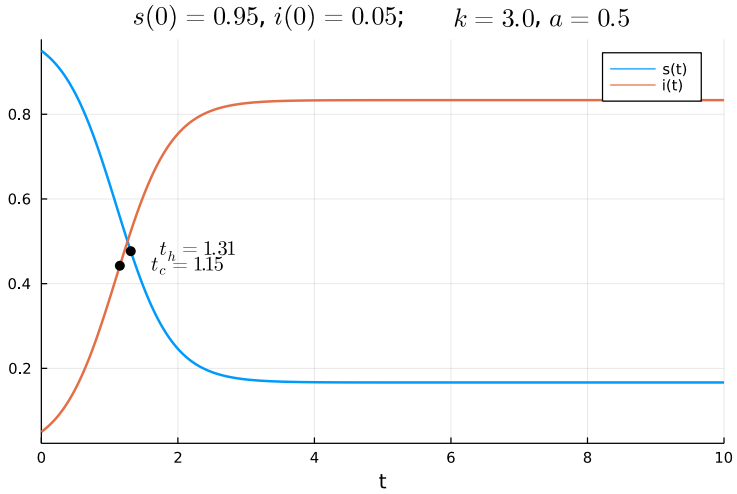

FIGURE 5. Epidemiological SIS model in the case of a disease outbreak

The mechanisms envisaged are similar to those of the standard SIS model. The difference with the SIS model is in the presence of an exogenous catalyst C which may for instance be interpreted as an environmental factor that impacts the speed of the reaction. The concentration of the exogenous catalyst C is assumed to be a known function of time, $c(t)$.

The reaction network above results to the following dynamical system:

$$\begin{aligned} s' &= ai - kcis \\ i' &= -ai + kcis \end{aligned} \tag{8}$$

The initial conditions for this model are as follows:

$$s(0) = s_0 > 0,\ i(0) = i_0 > 0. \tag{9}$$

The model is characterized by the conservation relation

$$s' + i' = 0 \quad \Rightarrow \quad s + i = s_0 + i_0 = const.$$

To provide a specific illustrative implementation, let us consider the case when the exogenous catalyst exhibits some kind of cyclical behavior, for example induced by seasonal factors. One version of such a dynamical system may be given by the following ordinary differential equations:

$$\begin{aligned} c' &= k_1 \cos(t) \\ s' &= k_3 i - k_2 cis \\ i' &= -k_3 i + k_2 cis \end{aligned}$$

The model in question is capable of generating different types of epidemiological outcomes. Depending on the velocities of transition between the groups, one can obtain a situation with a disease-free equilibrium (Figure 6). It is also possible to have outcomes where the masses of susceptible and infected individuals fluctuate around different levels, corresponding to low or high incidences of the disease (Figures 7 and 8).

Epidemiological SEIS model

The epidemiological SEIS model is represented by the following reaction network:

$$\begin{aligned} S + I &\xrightarrow{k} E + I \\ E &\xrightarrow{m} I \\ I &\xrightarrow{a} S \end{aligned}$$

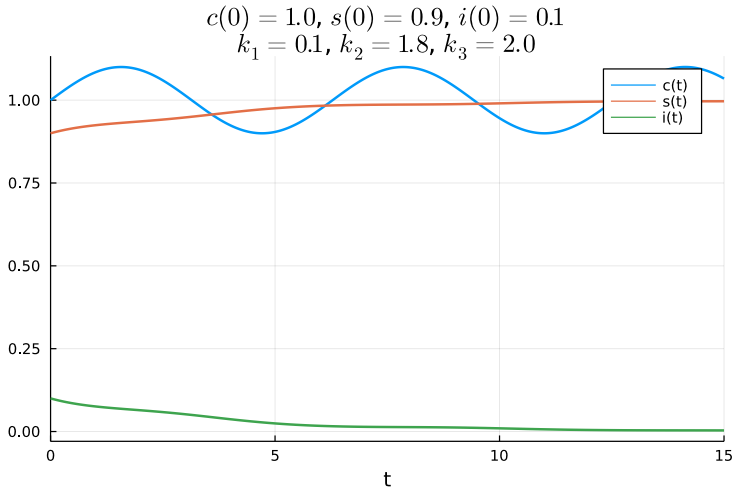

FIGURE 6. SIS model with exogenous catalytic species: no disease outbreak

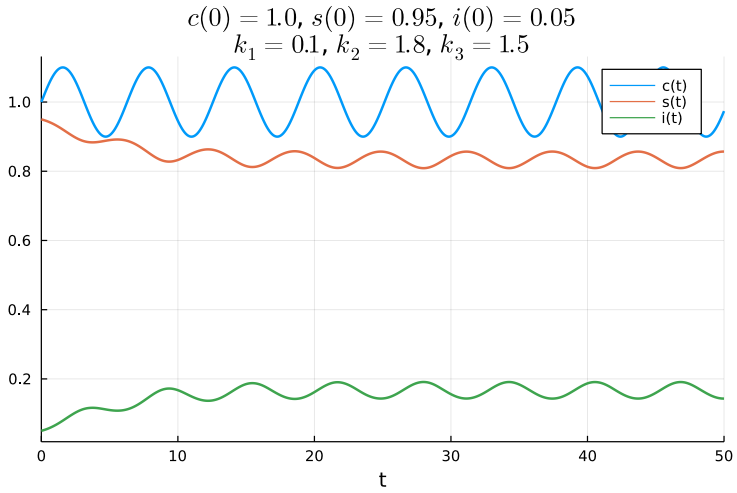

FIGURE 7. SIS model with exogenous catalytic species: low incidence equilibrium

The assumption of this model is that, upon contracting the disease, individuals spend a certain amount of time in a latent state where they are not yet infectious. These individuals are referred to as exposed (E). After a while exposed members of the population become infectious and start spreading the disease on contact.

This reaction network is associated with the dynamical system:

$$\begin{aligned} s' &= ai - kis \\ e' &= -me + kis \\ i' &= me - ai \end{aligned} \tag{10}$$

System (10) is coupled with the initial conditions

$$s(0) = s_0 > 0, e(0) = e_0 \geq 0,\ i(0) = i_0 \geq 0. \tag{11}$$

The conservation relation for this model is:

$$s' + e' + i' = 0 \quad \Rightarrow \quad s + e + i = s_0 + e_0 + i_0 = \text{const.}$$

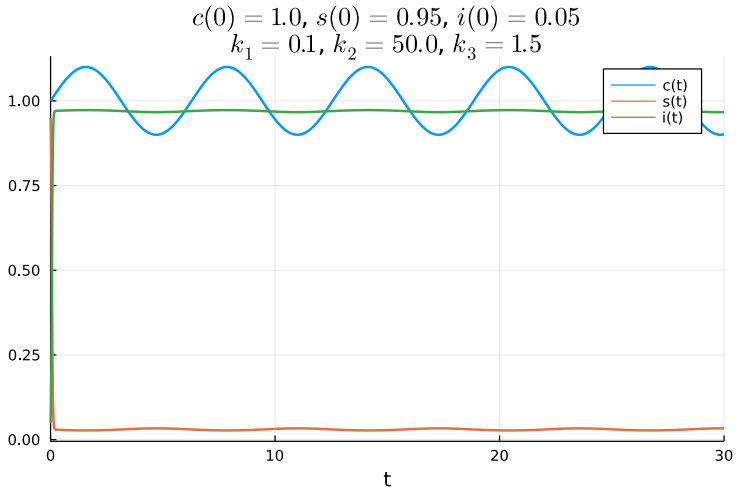

FIGURE 8. SIS model with exogenous catalytic species: high incidence equilibrium

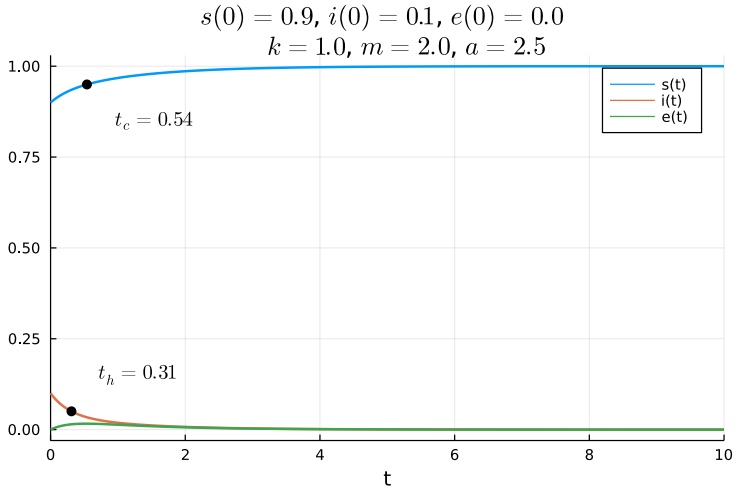

FIGURE 9. Epidemiological SEIS model in the case of no disease outbreak

Similarly to the SIS model, the SEIS model can support situations where there is a disease-free equilibrium (Figure 9) or where an endemic equilibrium obtains (Figure 10). The type of equilibrium again can be inferred from the basic reproduction number $\mathscr{R}_0$ (see [15], where the precise set of assumptions is detailed). Based on that, we have the following result:

Proposition 2 *For the SEIS model in the case* $s0 + e0 + i0 = 1$ *the basic reproduction number* $\mathscr{R}_0$ *equals* $\frac{k}{a}$. *When* $\mathscr{R}_0 \leq 1$, *the disease-free equilibrium obtains and when* $\mathscr{R}_0 > 1$, *an endemic equilibrium obtains.*

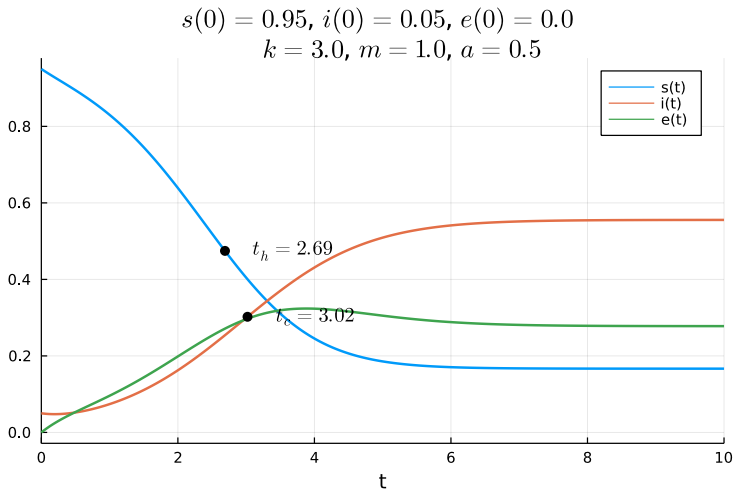

FIGURE 10. Epidemiological SEIS model in the case of a disease outbreak

Epidemiological SEIS model with exogenous catalytic species

The epidemiological SEIS model with an exogenous catalytic species is represented by the reaction network

$$\begin{aligned} C+S+I &\xrightarrow{k} C+E+I \\ E &\xrightarrow{m} I \\ I &\xrightarrow{a} S, \end{aligned}$$

where the catalyst is denoted by C. The model is a straightforward adaptation of the SIS model with exogenous catalytic species, as discussed above, to the SEIS case.

The corresponding dynamical system is formed by the following ordinary differential equations

$$\begin{aligned} s' &= ai - kcis \\ e' &= -me + kcis \\ i' &= me - ai, \end{aligned}$$

where the initial conditions are as follows:

$$s(0) = s_0 > 0, e(0) = e_0 \geq 0,\ i(0) = i_0 \geq 0. \tag{12}$$

Here the conservation relation is given by:

$$s' + e' + i' = 0 \quad \Rightarrow \quad s + e + i = s_0 + e_0 + i_0 = \text{const.}$$

An illustrative implementation is again given by taking the catalytic species as governed by a given periodic function. For this implementation the dynamical system is:

$$\begin{aligned} c' &= k_1 \cos(t) \\ s' &= k_4 i - k_2 cis \\ e' &= -k_3 e + k_2 cis \\ i' &= k_3 e - k_4 i \end{aligned}$$

In a manner analogical to the SIS model with exogenous catalytic species, our numerical results indicate that we can have outcomes where there is no disease outbreak, as shown in Figure 11, or where fluctuations are observed around different incidence levels (Figures 12 and 13).

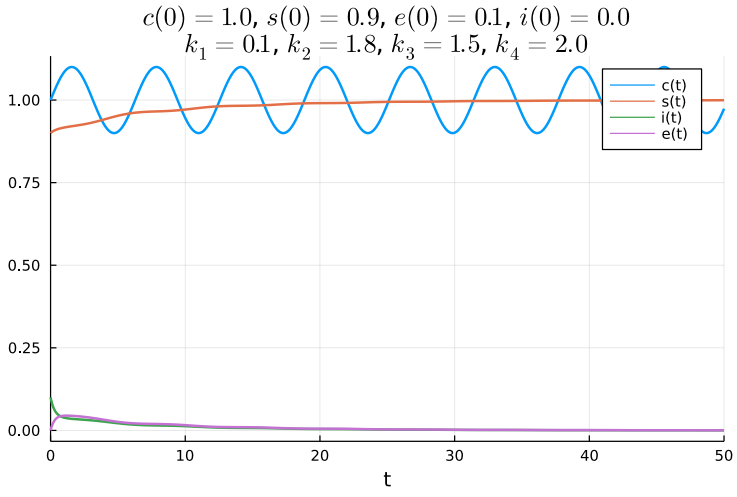

FIGURE 11. SEIS model with exogenous catalytic species: no disease outbreak

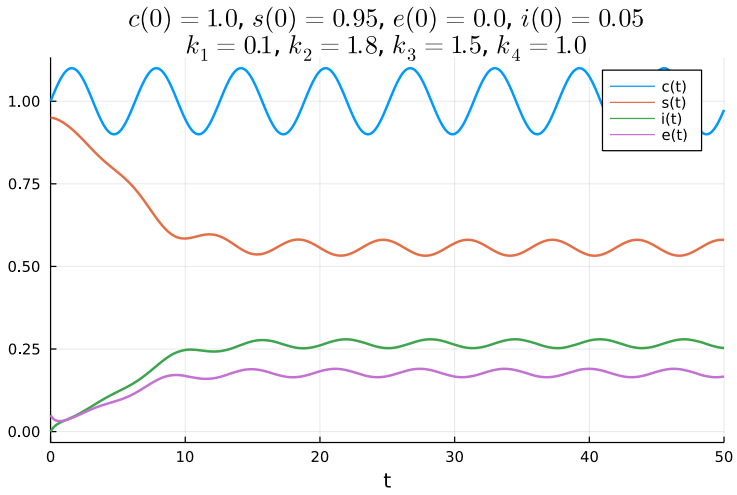

FIGURE 12. SEIS model with exogenous catalytic species: low incidence equilibrium

CONCLUSION

We study the 1-step and 2-step growth-decay models to analyze properties that are exhibited by more complex models with a growth or decay component.We define and compute several characteristics of growth and decay functions that measure globally the speed of development of the respective phenomenon. Our work also looks at implementations of the SIS and SEIS epidemiological models in terms of appropriate reaction networks.We propose modifications of the SIS and SEIS models that feature an exogenous catalytic species and show that multiple outbreaks of an infection can be generated in this framework. An open issue which arises in this setup is the comparison of our approach with models featuring time-dependent velocities.

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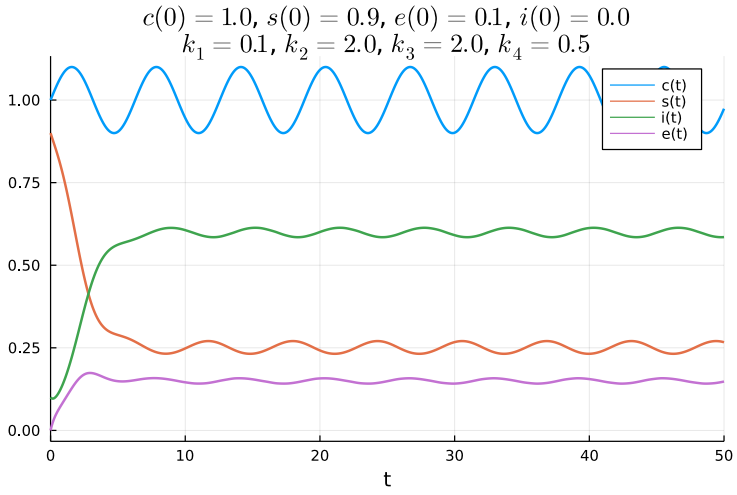

FIGURE 13. SEIS model with exogenous catalytic species: high incidence equilibrium

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