Journal of Mathematical Chemistry
https://doi.org/10.1007/s10910-021-01240-8

ORIGINAL PAPER

The two-step exponential decay reaction network: analysis of the solutions and relation to epidemiological SIR models with logistic and Gompertz type infection contact patterns

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Received: 13 May 2020 / Accepted: 22 February 2021

Abstract
We mathematically analyze the solutions to the dynamical system induced by the two-step exponential (growth-)decay (2SED) reaction network involving three species and two rate parameters. We study the influence of the rate parameters on the shape of the solutions. We compare the latter to those of the classic Kermack–McKendrick epidemiological SIR model. We then discuss the similarities and differences between the 2SED and the SIR models from the perspective of chemical reaction network theory (CRNT), as well as from epidemiological modelling view-point. The CRNT approach suggests that the classical SIR model, based on the logistic reaction mechanism, describes well epidemic events related to diseases spreading via a 'one-to-one' contact pattern between individuals. On the other side, the 2SED model can be used to simulate epidemic data coming from non-communicable diseases. Our comparative analysis naturally suggests the formulation of a SIR-type model, which is situated between the classic SIR model and the 2SED model, such that the logistic 'one-to-one' contact mechanism is replaced by a catalytic (Gompertzian) one. The proposed G-SIR model can be considered as an intermediate step between the SIR and the 2SED models. We compare the shapes of the solutions to the three discussed models and formulate a hypothesis that relates the characteristics of the solution shapes to the model reaction mechanism, resp. to the contact patterns of the particular disease.

Keywords Reaction networks · Chemical reaction network theory · Exponential growth-decay reaction chain · Epidemiological model

Mathematics Subject Classification 92E99 · 92D30

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Published online: 20 March 2021

1 Introduction

In his popular book on Mathematical Biology J. D. Murray writes: "Suppose the disease is such that the population can be divided into three distinct classes: the susceptible, S, who can catch the disease; the infectives, I, who have the disease and can transmit it; and the removed class, R, namely, those who have either had the disease, or are recovered, immune or isolated until recovered. The progress of individuals is schematically represented by $S \longrightarrow I \longrightarrow R$. Such models are often called SIR models" [32, Chap. 10.2, p. 320].

The "schematical representation" $S \longrightarrow I \longrightarrow R$ of the dynamics of a SIR model is mentioned by many authors, some of them calling it "diagram scheme". This "scheme" gives a general idea of the dynamics of a disease, however, it rises the natural question: what is the relation between the SIR model and the "diagram scheme" $S \longrightarrow I \longrightarrow R$, if the latter is interpreted as a reaction network in the sense of chemical reaction network theory (CRNT) [12, 15, 25], that is as a two-step exponential (radioactive decay) chain?

To answer this question, we have to compare the reaction network $S \longrightarrow I \longrightarrow R$ with the reaction network $S + I \longrightarrow 2I, I \longrightarrow R$ inducing the SIR model under mass action kinetics. Note that the first reaction in the SIR network is a (self-)catalyzed reaction where species I catalyzes the first-order reaction $S \longrightarrow I$. The catalytic action of species I over species S corresponds to the requirement on the disease to be communicable (contagious). Otherwise, if the disease is not communicable, the logistic type reaction network inducing the SIR model, will turn into a first-order exponential reaction.

The aim of this work is to investigate the relation between the two models considered as reaction networks. To this end we first mathematically analyze the solutions to the two-step exponential model in the spirit of the familiar analysis of the solutions to the SIR model [18, 19, 32]. We then focus on some analogies between the two models and certain new interpretations of the two-step exponential model.

The two-step exponential chain is a special case of the n-step exponential chain, known in the field of nuclear physics as exponential radio-active decay. The n-step exponential chain induces a dynamical system of equations, known as Bateman's system of differential equations [4]. Bateman's equations are extensively used in nuclear physics to study radioactive decay chains of particular nuclides. Nuclear physicists and chemists are mostly interested in the half-life characteristics of the nuclides involved in the reaction chain. The mathematical formulae for the solutions of Bateman's equations in the theory of radioactive decay are usually presented in matrix form [31]. Such a compact form is suitable for the description and study of reaction chains involving many nuclides—normally 4, 5 and more. In the case of the two-step exponential reaction chain the number of species is only three and some characteristics of the shape of the solutions, such as extremum and inflection points are of significant interest especially when it comes to fitting the solutions to measurement data describing dynamical processes. For the latter purposes one needs a detailed knowledge of the properties of the solutions to the two-step exponential chain, which we did not find in the available scholarly literature.

From the perspective of the chemical reaction network theory (CRNT), the two-step exponential chain model is tightly related to some of the most familiar mathematical models used for fitting life science data, such as the logistic and the Gompertz models. This is another motivation to analyze mathematically the solutions to the two-step exponential chain.

When studying the properties of the solutions to the two-step system of Bateman's differential equations, we focus our attention on characteristics, such as monotonicity, convexity, extremums, inflection points, etc. We examine situations when one of the chain-links is (much) faster than the other one, that is the values of the two rate parameters differ significantly. We formulate and prove some new properties of the solutions to the two-step Bateman system of differential equations focusing especially on the intermediate function and the sigmoidal growth function describing the temporal evolution of the final third species in the reaction chain. We consider the limiting cases when the much faster chain-link can be eliminated so that the two-step chain can be reduced to (approximated with) an one-step growth-decay reaction ($n = 1$).

The paper is structured as follows. In the preliminary Sect. 2 we introduce the language of chemical reaction network theory recalling the well-known first-order one-step exponential growth-decay model. The use of CRNT approach throughout the paper allows for treating all model networks as two-compartmental growth-decay processes and to keep an eye on the chemical meaning of all variables and parameters of the discussed models.

In Sect. 3 we introduce the two-step exponential decay reaction chain and analyze the solutions to the induced dynamical system as functions of time. We also study the influence of the rate parameters on the shape of the solutions.

In Sect. 4 we briefly recall the familiar logistic and Gompertz models formulating them as chemical reaction networks. This allows us to demonstrate the two-compartmental growth-decay nature of the models as involving two equally important parts: a "decaying" part (species, compartment) and a "growing" part. We then introduce the classic Kermack–McKendrick SIR model again as reaction network, emphasizing its relation to the logistic model. Our CRNT approach suggests a natural "Gompertzian" SIR (G-SIR) variant of the classic SIR model, such that the SIR logistic reaction is replaced by a Gompertzian one.

In Sect. 5 we introduce and analyze a so-called G-SIR model, which is a SIR-type epidemiological model with Gompertzian disease spread mechanism instead of the familiar logistic one.

In Sect. 6 we consider the two-step exponential growth-decay model from the perspective of the SIR-type epidemiological models. We conclude that the two-step exponential model can be used to simulate epidemic outbreaks related to non-communicable diseases caused by environmental factors, whenever the spread of the disease is not necessarily due to contacts within the individuals.

2 Preliminaries: the one-step exponential growth-decay model

Throughout the paper we shall denote (biological) species by uppercase letters, say S, P, Q, and shall assume that all species are homogeneously distributed in a fixed volume (space, areal). We shall consider the concentrations (masses) of the species as functions of time t, and denote them by corresponding lowercase letters, such as $s = s(t), p = p(t), q = q(t)$. We shall also assume that the species are involved in a reaction network which is governed by mass action kinetics. Therefore the reaction network induces an unique dynamical system of reaction equations for the rates $s' = ds(t)/dt$, $p' = dp(t)/dt$, ..., of the concentrations.

We next recall a familiar example of a growth-decay model induced by a reaction network.

2.1 The one-step exponential growth-decay model

The familiar n-step exponential growth-decay reaction network (chain) $S_1 \longrightarrow S_2 \longrightarrow \cdots \longrightarrow S_n \longrightarrow P$ is used in the study of radio-active (nuclear) decay phenomena. Under the assumption of mass action kinetics the exponential decay chain induces a dynamical system of reactant equations known as *Bateman's differential equations*, named on H. Bateman, who has shown that the dynamical system of radioactive decay possesses an exact algebraic solution [4].

In the simplest case of just one step $n = 1$, that is: $S_1 \longrightarrow P$ the exponential decay reaction is known as "first-order decay reaction" or as "saturation growth model"; in the field of marine ecology and fishery the name "von Bertalanffy model" is also used [43].

Let us write the one-step first-order reaction (network) as:

$$S \xrightarrow{k} P, \tag{1}$$

where $k > 0$ is a positive rate parameter. Assuming that reaction (1) is governed by mass action kinetics leads to the dynamical system:

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

System (2) implies the relation $s' + p' = 0$ which after integration gives the conservation relation

$$s + p = c = \text{ const }. \tag{3}$$

Consider initial values

$$s(0) = s_0 > 0, \quad p(0) = p_0 \geq 0. \tag{4}$$

When equipped with initial conditions (4) dynamical system (2) turns into an initial value problem (IVP) (2)–(4) and relation (3) becomes $s + p = c = s_0 + p_0$. This allows to obtain an autonomous ordinary differential equation for the growth function p of the form:

$$p' = k(c - p),$$

with initial condition $p(0) = p_0$.

The differential equations for s and p under initial conditions (4) admit explicit solutions as functions of $t \geq 0$:

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

Function p is also known as saturation growth model, function s is usually known as first-order exponential decay model.

The purpose of this example is to suggest that throughout this work all models will be formulated as chemical reaction networks involving both growth and decay species (functions, compartments) and both species will receive equal attention, moreover special consideration will be given to relations between the two functions, such as relation (3) in our example.

3 The two-step exponential growth-decay model: properties of the solutions

In this section we consider some properties of the solutions to the two-step exponential growth-decay model.

3.1 The two-step exponential growth-decay model and its solutions

Definition 1 An exponential growth-decay mechanism involving two sequential first order steps in the transformation of three species S, P, Q is presented in the following reaction network:

$$S \xrightarrow{k_1} P \xrightarrow{k_2} Q, \tag{5}$$

where k_1, k_2 are positive rate parameters.

Denote the concentrations (masses) of species S, P, Q as functions of time t by $s = s(t), p = p(t), q = q(t)$ and their derivatives respectively by s', p', q'.

Under the assumption of homogeneity and mass action kinetics, reaction network (5) induces the following dynamical system of reaction equations:

$$\begin{aligned} s' &= -k_1 s, \\ p' &= k_1 s - k_2 p, \\ q' &= k_2 p. \end{aligned} \tag{6}$$

Dynamical system (6) induces the following conservation relation

$$s + p + q = c = \text{ const }. \tag{7}$$

Indeed, dynamical system (6) follows by the general theory of reaction networks [25] under the assumption that reaction network (5) is governed by mass action

kinetics. The conservation equation follows from the relation $s' + p' + q' = 0$ induced by system (6).

We assume a set of initial value conditions to dynamical system (6) as follows:

$$s(0) = s_0 > 0; \quad p(0) = p_0 = 0; \quad q(0) = q_0 = 0. \tag{8}$$

Remark 2 The more general assumption $p_0 \geq 0$ will be discussed in Sect. 4.

Under initial conditions (8) the constant c becomes $c = s_0 > 0$, hence the conservation relation obtains the form:

$$s + p + q = s_0.$$

Solutions to initial value problem (6)–(8).

Definition 3 Consider the following functions defined in the interval $T = [0, \infty)$:

$$s(t) = s_0 e^{-k_1 t}; \tag{9}$$

$$p(t) = \begin{cases} \frac{s_0 k_1}{k_2 - k_1}(e^{-k_1 t} - e^{-k_2 t}), & k_1 \neq k_2, \\ s_0 k t e^{-kt}, & k_1 = k_2 = k; \end{cases} \tag{10}$$

$$q(t) = \begin{cases} \frac{s_0}{k_2 - k_1}\left(k_2(1 - e^{-k_1 t}) - k_1(1 - e^{-k_2 t})\right), & k_1 \neq k_2, \\ s_0(1 - (1 + kt)e^{-kt}), & k_1 = k_2 = k. \end{cases} \tag{11}$$

Remark 4 The expression (11) for function q in the case $k_1 \neq k_2$ can be also written in the following form:

$$q(t) = s_0\left(1 - \frac{k_2 e^{-k_1 t} - k_1 e^{-k_2 t}}{k_2 - k_1}\right).$$

In order to study the behaviour of functions s, p, q with respect to properties such as monotonicity, equilibrium points, asymptotes, extremums, inflection points, etc., we need to examine their derivatives.

The first derivatives of functions s, p, q defined by (9), (10), (11) can be presented by means of the following expressions:

$$s'(t) = -s_0 k_1 e^{-k_1 t}; \tag{12}$$

$$p'(t) = \begin{cases} \frac{s_0 k_1}{k_2 - k_1}(-k_1 e^{-k_1 t} + k_2 e^{-k_2 t}), & k_1 \neq k_2, \\ s_0 k e^{-kt}(1 - kt), & k_1 = k_2 = k; \end{cases} \tag{13}$$

$$q'(t) = \begin{cases} \frac{s_0 k_1 k_2}{k_2 - k_1}\left(e^{-k_1 t} - e^{-k_2 t}\right), & k_1 \neq k_2, \\ s_0 k^2 t e^{-kt}, & k_1 = k_2 = k. \end{cases} \tag{14}$$

Remark 5 Using expressions (9)–(11), (12)–(14) for functions s, p, q and their derivatives s', p', q', we can state that functions s, p, q are the unique solutions to initial value problem (6)–(8). Indeed, using expressions (9)–(14), it is easy to check that functions s, p, q satisfy IVP (6)–(8). For example, to see this for function p, substitute the expressions for s, p, p' in the second equation: $p' = k_1 s - k_2 p$ of dynamical system (6) to obtain an identity. Similarly identities for s and q can be checked and thus the existence part of our statement is validated. Uniqueness of solutions s, p, q follows from the smoothness of the right-hand sides of dynamical system (6) according to the general theory of ODE's (Picard-Lindelöf theorem). We recall that solutions s, p, q can be obtained by integrating dynamical system (6)–(8) using Laplace transform as done in [4] or by using algebraic methods as in [31, 35].

3.2 Properties of the solutions to the two-step exponential growth-decay model

We next analyze in some detail the properties of solutions s, p, q to initial value problem (IVP) (6)–(8) with respect to monotonicity and extremum points.

Function s defined by (9) already appeared in Sect. 2, see IVP (2)–(4). Solution s is a positive monotone decreasing function in $T = [0, \infty)$ and asymptotically tends to 0 with $t \to \infty$. Indeed, property $s > 0$ follows from expression (9) and monotonicity is due to $s' < 0$ as seen from expression (12) of the derivative s' and the first equation in system (6), i.e. $s' = -k_1 s < 0$.

A practically important characteristics of decay function s is:

$$t_h = \ln 2 / k_1,$$

known in nuclear physics as half-life (time). The half-life t_h satisfies the condition $s(t_h) = s_0/2$, cf. Fig. 1. From (3.2) the rate parameter k_1 can be computed as:

$$k_1 = \ln 2 / t_h.$$

Functions p, q defined by expressions (10), (11), satisfy in T the properties: $p \geq 0, q \geq 0$.

Proposition 6 *Function p is unimodal in $T = [0, \infty)$, asymptotically tending to 0 with $t \to \infty$ and attaining its maximum value at time moment $t_p^* > 0$:*

$$t_p^* = \begin{cases} \frac{\ln k_2 - \ln k_1}{k_2 - k_1}, & k_1 \neq k_2, \\ 1/k, & k_1 = k_2 = k. \end{cases} \tag{15}$$

The maximum value of function p attained at t_p^* is:

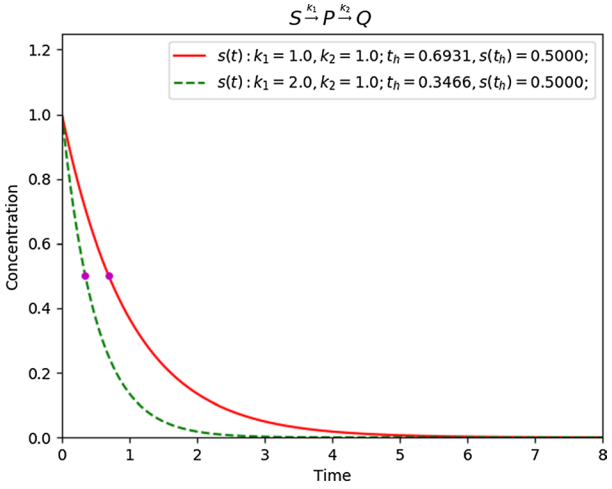


Fig. 1 The graph of the decay function s defined by (9) for $s_0 = 1$, visualized for two values of rate parameter k_1: $k_1 = 1$ and $k_1 = 2$. The half-life is shown on the two graphics

$$p(t_p^*) = \begin{cases} \frac{s_0 k_1}{k_2 - k_1} \left((\frac{k_2}{k_1})^{\frac{k_1}{k_1 - k_2}} - (\frac{k_2}{k_1})^{\frac{k_2}{k_1 - k_2}} \right), & k_1 \neq k_2, \\ s_0 e^{-1} \approx 0.36788 \times s_0, & k_1 = k_2. \end{cases} \tag{16}$$

Proof To investigate the maximum of function p we look for a time moment $t = t_p^*$, such that the derivative (13) of p annihilates: $p'(t_p^*) = 0$. The latter results in expressions (15), (16). □

Remark 7 Using an alternative to (15) expression for t_p^* for the case $k_1 \neq k_2$ we have:

$$t_p^* = \begin{cases} \ln \left((\frac{k_2}{k_1})^{(k_2 - k_1)^{-1}} \right), & k_1 \neq k_2, \\ 1/k, & k_1 = k_2 = k. \end{cases} \tag{17}$$

Note that the maximum value $p(t_p^*)$ of function p attained at t_p^* in the case of equal rate parameters $k_2 = k_1 = k$ does not depend on the value of k as shown in expression (16).

Proposition 8 *Solution q is a non-negative function in $T = [0, \infty)$, attaining value 0 if and only if $t = 0$. Function q is strictly monotone increasing in T. The steepest slope of q is achieved at time moment t_p^* given by (15). The value of the steepest slope of q is $q'(t_p^*) = k_2 p(t_p^*)$, where $p(t_p^*)$ is given by (16), that is*

$$q'(t_p^*) = k_2 p(t_p^*) = \begin{cases} \frac{s_0 k_1 k_2}{k_2 - k_1} \left((\frac{k_2}{k_1})^{\frac{k_1}{k_1 - k_2}} - (\frac{k_2}{k_1})^{\frac{k_2}{k_1 - k_2}} \right), & k_1 \neq k_2, \\ (s_0 k) e^{-1} \approx 0.36788 \times (s_0 k), & k_1 = k_2 = k. \end{cases} \tag{18}$$

The value $q(t_p^*)$ of function q at point t_p^* is

$$q(t_p^*)/s_0 = \begin{cases} 1 - \frac{k_2 (\frac{k_2}{k_1})^{\frac{k_1}{k_1 - k_2}} - k_1 (\frac{k_2}{k_1})^{\frac{k_2}{k_1 - k_2}}}{k_2 - k_1}, & k_1 \neq k_2, \\ 1 - 2e^{-1} \approx 0.2642, & k_1 = k_2 = k. \end{cases}$$

Proof To see that solution $q \geq 0$ is a non-negative monotone increasing function for $t \geq 0$, it is sufficient to note that the third equation of system (6) implies $q'(t) = k_2 p \geq 0$. Assumption $q'(t) = 0$ implies $t = 0$, hence q is (strictly) monotone increasing for $t > 0$. The derivative $q'(t)$ of q is proportional to p, hence the steepest slope of q (that is the largest reaction rate q' of q), is achieved at time moment t_p^* given by (15). Accordingly, the value of the maximum rate (slope) of q is given by (16). □

According to formulae (16) and (17) the time moment t_p^* as well as the values $p(t_p^*)$ and $q(t_p^*)$ depend on the rate parameters k_1, k_2. The next two propositions address this kind of dependence.

3.3 Dependence of the solutions to the two-step exponential growth-decay model on the rate parameters

Proposition 9 *Let (k_1, k_2) be such that $k_1 \geq 1, k_2 \geq 1$, then for any pair (k_1, k_2) the largest value of t_p^* is attained at $(k_1, k_2) = (1, 1)$, namely*

$$\max_{k_1 \geq 1, k_2 \geq 1} t_p^*(k_1, k_2) = t_p^*(1, 1) = 1.$$

Proof Geometrically expression (17) says that t_p^* is the slope of the secant to the graph of the natural logarithm function as function of k, $\ln(k)$, passing through the points $(k_1, \ln k_1)$ and $(k_2, \ln k_2)$. Clearly the secant with largest slope (= 1) is the tangent at the point $(1, \ln 1) = (1, 0)$. □

Proposition 10 *Let pair (k_1, k_2) be such that either* (i) $k_1 = 1, k_2 \longrightarrow \infty$, *or* (ii) $k_2 = 1, k_1 \longrightarrow \infty$. *Then*

$$p(t_p^*; k_1, k_2) \longrightarrow \begin{cases} 0, & k_1 = 1, \quad k_2 \longrightarrow \infty, \\ s_0, & k_2 = 1, \quad k_1 \longrightarrow \infty. \end{cases}$$

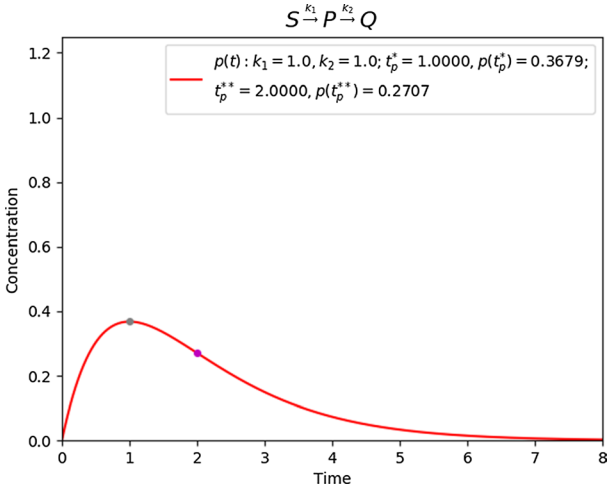


Fig. 2 The graph of solution p of the IVP (6)–(8) for initial conditions $s_0 = 1$, $p_0 = q_0 = 0$ and rate parameters $k_1 = k_2 = 1$. The maximum point $(t_p^*, p(t_p^*))$ and the inflection point $(t_p^{**}, p(t_p^{**}))$ are shown on the graph

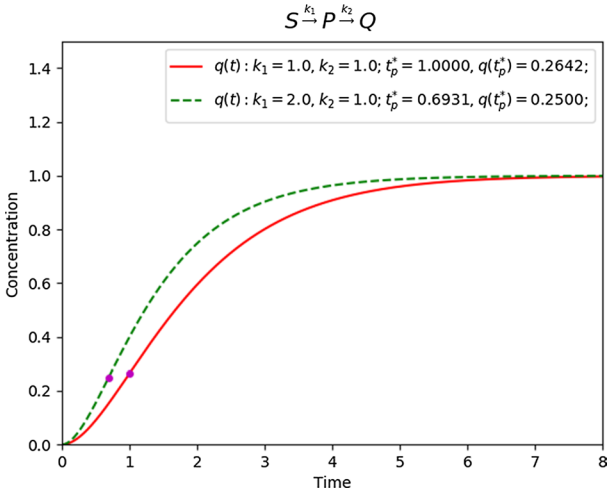


Fig. 3 The graph of solution q of IVP (6)–(8) for initial conditions $s(0) = 1$, $p_0 = q_0 = 0$ and two pairs of rate parameters: (i) $k_1 = k_2 = 1$, and (ii) $k_1 = 2$, $k_2 = 1$. The inflection points $(t_p^*, q(t_p^*))$ are shown on the graphs

Proof Follows from expression (16) when substituting alternatively one of the rate parameters by 1 and passing to limit the other rate parameter, using the limit $\lim_{n \longrightarrow \infty}(1/n)^n = 1$. □

Figures 1, 2 and 3 visualize the solutions s, p, q of problem (6–8) for fixed initial conditions $s(0) = 1$, $p(0) = q(0) = 0$ and diverse values of the rate parameters k_1, k_2.

3.4 More properties of the solutions to the two-step exponential growth-decay model

In order to analyse the solutions to IVP (6)–(8) with respect to properties, such as convexity and inflection points, consider the second derivatives of functions s, p, q.

$$s''(t) = s_0 {k_1}^2 e^{-k_1 t}; \tag{19}$$

$$p''(t) = \begin{cases} \frac{s_0 k_1}{k_2 - k_1}({k_1}^2 e^{-k_1 t} - {k_2}^2 e^{-k_2 t}), & k_1 \neq k_2, \\ s_0 k^2 e^{-kt}(kt - 2), & k_1 = k_2 = k; \end{cases} \tag{20}$$

$$q''(t) = \begin{cases} \frac{s_0 k_1 k_2}{k_2 - k_1}\left(-k_1 e^{-k_1 t} + k_2 e^{-k_2 t}\right), & k_1 \neq k_2, \\ s_0 k^2 (1 - kt) e^{-kt}, & k_1 = k_2 = k. \end{cases} \tag{21}$$

Using expressions (19)–(21) one obtains some additional properties of the solutions to IVP (6)–(8). Note that expression (19) implies $s''(t) > 0$, hence function s is strictly convex on T, which is clearly observed on Fig. 1. As regard to solution p, expression (20) contributes to the following result.

Proposition 11 *Solution p has an inflection at point $t_p^{**} = 2t_p^* > 0$:*

$$t_p^{**} = 2\begin{cases} \frac{\ln k_2 - \ln k_1}{k_2 - k_1}, & k_1 \neq k_2, \\ 1/k, & k_1 = k_2 = k, \end{cases} \tag{22}$$

where t_p^* is given by (15). The value $p(t_p^{**}) = p(2t_p^*)$ is given by

$$p(2t_p^*) = \begin{cases} \frac{s_0 k_1}{k_2 - k_1}\left((\frac{k_2}{k_1})^{2k_1/(k_1 - k_2)} - (\frac{k_2}{k_1})^{2k_2/(k_1 - k_2)}\right), & k_1 \neq k_2, \\ 2s_0 e^{-2} \approx 0.27067 \times s_0, & k_1 = k_2 = k; \end{cases} \tag{23}$$

Expressions (22)–(23) are obtained by elementary calculations, visualize on Fig. 4.

Proposition 12 *Solution q has an inflection at time moment $t_p^{**} = 2t_p^*$, where t_p^* is given by (15). The value of function q at time $2t_p^*$ is*:

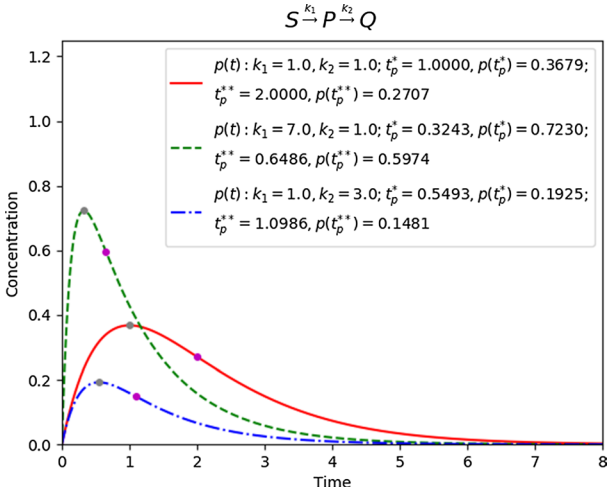


Fig. 4 Function p as defined in (10) for $s_0 = 1$ and three pairs of rate parameters $(k_1, k_2) = (1, 1), (k_1, k_2) = (7, 1)$, and $(k_1, k_2) = (1, 3)$ together with maximum points $(t_p^*, p(t_p^*))$ and inflection points $(t_p^{**}, p(t_p^{**}))$

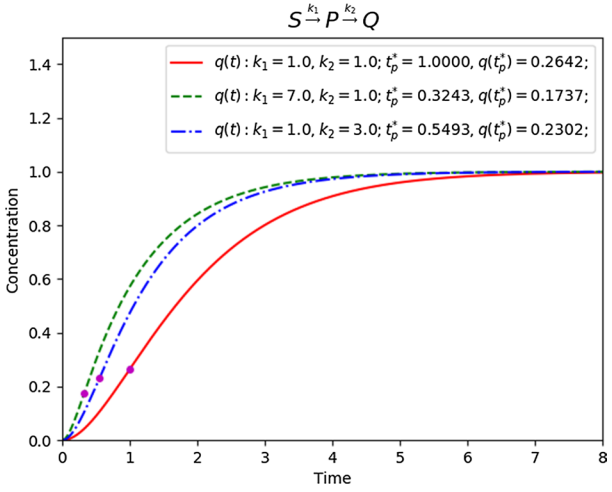


Fig. 5 Function q as defined in (11) for $s_0 = 1$, and three pairs of rate parameters $(k_1, k_2) = (1, 1), (k_1, k_2) = (7, 1)$, and $(k_1, k_2) = (1, 3)$ together with inflection points

$$q(2t_p^*) = \begin{cases} \frac{s_0}{k_2-k_1}\left(k_2\left(1-\left((\frac{k_2}{k_1})^{\frac{2k_1}{k_1-k_2}}\right)\right)\right. \\ \left.-k_1\left(1-\left((\frac{k_2}{k_1})^{\frac{2k_2}{k_1-k_2)}}\right)\right)\right), & k_1 \neq k_2, \\ s_0(1-3e^{-2}) \approx 0.59399 \times s_0, & k_1 = k_2 = k. \end{cases} \tag{24}$$

Proof Substitute the argument $2t_p^*$ in expression (11) for q gives:

$$q(2t_p^*) = \begin{cases} \frac{s_0}{k_2-k_1}\left(k_2\left(1-e^{\ln\left((\frac{k_2}{k_1})^{\frac{2k_1}{k_1-k_2}}\right)}\right)\right. \\ \left.-k_1\left(1-e^{\ln\left((\frac{k_2}{k_1})^{\frac{2k_2}{k_1-k_2}}\right)}\right)\right), & k_1 \neq k_2, \\ s_0(1-3e^{-2}), & k_1 = k_2 = k, \end{cases}$$

which gives (24). The graph of function q is visualized on Fig. 5. □

3.5 Remarks on the global behaviour of the two-step exponential growth-decay model

Let us comment on the global behaviour of the solutions s, p, q to the two-step exponential growth-decay model.

As seen above the shape of the solutions to dynamical system (6) varies relative to the variation of the values of the two rate parameters (k_1, k_2).

In the case of equal parameter rates $k_1 = k_2 = k$ the point $t_p^* = 1/k$ tends to zero with $k \to \infty$, i.e. $\lim_{k\to\infty} t_p^* \to 0$. Hence, in the limit no inflection takes place for the intermediate p. The maximum value of function p in the case of equal parameter rates does not depend on the value k of the rates, but just on s_0, namely $(100/e)\%s_0 \approx 36.7879\% \times s_0$. For the value of p at the inflection point $2/t$ we have $2(100/e^2)\%s_0 \approx 0.27067 \times s_0$.

We also wish to know how the solutions behave when one of the rate parameters k_1, k_2 is kept fixed to a certain value, while the other one is growing up to infinity.

Without loss of generality, we can fix the minimum value of the two rate parameters to be $\min(k_1, k_2) = 1$. Consider then separately the two possible cases as follows.

Special case $k_1 = 1, k_2 > 1$. In the case $k_1 = 1, k_2 > 1$ formula (15) becomes

$$\begin{aligned} t_p^* &= \frac{\ln k_2 - \ln k_1}{k_2 - k_1} \\ &= \ln(k_2)/(k_2 - 1) \\ &= \ln\left((k_2)^{\frac{1}{k_2-1}}\right) \end{aligned} \tag{25}$$

Substituting (25) in: $p(t)|_{k_1\neq k_2} = s_0 \frac{k_1}{k_2-k_1}(e^{-k_1 t} - e^{-k_2 t})$, we obtain

$$\begin{aligned} p(t_p^*)|_{k_1\neq k_2} &= p\left(\ln(k_2^{\frac{1}{k_2-1}})\right) \\ &= \frac{s_0}{k_2-1}\left(k_2^{\frac{1}{1-k_2}} - k_2^{\frac{k_2}{1-k_2}}\right). \end{aligned} \tag{26}$$

From expression (26) one concludes that if $k_1 = 1$ is fixed and k_2 increases to infinity $k_2 \to \infty$, then $\lim p(t^*)|_{k_1=1,k_2\to\infty} = 0$, and therefore function p globally tends to zero in $[0, \infty)$.

Remark 13 Since the maximum of the intermediate function p tends to zero with $k_2 \to \infty$, then function p vanishes globally in $[0, \infty)$. Moreover, the derivative of p also vanishes globally: $p' = k_1 s - k_2 p \to 0$, hence in the limit $k_1 s \to k_2 p$ with $k_2 \to \infty$. This implies that system (6)–(8) can be "approximated" by the following reduced system:

$$\begin{aligned} s' &= -k_1 s, \\ q' &= k_1 s, \end{aligned}$$

with initial conditions $s(0) = s_0, q(0) = q_0 = 0$, which is identical to the saturated first-order system (2) induced by reaction $S \longrightarrow Q$.

Special case $k_2 = 1, k_1 > 1$. In this case we have

$$t_p^* = \ln(k_2/k_1)/(k_2 - k_1) = \ln(1/k_1)/(1 - k_1) = \ln(k_1)/(k_1 - 1).$$

We thus obtain:

$$\begin{aligned} p(t_p^*)|_{k_1\neq k_2} &= s_0 \frac{k_1}{k_1-1}(e^{-k_1 t} - e^{-t})|_{t=t^*} \\ &= s_0 \frac{k_1}{k_1-1}(e^{-k_1 \ln(k_1)/(k_1-1)} - e^{-\ln(k_1)/(k_1-1)}). \end{aligned} \tag{27}$$

From expression (27) one concludes that if $k_2 = 1$ is fixed and k_1 increases $k_1 \to \infty$, then $\lim p(t_p^*)|_{k_2=1,k_1\to\infty} = s_0/e$. On the other side function s tends globally to zero with $k_1 \to \infty$ in $[\epsilon, \infty)$ for any $\epsilon > 0$. Hence the variable s can be eliminated from system (6) and the latter can be reduced (approximately) to the following system:

$$\begin{aligned} p' &= -k_2 p, \\ q' &= k_2 p, \end{aligned}$$

with initial conditions $p(0) = s_0, q(0) = q_0 = 0$, which is identical to the first-order system (2) induced by reaction $P \longrightarrow Q$.

Remark 14 The discussed reduction of the three-dimensional dynamical system (6) into a two-dimensional one can be formulated in terms of chemical reaction network theory, cf. [37, 38].

4 The epidemiological SIR model from the perspective of CRNT: relation to logistic and Gompertz growth-decay mechanisms

In this section we discuss the relations between the epidemiological SIR model and the logistic and Gompertz growth-decay models. These relations are clearly elucidated when the models are formulated in terms of chemical reaction network theory (CRNT).

We first briefly recall the logistic model which is a substantial ingredient part of the classic SIR model. We shall then consider the Gompertz model as tightly related to the logistic one and often used as a substitute of the logistic model when describing and simulating growth-decay evolutionary processes.

The main purpose of this section is to prepare the background for Sect. 5, where we replace the logistic reaction in the SIR reaction network by the Gompertzian reaction, obtaining thus a meaningful modification of the classic SIR model.

4.1 The logistic and the Gompertz growth-decay mechanisms

In the mathematical literature the logistic and Gompertz models are mostly considered as growth models, see e.g. [46], however, each of these two models consists of two closely related ingredients, a growth function and a decay function. This fact has been noticed by several authors who formulate the two models in the form of two-compartmental dynamical systems, such as $s' = -ksx,\ x' = kxs$ for the logistic model, and $s' = -\alpha s,\ x' = ksx$ for the Gompertz model. Such a "recasting" of the logistic and the Gompertz growth models is discussed by several authors, see e.g. [13, 44].

We next formulate the logistic and the Gompertz models in terms of CRNT. This allows to show the close relation between the two models and to elucidate their chemical mechanisms from an unified perspective. The knowledge of the logistic mechanism is needed for the discussion of the SIR model; the Gompertz mechanism will be used when introducing a Gompertzian type SIR (G-SIR) model in Sect. 5.

The logistic growth-decay model [42] is generated by the following reaction network involving species S and X [22, 23, 27]:

$$S + X \xrightarrow{k} 2X, \tag{28}$$

wherein k is a positive rate parameter. Under the assumption of mass action kinetics reaction network (28) induces the following dynamical system for the masses (concentrations, densities) s, x of species S, X, resp.:

$$s' = -ksx,\ x' = kxs. \tag{29}$$

Assuming initial conditions

$$s(0) = s_0 > 0,\ x(0) = x_0 > 0, \tag{30}$$

initial value problem (29)–(30) implies $s' + x' = 0$ generating thus the conservation relation

$$s + x = c, \ c = s_0 + x_0 = \text{ const }. \tag{31}$$

In addition, problem (29)–(30) implies the following autonomous differential equations for the growth function x and the decay function s:

$$x' = kx(c - x), \quad s' = -ks(c - s), \quad c = s_0 + x_0. \tag{32}$$

Equations (32) show that function s monotonically decreases approaching zero, whereas function x monotonically increases approaching the number c, known as (environmental) *carrying capacity*. Equations (32) possess explicit solutions for $t \in (-\infty, \infty)$. For instance, assuming carrying capacity $c = 1$ and initial conditions $x(0) = x_0 = 1/2$, $s_0 = x_0 = 1/2$, we have:

$$x = 1/(1 + e^{-kt}), \quad s = e^{-kt}/(1 + e^{-kt}).$$

Function x is referred as logistic growth, whereas function s is logistic decay.

Reaction network (28) exhibits a close relation between species S and X, mathematically expressed in equation (31). Roughly speaking, X consumes species S and grows for the expenses of S, which decays. We shall next see a rather distinct mechanism in the Gompertzian growth-decay model.

4.2 The Gompertz growth-decay model

The Gompertz growth function [14] initially designed for insurance purposes, and later used more generally as a growth function [46], is usually presented as solution to a differential equation, having an explicite algebraic expression. In the sequel we shall deduce the Gompertz function starting from a reaction network using CRNT terminology. This will allow us to obtain the Gompertz growth function together with its related decay function, giving us a general view on the Gompertzian growth-decay process, as well as a transparent physicochemical interpretation of the variables and rate parameters involved. To this end consider the following reaction network:

$$S \xrightarrow{\nu} Q, \quad S + X \xrightarrow{k} 2X + S, \tag{33}$$

wherein ν, k are positive rate parameters. From reaction $S + X \xrightarrow{k} 2X + S$ of reaction network (33) we see that X is growing species autocatalizing itself (as in the logistic case) and S is a second catalyst in this reaction. As a catalyst species S does not change, however S decays as result of reaction $S \xrightarrow{\nu} Q$. Species Q is an external species for the model system and can be ignored, in which case we use the symbol $\varnothing$ instead of Q: $S \xrightarrow{\nu} \varnothing$. Denoting by s, x the mass-related mathematical characteristics (like concentrations, masses, densities, etc.) of species S, X, resp., we formulate the following:

Proposition 15 *Cf.* [27]. *Under the assumption of mass action kinetics, reaction network* (33) *induces the following dynamical system*:

$$s' = -\nu s, \quad x' = kxs. \tag{34}$$

Assuming initial conditions (30), *initial value problem* (34)–(30) *induces the relation*

$$\gamma s + \ln x = \ln c = \text{ const}, \quad \ln c = \gamma s_0 + \ln x_0, \quad \gamma = k/\nu, \tag{35}$$

resp., the autonomous differential equation for the Gompertz growth function x:

$$x' = \nu x(\ln c - \ln x). \tag{36}$$

Under the choice $c = 1$, *resp.* $\ln c = 0$, *the solution to* (36) *can be presented as*

$$x = {x_0}^{e^{-\nu t}}. \tag{37}$$

Proof Dynamical system (34) implies the relation:

$$s'/\nu + x'/(kx) = 0. \tag{38}$$

Using initial value conditions (30) the integration of (38) yields the "conservation" relation (35), resp. the Gompertz equation (36). Let us fix $c = 1$, so that $\ln c = 0 = \gamma s + \ln x$, and, in particular $\gamma s_0 + \ln x_0 = 0$, $\gamma = k/\nu$. Substituting $c = 1$ in differential equation (36) yields

$$x' = \nu x(-\ln x) = \nu x \ln \frac{1}{x}.$$

The solution $s = s(t)$ of IVP (34)–(30) is the exponential decay function $s = s_0 e^{-\nu t}$, $t \in (-\infty, \infty)$, hence the solution $x = x(t)$ can be computed from relation (35) expressing x in terms of function s. Assuming $c = 1$, so that $\ln x_0 = -\gamma s_0$, we have for $x = x(t)$ the following expression:

$$\ln x = -\gamma s = -\gamma s_0 e^{-\nu t},$$

resp.

$$x = e^{-\gamma s} = e^{-\gamma s_0 e^{-\nu t}} = (e^{-\gamma s_0})^{e^{-\nu t}} = (e^{\ln x_0})^{e^{-\nu t}} = {x_0}^{e^{-\nu t}}.$$

This proves expression (37) and the proposition. □

Remarks

1. The integration constant c in relation (35) is conveniently accepted to be $c = 1$, so that $\ln c = \ln 1 = 0$. Such a choice limits the range of values of $\ln x$ to the negative half-line $(-\infty, 0]$ (since $\gamma s = -\ln x > 0$), and hence the range of x is limited to the interval $(0, 1]$. In other words, the integration constant $\ln c = \ln 1 = 0$, resp. $c = 1$, limits the growth of solution x up to asymptotic value 1. So, function x monotonically increases from some initial value $x_0 < 1$ approaching the "carrying capacity" asymptote $c = 1$. In simulation studies, fixing the value of $c = 1$ is a recommended normalization procedure. After fixing the carrying capacity $c = 1$ and choosing an initial value x_0, we have to calculate the value of s_0 as a function

of x_0 according to relation (35), namely: $0 = \rho s_0 + \ln x_0$, that is: $s_0 = -\ln x_0/\gamma$. Such an approach allows the computations with various initial conditions x_0 to be uniformly scaled. However, note that, differently to the logistic case, where $s_0 = 1 - x_0 < 1$, now the values of s_0 can be (much) larger than 1 for small values of x_0. Note that the physicochemical meaning of S is a catalyst, and not a (food) resource as in the logistic case.

2. In modelling and computer simulation of a particular real-world situations we choose first the scaling constant c (usually as $c = 1$), then the initial condition x_0 for the growth function using available empirical (experimental) data, then we determine s_0 from the conservation relation (35), and then we fit the Gompertz growth curve to empirical data varying the remaining free parameters in the model. The relation between S and X in the logistic case is 'purely' conservative: $s + x = c = 1$, in contrast to the Gompertzian case, where the sum $s + x$ is not constant, rather we have $\gamma s + \gamma \ln x = 0$. Respectively, in the Gompertzian case the variable s is proportional to $\ln x$, and not to x as in the logistic case, showing the specific role of the catalyst species S. More specifically, the growing species X is (much) less sensitive to changes of the catalyst values s in comparison to the logistic case, where x detains its growing "linearly" with the exhaust of the resource species s: $x = 1 - s$.
3. Reaction network (33), resp., dynamical system (34) involves two rate parameters ν, k. Without loss of generality any one of these parameters can be fixed to 1 leaving the other parameter free, as done by several authors, see e.g. [13], where $\nu = 1$, or [44], where $k = 1$. Equivalently the ratio γ can be used instead of the two rate parameters. This explains why some basic expressions, such as (35), involve just the ratio γ and not any of the single rate parameters ν, k. The derivation of the Gompertz equations from relation (35), such as the expression (37) contributes to a physicochemical interpretation of the participating variables and rate parameters.

The solution x to the Gompertz equation (36), resp. function (37) is further referred to as Gompertz growth function (model, mechanism).

4.3 Relation between the logistic and the Gompertz models

A detailed mathematical comparison analysis of the logistic and the Gompertz growth functions, as defined by their algebraic expressions, is presented already in the early work by Winsor [46]. The present use of a CRNT approach contributes to an additional comparison between the two models emphasizing both their dual growth-decay nature, as well as the physicochemical meaning of the variables and parameters of the two models. In both models species X reproduces by a doubling mechanism, being constrained by a species S which declines with time until vanishing. However, both models adopt distinct reaction mechanisms for the time evolution of the two reacting species. Formally, the logistic dynamical system (29) differs from the Gompertz dynamical system (34) by the form of the differential equation for the decaying variable s. More specifically, equation $s' = -ksx$, in the logistic

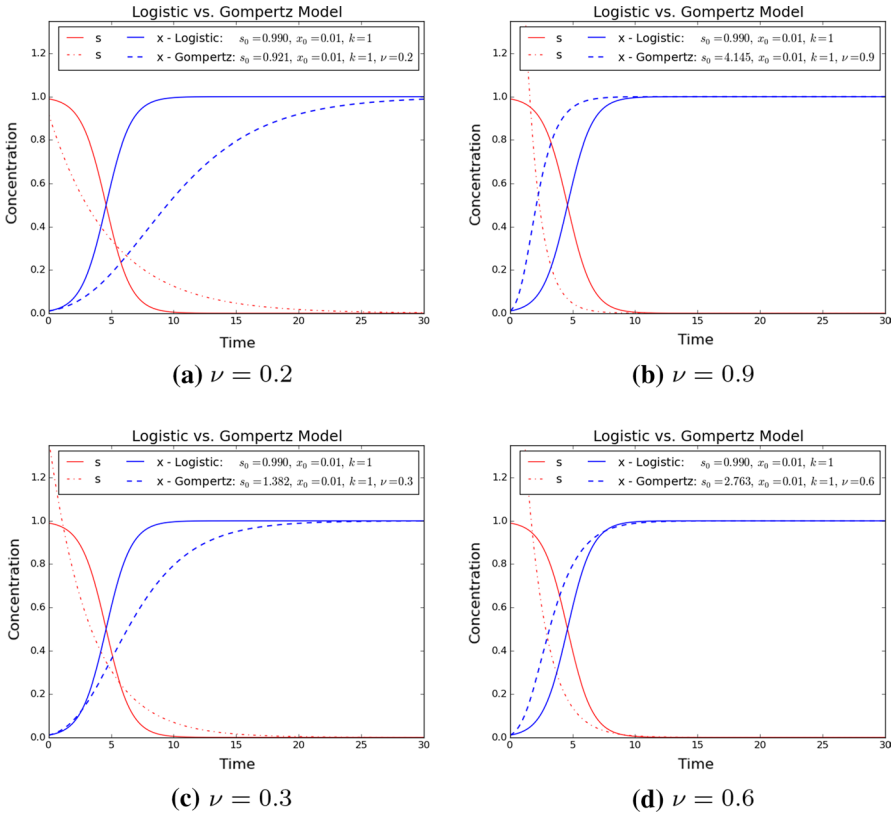


Fig. 6 The solutions to the logistic and the Gompertz models for same carrying capacity $c = 1$, equal initial conditions $x_0 = 0.001$ and equal rate parameters $k = 1$ for the growth function. The rate parameters for the Gompertzian decay function s are: $\nu = 0.2$ in (**a**), $\nu = 0.9$ in (**b**), $\nu = 0.3$ in (**c**) and $\nu = 0.6$ in (**d**)

model (29) turns to equation $s' = -\nu s$ in the Gompertz model (34), so that variable s becomes independent on the growth variable x (including the rate parameter of the latter). This is a consequence of the different roles of species S in the two models, namely a reactant (resource, food) in the logistic case and a catalyst in the Gompertzian case. The specific role of the catalyst is determined in each particular real-world natural phenomenon application of the model. For example, in cancer research, when modelling solid tumour growth, some authors relate the variable s to the functional activity of the non-proliferating cells in tumours, cf. [13, 44]. As another example, the suitability of the logistic and Gompertz functions to modelling of microbial growth is discussed in a number of articles, cf. [47].

On Fig. 6 both the decay and growth solutions to the logistic and the Gompertz models for same carrying capacity $c = 1$ and equal initial conditions $x_0 = 0.001$ are graphically presented. The rate parameters $k = 1$ are also equal, however the values of the rate parameter ν in the Gompertz model are chosen differently:

$\nu = 0.2$ in the left upper part (A), $\nu = 0.6$ in the right upper part (B), $\nu = 0.3$ in the left lower part (C), and $\nu = 0.6$ in the right lower part (D). The differences of the shapes of the logistic and the Gompertz solutions are apparent—the symmetry of the logistic solutions versus the "skewness" of the Gompertzian ones. As it is often underlined, cf. [46], the inflection of the Gompertzian growth curve is at appr. 37% of the carrying capacity whereas the inflection of the logistic growth curve is at 50% of the carrying capacity.

We shall next briefly discuss the classic SIR model from the perspective of CRNT, emphasizing the involvement of the logistic reaction in the SIR model. In the next Sect. 5 we shall show that the logistic reaction in the SIR model can be naturally replaced by the Gompertzian one and shall discuss on possible applications of the resulting model.

4.4 The epidemiological SIR model as based on the logistic reaction mechanism

The classic Kermack–McKendrick epidemiological SIR model is usually formulated as a dynamical system and is discussed in a huge number of references, e.g. [11, 17–21, 32]. Here we propose a brief presentation of the SIR model in the spirit of mathematical chemistry.

The classic SIR model can be formulated as a chemical reaction network in the following way:

$$\begin{array}{lcl} S + I & \overset{k}{\longrightarrow} & 2I, \\ I & \overset{a}{\longrightarrow} & R, \end{array} \tag{39}$$

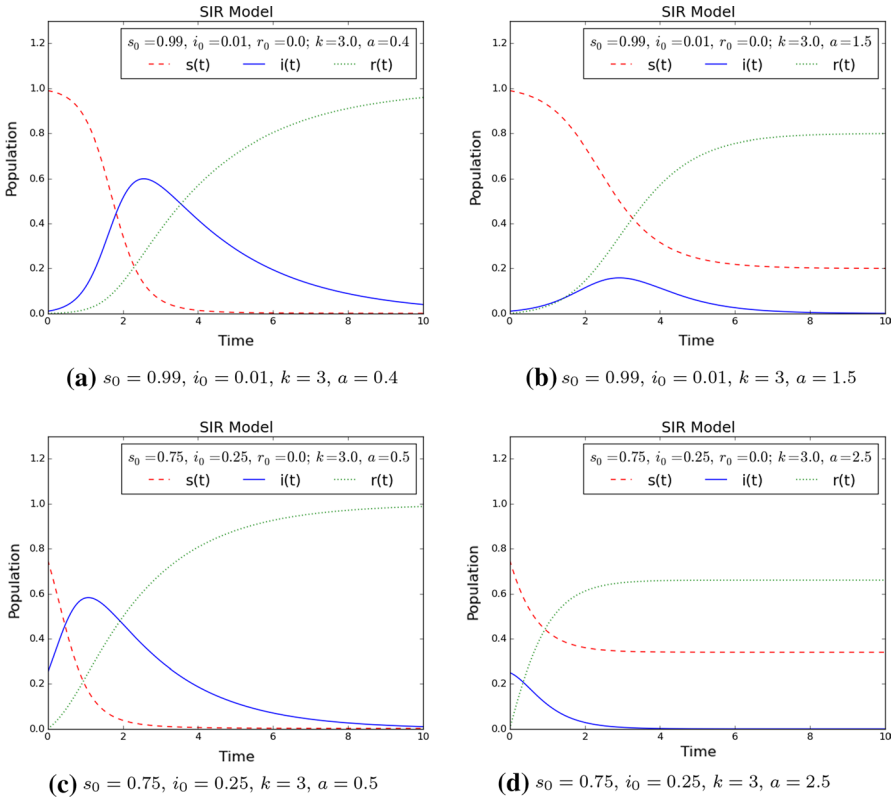
where S, I, R denote three classes (compartments) of individuals (populations, species): susceptibles S, infectives I and removed R, and $k, a > 0$ are rate parameters. More specifically, $k > 0$ is called the "infection" rate parameter and $a > 0$ is the "removal" rate parameter. Obviously, reaction network (39) combines two reactions: a logistic reaction (28) and an one-step exponential first-order growth-decay reaction (1).

It is supposed that the three classes of species S, I, R are homogeneously distributed in a certain space (area) and their densities (masses) as functions of time are denoted resp. $s = s(t), i = i(t), r = r(t)$. Assuming that reaction network (39) is governed by the mass action law, we obtain the familiar dynamical system for the variables s, i, r:

$$\begin{aligned} s' &= -ksi, \\ i' &= ksi - ai, \\ r' &= ai. \end{aligned} \tag{40}$$

The initial value conditions associated to the SIR dynamical system (40) are of the form

$$s(0) = s_0 > 0; \quad i(0) = i_0 > 0; \quad r(0) = r_0 = 0. \tag{41}$$



(a) $s_0 = 0.99,\ i_0 = 0.01,\ k = 3,\ a = 0.4$ **(b)** $s_0 = 0.99,\ i_0 = 0.01,\ k = 3,\ a = 1.5$

(c) $s_0 = 0.75,\ i_0 = 0.25,\ k = 3,\ a = 0.5$ **(d)** $s_0 = 0.75,\ i_0 = 0.25,\ k = 3,\ a = 2.5$

Fig. 7 The solutions to the SIR model

Adding up the reaction equations of SIR dynamical system (40) we obtain the relation $s' + i' + r' = 0$, which after integration and taking into account initial conditions (41) yields the conservation equation:

$$s + i + r = s_0 + i_0. \tag{42}$$

A visualization of an epidemic outbreak is shown on Fig. 7 parts (A), (B), (C); on part (D) the absence of an outbreak is presented. Note the logistic decay form of solution s and the wave-like form of the intermediate solution i that can be seen in a number of research articles on the classic SIR model, e.g. [19, 26]. We especially emphasize the following two features of solutions s, i: (i) an well-expressed ("logistic-type") inflection of function i between 0 and the maximum (better observed on Fig. 7a, and (ii) that function s tends to some strictly positive value $s_\infty > 0$ as $t \longrightarrow \infty$ (better observed on Fig. 7b.

A situation when there is no epidemic outbreak is visualized on Fig. 7 (D), where the value of rate parameter a is sufficiently large (in this case $a = 2.5$).

Analogously to dynamical system (6), system (40) does possess an exact algebraic expressions for the solutions s, i, r, as recently shown in [16].

Remark The SIR model (39)–(40) involves an auto-catalytic action exercised by species I over the one-step exponential reaction $S \longrightarrow I$, turning the latter into a logistic reaction of the form $S + I \longrightarrow I + I$. Such a logistic autocatalytic reaction is typical for models of infectious diseases that are transmitted via one-to-one contacts between individuals in a more or less dense population. Note the similarity with the reaction mechanism in the Lotka-Volterra predator-prey model [8], where the contacts between the pray and the predator are modelled also by means of a logistic reaction. In the classic SIR model the susceptibles play the role of the prey, and the infectives are the predators.

For an epidemic outbreak threshold of the SIR model we have:

$$i'|_{t=0} = ks_0 i_0 - ai_0 = i_0(ks_0 - a) = 0,$$

so, if $s_0 > \rho = a/k$, then $i'|_{t=0} > 0$, leading to an epidemic outbreak. The epidemic outbreak threshold is usually expressed in terms of the *reproduction number* R_0, which in the case of the classic SIR model is given by:

$$R_0^{sir} = (k/a)s_0 = s_0/\rho, \quad \rho = a/k. \tag{43}$$

Using the reproduction number (43), the threshold condition for an epidemic outbreak is expressed as $R_0^{sir} > 1$, which is equivalent to condition $s_0 > \rho$, cf. [6].

5 The G-SIR model: a SIR-type epidemiological model with Gompertzian disease spread mechanism

The first reaction in the classic SIR reaction network (39), namely $S + I \xrightarrow{k} 2I$, describes an infection dynamics of logistic type (28) which is characterized by a disease spread mechanism based on the one-to-one contacts between individuals. The close relation between the logistic and the Gompertz growth-decay mechanisms [27] suggests to examine the behaviour of a SIR-type model when the logistic reaction is replaced by a Gompertzian one (33). To this end we introduce the following reaction network:

$$\begin{array}{lcl} S & \xrightarrow{\nu} & Q, \\ S + I & \xrightarrow{k} & 2I + S, \\ I & \xrightarrow{a} & R, \end{array} \tag{44}$$

wherein S, I, R denote the classes analogous to the respective compartments in the classic SIR reaction network (39). More specifically, I is the class of infective individuals and R is the class of removed ones. The class S corresponds to susceptibles that exercise catalytic action on the disease spread process. Class Q is an "external" class of species, could be written as $\varnothing$. The constants k, ν, a are positive rate parameters.

Assuming that classes S, I, R are homogeneously distributed in a fixed space, denote their densities as functions of time t, resp. $s = s(t), i = i(t), r = r(t)$.

Proposition 16 *Assuming mass action kinetics, reaction network* (44) *generates the following dynamical system for functions* s, i, r:

$$\begin{aligned} s' &= -\nu s, \\ i' &= ksi - ai, \\ r' &= ai. \end{aligned} \tag{45}$$

Initial value problem (45)–(41) *admits an exact solution for functions* $s = s(t)$, $i = i(t)$, *namely* $s = s_0 e^{-\nu t}$, *and*

$$i = i_0 \exp\left(\gamma(s_0 - s) - at\right) = i_0 \exp\left(\gamma s_0(1 - e^{-\nu t}) - at\right), \quad \gamma = \frac{k}{\nu}. \tag{46}$$

Proof Dynamical system (45) follows by general CRNT considerations [25]. The first uncoupled differential equation in dynamical system (45) $s' = -\nu s$ has the solution $s = s_0 e^{-\nu t}$. In the second differential equation of system (45): $i' = ksi - ai = (ks - a)i$ we replace s by $-s'/\nu$ to obtain:

$$\frac{i'}{i} = -\gamma s' - a, \quad \gamma = \frac{k}{\nu}. \tag{47}$$

Integrating (47) yields an equation for solutions i and s:

$$\ln i = -\gamma s - at + c, \quad c = \gamma s_0 + \ln i_0,$$

resp.

$$\ln \frac{i}{i_0} = \gamma(s_0 - s) - at. \tag{48}$$

Relation (48) yields expression (46) for the solution i as function of t. □

Reaction network (44), resp. dynamical system (45), will be further referred as Gompertz-type SIR model, briefly: G-SIR model.

5.1 Analysis of solution *i*

From expression (46) we can compute the asymptote for solution i when $t \longrightarrow \infty$. To this end we write solution i in the form

$$i = i_0 \exp\left(\gamma(s_0 - s) - at\right) = i_0 \exp\left(\gamma(s_0 - s)\right) \exp(-at). \tag{49}$$

Using that the multiplier $\exp\left(\gamma(s_0 - s)\right)$ is bounded, whereas $\exp(-at)$ tends to 0, we obtain $i(\infty) = 0$.

The condition for an epidemic disease outbreak of the G-SIR model is $i'|_{i=0} > 0$, that is $ks_0 - a > 0$. So, the reproduction number for the G-SIR model is given by the same expression (43) as the one for the SIR model, that is:

$$R_0^{G\text{-}SIR} = s_0/\rho, \quad \rho = a/k. \tag{50}$$

Using the reproduction number (50), the threshold condition for an epidemic outbreak can be expressed as $R_0^{G-SIR} > 1$.

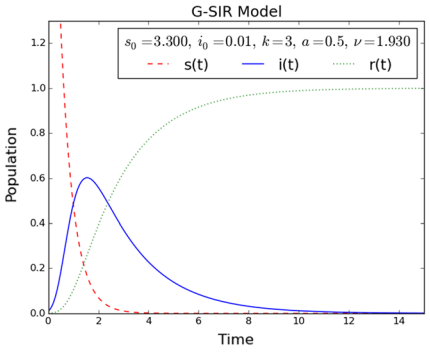
To find a maximum value of function i in the case of an outbreak ($\rho < s_0$), we have to solve for $t > 0$ the equation $i' = (ks - a)i = 0$, that is $ks - a = 0$. Let t_i^* be the solution to the latter equation, so that

$$s(t_i^*) = a/k = \rho. \tag{51}$$

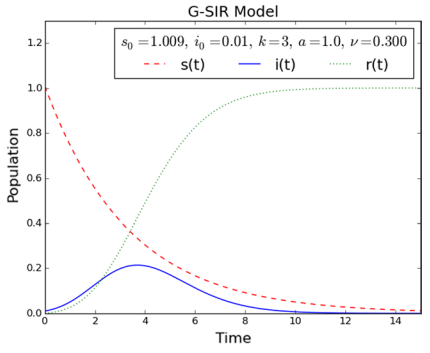
Using the expression for $s = s(t)$ we have $s(t_i^*) = s_0 e^{-\nu t_i^*} = \rho$, which yields

$$-\nu t_i^* = \ln(\rho/s_0) = -\ln(s_0/\rho),$$

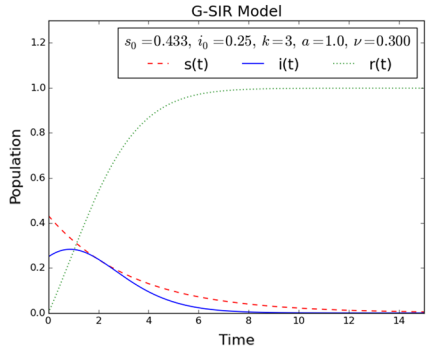
hence for the time moment of the maximum of function i we obtain



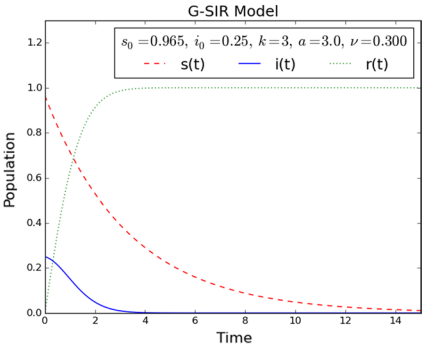
(a) $s_0 = 3.3$, $i_0 = 0.01$, $k = 3$, $a = 0.5$, $\nu = 1.93$



(b) $s_0 = 1.009$, $i_0 = 0.01$, $k = 3$, $a = 1.0$, $\nu = 0.3$



(c) $s_0 = 0.433$, $i_0 = 0.25$, $k = 3$, $a = 1.0$, $\nu = 0.3$



(d) $s_0 = 0.965$, $i_0 = 0.25$, $k = 3$, $a = 3.0$, $\nu = 0.3$

Fig. 8 Solutions to the G-SIR model

$$t_i^* = (1/\nu)\ln(s_0/\rho) = \ln(s_0/\rho)^{(1/\nu)},\ \ \rho < s_0. \tag{52}$$

The value of function i at time t_i^* is computed by substituting expression (52) in equation (46). Using (51), we obtain for $i^* = i(t_i^*)$ the following expression:

$$\ln i^* = -\frac{k}{\nu}\frac{a}{k} - at_i^* + c = -\frac{a}{\nu} - a\ln(s_0/\rho)^{(1/\nu)} + \gamma s_0 + \ln i_0. \tag{53}$$

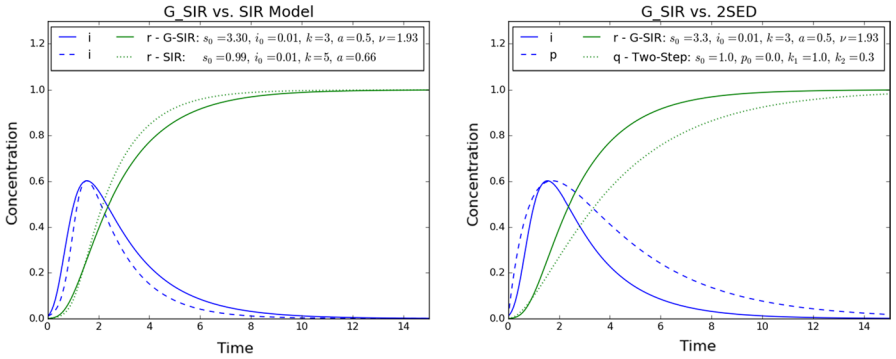
Assuming $c = \gamma s_0 + \ln i_0 = 0$, we have

$$i^* = \exp\left(-\frac{a}{\nu} - \ln(s_0/\rho)^{(a/\nu)}\right) = \exp\left(-\frac{a}{\nu}\right)(s_0/\rho)^{(\nu/a)}. \tag{54}$$

The above results characterizing solution i are summarized in the following:

Proposition 17 *In the case of an epidemic outbreak* $R_0^{G-SIR} = s_0/\rho > 1,\ \rho = a/k$, *the maximum value of function i of the G-SIR model is attained at time moment* t_i^* *given by* (52). *The value of function i at time* t_i^* *is given by expression* (54).

A visualization of the solutions of the G-SIR model is shown on Fig. 8. A typical epidemic outbreak is graphically presented on part (A). Note the wave-like form of the intermediate solution i and the sigmoidal form of function r. Both solutions have there inflections at (much) lower positions than those for the SIR model. Note also the exponential decay form of solution s tending to zero. The different shapes of the solutions of the SIR and the G-SIR models are clearly expressed on Fig. 9a.



(a) G-SIR vs. SIR model **(b)** G-SIR vs. 2SED model

Fig. 9 Comparison between the SIR, G-SIR and the 2SED models

6 The two-step exponential chain as an epidemiological model

Let us examine the two-step exponential chain $S \longrightarrow I \longrightarrow R$ with respect to possible applications to modelling epidemic outbreaks. Coming back to J. D. Murray's definition of a SIR epidemiological model, consider a situation when the infectives are not necessarily capable to transmit the disease in a one-to-one contact pattern to healthy susceptible individuals (possibly due to restrictions imposed). We then ask how to formulate a SIR three-compartmental model so that it is not necessarily subject to the logistic assumption for the disease transmission. Indeed certain diseases are capable to spread independently on one-to-one contacts between susceptible and diseased individuals. There are so-called "noncommunicable" diseases (NCD's), that can be catched without contacts between healthy and diseased individuals. The spread of such NCD's is facilitated by various factors, such as certain environmental factors, e.g. contaminated water, air pollution, socio-economic factors, etc., cf. [3, 5, 7, 36, 39].

Recall that reaction network (39) inducing the classic SIR model (40) involves an (auto-)catalytic action of species I over the reaction $S \longrightarrow I$. In contrast, the two-step reaction chain $S \longrightarrow I \longrightarrow R$ does not presume any catalytic action.

We are going to comparatively study the two-step exponential model as based on a reaction network closely related to those of the SIR model. Furthermore, we shall examine to what extent the two-step exponential model can be applied to simulate epidemiological data.

6.1 The two-step exponential chain: epidemic outbreaks

In order to compare the two-step exponential decay (2SED) model to the classic SIR and the G-SIR models, we shall consider species S, P, Q as having similar meaning as species S, I, R in the SIR model, resp., that is: susceptible S, diseased P, and removed Q classes of individuals. Further, in the initial value conditions (8) we shall allow for the initial value of diseased population $p(0) = p_0$ to be positive, as accepted in the SIR model, cf. (41). We thus assume in the sequel:

$$s(0) = s_0 > 0; \quad p(0) = p_0 \geq 0; \quad q(0) = q_0 = 0. \tag{55}$$

Under initial value conditions (55) the number $c > 0$ from relation (7) giving the (constant) total population becomes:

$$c = s_0 + p_0. \tag{56}$$

In accordance to assumption (56), expression (10) for p becomes:

$$p(t) = \begin{cases} \frac{s_0 k_1}{k_2 - k_1}(e^{-k_1 t} - e^{-k_2 t}) + p_0 e^{-k_2 t}, & k_1 \neq k_2, \\ s_0 k t e^{-kt} + p_0 e^{-kt}, & k_1 = k_2 = k. \end{cases} \tag{57}$$

Differentiating expression (57) we obtain for the derivative of p:

$$p'(t) = \begin{cases} \frac{s_0 k_1}{k_2 - k_1}(-k_1 e^{-k_1 t} + k_2 e^{-k_2 t}) - p_0 k_2 e^{-k_2 t}, & k_1 \neq k_2, \\ s_0 k e^{-kt}(1 - kt) - p_0 k e^{-kt}, & k_1 = k_2 = k. \end{cases} \tag{58}$$

Let us check whether the two-step exponential IVP (6)–(55) is capable to simulate an epidemic outbreak. To this end we need to find out the sign of function $p'(t)$ at $t = 0$.

Denote for brevity $\delta = k_2 - k_1$, $\rho = k_2/k_1$, $\eta_i = \eta_i(t) = e^{-k_i t}$, $i = 1, 2$. Note that conditions $\delta = 0$ and $\rho = 1$ are equivalent. We also have $\eta_2/\eta_1 = e^{-\delta t}$.

Consider first the case: $\delta = k_2 - k_1 \neq 0$. Then, from (58) we can write equation $p'(t) = 0$ for t as:

$$\frac{s_0 k_1}{\delta}(-k_1 \eta_1 + k_2 \eta_2) - p_0 k_2 \eta_2 = 0,$$

hence

$$-k_1 \eta_1 + k_2 \eta_2 = \frac{p_0}{s_0} \rho \delta \eta_2. \tag{59}$$

Substituting $t = 0$ in (59), we obtain $-k_1 + k_2 = \frac{p_0}{s_0}\rho\delta$, that is $\delta = \frac{p_0}{s_0}\rho\delta$. So, we have $1 = \frac{p_0}{s_0}\rho$, or the threshold expression:

$$\rho = \frac{s_0}{p_0} = \frac{s_0}{c - s_0},$$

using relation (56).

Consider now the case: $\delta = k_2 - k_1 = 0$, $k_2 = k_1 = k$. Then, using (58), we can write the equation $p'(t) = 0$ for t as: $s_0 k e^{-kt}(1 - kt) - p_0 k e^{-kt} = 0$, or $s_0(1 - kt) - p_0 = 0$, that is

$$1 - kt = \frac{p_0}{s_0}.$$

For $t = 0$ we obtain the threshold condition $1 = \frac{p_0}{s_0}$ or $p_0 = s_0$. Note that this result can be considered as a consequence of the case $\delta \neq 0$: $1 - \frac{p_0}{s_0}\rho = 0$ when $\rho = 1$, which is identical to $\delta = 0$.

We summarize the two cases in the following:

Proposition 18 *For the IVP (6)–(55) we have*

$$p'(t)|_{t=0} \text{ is: } \begin{cases} < 0, & \rho > \frac{s_0}{p_0}, \\ > 0, & \rho < \frac{s_0}{p_0}, \\ = 0, & \rho = \frac{s_0}{p_0}, \end{cases}$$

that is, in the first and third cases $\rho \geq \frac{s_0}{p_0}$ there is no epidemic outbreak, whereas in the second case $\rho < \frac{s_0}{p_0}$ there is an outbreak. The threshold condition is $\rho = \frac{s_0}{p_0}$.

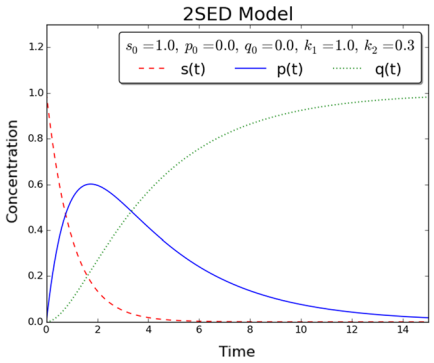
Analogously to expression (43) for the SIR reproduction number, we compute:

$$R_0^{2SED} = \frac{s_0}{p_0}\frac{k_1}{k_2} = \frac{s_0}{p_0}\rho^{-1} = \frac{s_0}{c - s_0}\rho^{-1}. \tag{60}$$

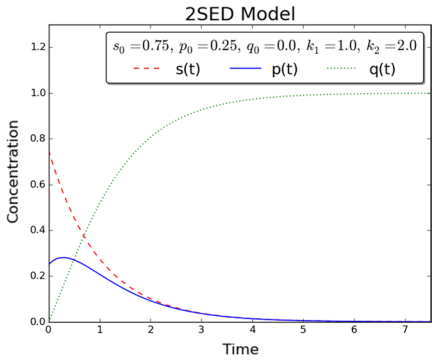
According to expression (60) the threshold condition $R_0^{2SED} > 1$ ensues an epidemic outbreak.

Let us find out the time moment t^* when the 2SED model epidemic outbreak attains its maximum value. To this end we have to solve the equation $p'(t) = 0$ with respect to t, whenever $p_0 > 0$ and $R_0^{2SED} > 1$, that is $\rho < s_0/p_0$. Using expression (59) and the abbreviate notations we obtain

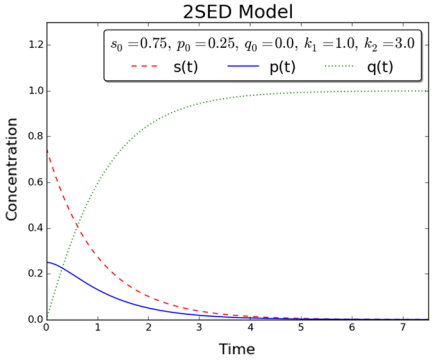
$$e^{\delta t} = \frac{1}{k_1}\left(k_2 - \frac{p_0}{s_0}\rho\delta\right) = \rho\left(1 - \frac{p_0}{s_0}\delta\frac{1}{k_1}\right),$$



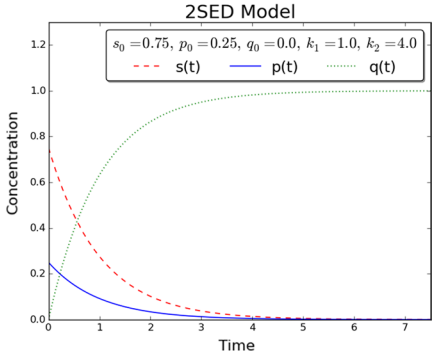
(a) Parameter values $s_0 = 1.0, p_0 = 0.0, q_0 = 0, k_1 = 1.0, k_2 = 0.3$.



(b) Parameter values $s_0 = 0.75, p_0 = 0.25, q_0 = 0, k_1 = 1, k_2 = 2$. As $\rho < \frac{s_0}{p_0}$ there is an epidemic outbreak.



(c) Parameter values $s_0 = 0.75, p_0 = 0.25, q_0 = 0, k_1 = 1, k_2 = 3$. Due to threshold condition $\rho = \frac{s_0}{p_0}$, there is no epidemic outbreak.



(d) Parameter values $s_0 = 0.75, p_0 = 0.25, q_0 = 0, k_1 = 1, k_2 = 4$. As $\rho > \frac{s_0}{p_0}$ there is no epidemic outbreak.

Fig. 10 Graphical presentation of of the solutions to the two-step exponential model (6)–(55)

hence

$$t^* = (1/\delta) \ln \left(\rho \left(1 - \frac{p_0}{s_0} \delta \frac{1}{k_1} \right) \right). \tag{61}$$

So, the maximum value of solution p is attained at point t^* given by (61).

6.2 The 2SED model: graphical comparison with the SIR and the G-SIR models

Figure 10 shows the solutions to the 2SED model for four different parameter sets. Figure 10a, b present an outbreak, whereas Fig. 10c, d show an absence of an outbreak. The solutions of the 2SED model on Fig. 10a are compared with the solutions of the G-SIR model on Fig. 8a by a common plot on Fig. 9b. Looking at Fig. 9b we clearly see the differences in the shapes of the solutions p, i, modelling the infective individuals resp. in the 2SED model and the G-SIR model.

Comparing the shapes of the solutions i to both SIR type models—the classic (logistic type) SIR and the (Gompertzian type) G-SIR model—and the solution p to the 2SED model, we can distinguish three types (modes) of shapes regarding outbreaks during the initial interval $[0, t^*]$ as follows:

(i) a "logistic mode" (L-mode): a strongly expressed inflection at a height appr. 50% of the carrying capacity c in the initial interval $[0, t^*]$, as in the classic SIR model;
(ii) a "Gompretzian mode" (G-mode): a mildly expressed inflection at a height appr. 37% of the carrying capacity c leasing to an almost linear shape, in the initial interval $[0, t^*]$, as in the G-SIR model;
(iii) an "exponential mode" (E-mode): a lack of inflection in the initial interval $[0, t^*]$; as in the case of the 2SED model.

As we see, the G-SIR model is situated between the two extreme cases of a high positioned inflection point and no inflection point.

It seems remarkable that from the perspective of CRNT the G-SIR model takes an intermediate place between the SIR and the 2SED models with respect to disease spread patterns:

(i) an explicit strongly expressed one-to-one "logistic mode" , resulting from the logistic reaction mechanism as in the case of the classic SIR model;
(ii) an implicit "catalytic mode" as result of the Gompertzian growth-decay mechanism as in the case of the G-SIR model;
(iii) the spontaneous disease transmission due to a exponential "radioactive decay" mechanism as in the 2SED model.

Particular epidemiological events depend both on the spread contact patterns of the infective agents (bacteria, viruses, transmission vectors, etc.) as well as on the social behaviour of the involved population (hygienic precautions, contact restrictions,

etc). It is to be expected that the epidemiological characteristics of a particular epidemic outbreak reflect on the shape of the collected measurement date of the epidemic event.

The parallelism between the three characteristic graph shapes and their generating reaction mechanisms suggest the following:

6.3 Hypothesis

The shape of the measurement data series of a particular epidemic outbreak is indicative for the disease spread pattern of the epidemic event and may be helpful for the choice of a mathematical model possessing the appropriate reaction mechanism.

Future work should be performed in order to validate or disvalidate the above hypothesis by testing the discussed three models on various available measurement data series. If necessary the presented models should be modified in order to take into consideration various demographic, social, environmental, etc. factors.

7 Concluding remarks

We analyze mathematically in some detail the solutions to the two-step exponential (radioactive) decay (2SED) reaction chain involving three species and two rate parameters. We study the influence of the rate parameters on the shape of the solutions. We compare the 2SED model solutions with those to the classic Kermack–McKendrick SIR model [7, 11, 17–19, 21, 26].

The chemical reaction network theory (CRNT) approach suggests that the 2SED model turns into the classic epidemiological SIR model whenever the first reaction in the 2SED reaction chain is catalyzed by the intermediate (second) species in the chain. The CRNT approach also suggests that the SIR and the 2SED reaction chains can be modified in order to simulate various epidemiological phenomena. The present work is a step into this direction by proposing a modification of the classic SIR model by replacing the first (logistic) SIR reaction with a Gompertzian growth-decay catalytic reaction. We thus obtain a variant of the classic logistic SIR model denoted as Gompertzian or G-SIR model.

The G-SIR model finds an intermediate place between the SIR and the 2SED models. Based on its characteristics we hypothesize that the G-SIR model might be suitable to simulate epidemic outbreaks related to diseases that are not necessarily communicable according to the one-to-one contact spread pattern.

The similarities and differences between the discussed three epidemiological models (SIR, G-SIR and 2SED) are clearly elucidated using the CRNT approach. The three models are similar in that they involve three spices variables with roughly similar solution shapes: a monotonically decreasing (decaying) variable, an unimodal wave-like (in case of an outbreak) variable and a monotonically increasing (sigmoidally growing) solution. The differences are in the specific characteristics of the solution shapes. The SIR model possesses two distinctive

features with respect to the unimodal (outbreak) solution: (i) a strongly expressed highly situated inflection (before the maximum), and (ii) the decaying variable does not tend to zero at infinity ($s_\infty > 0$). The G-SIR model possesses modestly expressed first feature of the SIR model (initial inflection) and does not have the second feature (since $s_\infty = 0$). The 2SED model does not have either of the two features characteristic for the SIR outbreaks. However, the CRNT approach suggests that the 2SED model will be appropriate for simulation epidemiological phenomena with particular disease spread contact patterns, such as NCD's.

We conclude that the 2SED model can be used to simulate epidemic outbreaks related to diseases caused by environmental factors, where the spread of the disease does not depend significantly on one-to-one contacts between the susceptible (healthy) and diseased individuals. Particular epidemic outbreaks of NCDs, induced by environmental factors, such as contaminated air/water, socio-economic disturbances, etc., are reported in a number of research articles, cf. [1, 3, 5, 7, 9, 33, 34, 36, 39–41, 45]. Epidemiological models implementing various disease transmission contact patterns are discussed in [10].

In the literature on mathematical modelling there exist a large number of mathematical models involving the logistic mechanism; for some of these models it is a challenge to be reformulated as models based on the Gompertz mechanism. The simplest way to perform the transition of a model with logistic mechanism into a model with Gompertzian mechanism, is to formulate the models in terms of reaction networks, cf., models (28) and (33). The the logistic-to-Gompertz transition can be also done on the level of growth-decay dynamical systems as well, cf. the level of systems (29) and (34). In the latter case we formally eliminate the growth function variable from the right-hand side of the differential reaction equation for the decay function. In effect, the rate of the decay function does not depend on the value of the growth function any more. In addition the decay function becomes a second catalyst for the autocatalytic reaction that reproduces the growth function. However, such a logistic-to-Gompertz transition of a model is not easily possible if the logistic part concerns only the growth function as is often the case in practice.

Growth-decay functions that are solutions to dynamical systems (possibly induced by reaction networks), are of considerable interest for modelling and simulation of various natural growth-decay processes, cf. [2, 22–24, 27–30].

Acknowledgements This paper is supported by the National Scientific Program "Information and Communication Technologies for a Single Digital Market in Science, Education and Security (ICTinSES)", contract No. DO1-205/23.11.2018, financed by the Ministry of Education and Science in Bulgaria. The authors are grateful to Dr. Roumen Anguelov and Dr. Nikolay Kyurkchiev for their critical remarks and meaningful suggestions. We appreciate very much the careful work done by the reviewers and their critical remarks and meaningful suggestions.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

References

1. L. Allen, Are we facing a noncommunicable disease pandemic? J. Epidemiol. Global Health **7**(1), 5–9 (2017)
2. R. Anguelov, M. Borisov, A. Iliev, N. Kyurkchiev, S. Markov, On the chemical meaning of some growth models possessing Gompertzian-type property. Math. Meth. Appl. Sci. **2017**, 1–2 (2017). https://doi.org/10.1002/mma.4539
3. J.P. Aparicio, C. Castillo-Chavez, Mathematical modelling of tuberculosis epidemics. Math. Biosci. Eng. **6**(2), 209–237 (2009). https://doi.org/10.3934/mbe.2009.6.209
4. H. Bateman, The solution of a system of differential equations occurring in the theory of radioactive transformations. Proc. Camb. Phil. Soc. **15**, 423–427 (1910)
5. S. Blower, A. Mclean, T. Porco et al., The intrinsic transmission dynamics of tuberculosis epidemics. Nat. Med. **1**, 815–821 (1995). https://doi.org/10.1038/nm0895-815
6. F. Brauer, C. Castillo-Chávez, *Mathematical Models in Population Biology and Epidemiology* (Springer, London, 2001)
7. R. Bürger, G. Chowell, L. Yissedt Lara-Díıaz, Comparative analysis of phenomenological growth models applied to epidemic outbreaks. Math. Biosci. Eng. **16**(5), 4250–4273 (2019). https://doi.org/10.3934/mbe.2019212
8. V. Chellaboina, S.P. Bhat, W.M. Haddat, D.S. Bernstein, Modeling and analysis of mass-action kinetics. IEEE Control Syst. Mag. **29**, 60–78 (2009)
9. A. Das, Diabetic retinopathy: battling the global epidemic. Invest. Ophthalmol. Vis. Sci. **57**(15), 6669–6682 (2016). https://doi.org/10.1167/iovs.16-21031
10. S.Y. Del Valle, J.M. Hyman, N. Chitnis, Mathematical models of contact patterns between age groups for predicting the spread of infectious diseases. Math. Biosci. Eng. **10**(5–6), 1475–1497 (2013). https://doi.org/10.3934/mbe.2013.10.1475
11. O. Diekmann, J.A.P. Heesterbeek, J.A. Metz, On the definition and the computation of the basic reproduction ratio R0 in models for infectious diseases in heterogeneous populations. J. Math. Biol. **28**, 365–382 (1999)
12. M. Feinberg, *Foundations of Chemical Reaction Network Theory* (Springer, London, 2019)
13. P. Gerlee, The model muddle: in search of tumor growth laws. Cancer Res. **73**(8), 2407–11 (2013)
14. B. Gompertz, On the nature of the function expressive of the law of human mortality, and on a new mode of determining the value of life contingencies. Philos. Trans. R. Soc. Lond. **115**, 513–585 (1825)
15. J. Gunawardena, *Chemical reaction network theory for in-silico biologists*. Technicalreport (2003). http://vcp.med.harvard.edu/papers/crnt.pdf
16. T. Harko, F.S.N. Lobo, M.K. Mak, Exact analytical solutions of the susceptible-infected-recovered (SIR) epidemic model and of the SIR model with equal death and birth rates. Appl. Math. Comput. **236**, 184–194 (2014)
17. H.W. Hethcote, Qualitative analyses of communicable disease models. Math. Biosci. **28**, 335–356 (1976)
18. H.W. Hethcote, The mathematics of infectuous diseases. SIAM Rev. **42**(4), 599–653 (2000)
19. W.O. Kermack, A.G. McKendrick, A contribution to the mathematical theory of epidemimcs. R. Soc. Publ. (1927). https://doi.org/10.1098/rspa.1927.0118
20. W.O. Kermack, A.G. McKendrick, A contribution to the mathematical theory of epidemics. II. The problem of endemicity. Proc. R. Soc. Lond. A **138**, 55–83 (1932). https://doi.org/10.1098/rspa.1932.0171)
21. W.O. Kermack, A.G. McKendrick, A contribution to the mathematical theory of epidemics. III. Further studies of the problem of endemicity. Proc. R. Soc. Lond. A **141**, 94–122 (1933). https://doi.org/10.1098/rspa.1933.0106)
22. N. Kyurkchiev, S. Markov, On the numerical solution of the general kinetic "K-angle'' reaction system. J. Math. Chem. **54**, 792–805 (2016)
23. N. Kyurkchiev, S. Markov, On the Hausdorff distance between the Heaviside step function and Verhulst logistic function. J. Math. Chem. **54**, 109–119 (2016)
24. N. Kyurkchiev, On a sigmoidal growth function generated by reaction networks. Some extensions and applications. Commun. Appl. Anal. **23**(3), 383–400 (2019)
25. G. Lente, *Deterministic Kinetics in Chemistry and Systems Biology. Briefs in Molecular Science* (Springer, London, 2016)

26. Q.-H. Liu, M. Ajelli, A. Aleta, S. Merler, Y. Moreno, A. Vespignani, Measurability of the epidemic reproduction number in data-driven contact networks. Proc. Natl. Acad. Sci. **115**(50), 12680–12685 (2018). https://doi.org/10.1073/pnas.1811115115
27. S. Markov, Reaction networks reveal new links between Gompertz and Verhulst growth functions. Biomath **8**, 1904167 (2019). https://doi.org/10.11145/j.biomath.2019.04.167
28. S. Markov, On a class of generalized Gompertz–Bateman growth-decay models. Biomath Commun. **6**, 51–64 (2019). https://doi.org/10.11145/bmc.2019.07.307
29. S. Markov, A. Iliev, A. Rahnev, N. Kyurkchiev, A note on the three-stage growth model. Dyn. Syst. Appl. **28**(1), 63–72 (2019)
30. S. Markov, A. Iliev, A. Rahnev, N. Kyurkchiev, A note on the n-stage growth model. Overview Biomath Commun. **5**, 79–100 (2018). https://doi.org/10.11145/bmc.2018.11.117
31. L. Moral, A.F. Pacheco, Algebraic approach to the radioactive decay equations. Am. J. Phys. **71**(7), 684–686 (2003). https://doi.org/10.1119/1.1571834
32. J.D. Murray, *Mathematical Biology: I. An Introduction*, 3rd edn. (Springer, London, 2002)
33. K.A. Murray et al., Global biogeography of human infectious diseases. Proc. Natl Acad. Sci. USA **112**, 12746–12751 (2015)
34. R.A. Nianogo, O.A. Arah, Agent-based modeling of noncommunicable diseases: a systematic review. Am. J. Public Health **105**(3), e20–e31 (2015). https://doi.org/10.2105/AJPH.2014.302426
35. D.S. Pressyanov, Short solution of the radioactive chain equations. Am. J. Phys. **70**, 444–445 (2002)
36. A. Pruess-Ustuen, J. Wolf, C. Corvalán, T. Neville, R. Bos, M. Neira, Diseases due to unhealthy environments: an updated estimate of the global burden of disease attributable to environmental determinants of health. J. Public Health **39**(3), 464–475 (2017). https://doi.org/10.1093/pubmed/fdw085
37. O. Radulescu, A. Gorban, A. Zinovyev, A. Lilienbaum, Robust simplifications of multiscale biochemical networks. BMC Syst. Biol. **2**, 86 (2008)
38. O. Radulescu, A.N. Gorban, A. Zinovyev, V. Noel, Reduction of dynamical biochemical reactions networks in computational biology. Front. Genetics **3**, 131 (2012)
39. D.W. Redding, P.M. Atkinson, A.A. Cunningham et al., Impacts of environmental and socio-economic factors on emergence and epidemic potential of Ebola in Africa. Nat. Commun. **10**, 4531 (2019). https://doi.org/10.1038/s41467-019-12499-6
40. J. Seeberg, L. Meinert, Can epidemics be noncommunicable? Reflections on the spread of "noncommunicable'' diseases. Med. Anthropol. Theory **2**(2), 54–71 (2015)
41. T. Stocks, *Dynamic Modelling of Communicable and Non-Communicable Diseases* (Stockholm University, Department of Mathematics, 2017). Retrieved from http://urn.kb.se/resolve?urn=urn:nbn:se:su:diva-137860
42. P.-F. Verhulst, Notice sur la loi que la population poursuit dans son accroissement. Correspond. Math. Phys. **10**, 113–121 (1838)
43. L. von Bertalanffy, A quantitative theory of organic growth (inquiries on growth laws. II). Hum. Biol. **10**, 181–213 (1938)
44. J. West et al., An evolutionary model of tumor cell kinetics and the emergence of molecular heterogeneity driving Gompertzian Growthm SIAM review. Soc. Ind. Appl. Math. **58**(4), 716–736 (2015). https://doi.org/10.1137/15M1044825
45. World Health Organization (WHO), Global Status Report on Noncommunicable Diseases 2010, Geneva: WHO, 2011. http://www.who.int/nmh/publications/ncd_report2010/en/
46. C. Winsor, Gompertz curve as a growth equation. Proc. Natl. Acad. Sci. **18**(1–8), 1932 (1932)
47. M.H. Zwietering, I. Jongenburger, F.M. Rombout, K. van't Riet, Modeling of the bacterial growth curve. Appl. Environ. Microbiol. **56**(6), 1875–1881 (1990). https://doi.org/10.1128/AEM.56.6.1875-1881.1990

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