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The Gompertz model revisited and modified using reaction networks: Mathematical analysis

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The paper is dedicated to Prof. Dr. Roumen Anguelov on the occasion of his 65th birthday.

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***Abstract*— In the present work we discuss the usage of the framework of chemical reaction networks for the construction of dynamical models and their mathematical analysis. To this end, the process of construction of reaction-network-based models via mass action kinetics is introduced and illustrated on several familiar examples, such as the exponential (radioactive) decay, the logistic and the Gompertz models. Our final goal is to modify the reaction network of the classic Gompertz model in a natural way using certain features of the exponential decay and the logistic models. The growth function of the obtained new Gompertz-type hybrid model possesses an additional degree of freedom (one more rate parameter) and is thus more flexible when applied to numerical simulation of measurement and experimental data sets. More specifically, the ordinate (height) of the inflection point of the new generalized Gompertz model can vary in the interval $(0, 1/e]$, whereas the respective height of the classic Gompertz model is fixed at $1/e$ (assuming the height of the upper asymptote is one). It is shown that the new model is a generalization of both the classic Gompertz model and the one-step exponential decay model. Historically the Gompertz function has been first used for statistical/insurance purposes, much later this function has been applied to simulate biological growth data sets coming from various fields of science, the reaction network approach explains and unifies the two approaches.**

***Keywords*-Systems of ordinary differential equations, Reaction networks, Chemical reaction networks, Evolutionary growth-decay models, Relative growth rate, Exponential (radioactive) decay, Logarithmic change rate, Logistic model, Gompertz model.**

I. Introduction: reaction networks and evolutionary growth-decay models

The present study is devoted to mathematical models induced by chemical reaction networks describing evolutionary changes of biolog-

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ical species. We are interested in smooth changes that are described either as monotone growth, or monotone decay, in certain (large) time intervals, oscillation processes will not be considered in this work. We briefly call such changes, resp. functions, *g*rowth-decay changes/functions. The exponential radioactive decay, the Gompertz and the logistic models are three textbook examples, where we can consider the state variables involved as species that react between each others or are catalysts of certain reaction(s).

The main purpose of this work is to propose a new modification of the classic Gompertz model possessing more flexibility and functionalities. On the way to achieve this goal we offer a brief introduction into the method of chemical reaction networks, which turns to be essential in the construction of new meaningful mathematical models, in particular when it comes to biological growth and decay processes.

In the preliminary part of this work we present several examples demonstrating the role of the chemical reaction network theory (CRNT) in tracing the characteristics of elementary familiar mathematical models for the numerical simulation of complex phenomenological (biological) processes. The example with the Gompertz model demonstrates the need of a detailed knowledge on the basics of elementary reaction networks.

Biological growth-decay functions, describing evolutionary processes, are often presented in the literature by means of explicit algebraic expressions. Such a presentation offers little or no information on the physico-chemical mechanism of the studied process. More information in this direction is provided when the growth-decay functions are defined as solutions to systems of ordinary differential equations. In the latter case we may look for a possible *(chemical) reaction network*, which implies the particular dynamical system via mass action kinetics [20]. If such a network does exist, we say that the differential system has a realization (formulation) in terms of a (chemical) reaction network [6].

Models formulated in terms of reaction networks offer additional knowledge for the particular biological process, possibly leading to further modifications and improvements of the particular model.

An essential step towards the generalizion of *purely chemical reaction network*, involving just particular chemical substances towards a more generalized chemical objects, such as enzymes and substrates, seem to be done first by the prominent scientist Victor Henri, who proposed the enzyme kinetic reaction network, see example 7 below. Later on scientists working in fields, such as population dynamics and epidemiological modelling, began to realize that many of their models can be based on reaction networks, wherein the chemical substances are considered as more generalized biological objects often denoted as species [6].

The logistic model is an instructive example of a growth-decay model possessing a chemical reaction network [6], [13], [21]. The reaction network presentation enables an easy identification of the logistic model as a constituent part of other (more complex) growth-decay models and to expect similar behaviour of the growth and decay functions, such as sigmoidal growth and exponential decay.

Section 2 is intended for readers who are not familiar with the *Chemical Reaction Network Theory (CRNT)* and its application to mathematical modelling in biology. On several examples we give a brief introduction of method of "translation" of a reaction network into a system of ordinary differential equations (ODE's) using the simple "mass action kinetic" principle. Such a translation turns the reaction network into an unique mathematical problem for the time evolution of the masses (concentrations , densities) of the species. Readers who are interested in the implementation of the more involved "power law kinetic" postulates may consult some textbooks on CRNT [8], [20].

In Section 3 we consider the classical Gompertz model from the perspective of CRNT. For this purpose we formulate the Gompertz model in terms of a reaction network. Readers already equipped with the technique of translation will be able to easily

trace the relation between the "chemical" reaction network and the classical ODE's involved. This approach allows us to enlighten certain characteristics of the Gompertz growth function and the closely related Gompetz decay function involved (known as mortality law).

In Section 4 we propose a new modification of the reaction network of the classic Gompertz model obtaining thus an original Gompertz-like model possessing one more degree of freedom. The proposed new model is mathematically analysed in the spirit of the reaction network approach. It is shown that the model is a generalization of both the classic Gompertz model and the one-step radioactive exponential decay model, forming thus a hybrid between these two familiar models.

II. Preliminaries: reaction networks and their translation into ODE's

We briefly recall some features of growth-decay models based on reaction networks as well as some appropriate terminology and notation.

A. Reaction networks.

Canonical forms. Systems of chemical reactions, briefly: *reaction networks*, are symbolically presented as systems of elementary reactions of the following *canonical form*:

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

showing that one, two or more species on the left side of the *reaction arrow*, called *reactants* or *reagents* (in this example species S and Q), react, and, as result of the reaction, one, two or more species, named *products* (here P and R), are produced. Note that the arrow should point to the right and the sign "+" has different meaning when placed on the left or on the right side of the reaction arrow: on the left side the "+" means reaction between the enlisted reactants, whereas on the right no reaction is assumed between the product speciess; if such a reaction exists, then it should be described by a separate elementary reaction. Just one species on each side of the arrow is also possible, in fact, as we shall see below, a reaction of the form $S \xrightarrow{k} P$ is a basic one. Note that a presentation, such as $S \xrightarrow{k} P \xrightarrow{k_1} Q$, is not canonical, the corresponding canonical presentation for this reaction network is: $S \xrightarrow{k} P,\ P \xrightarrow{k_1} Q$. As another example, the often used non-standard presentation of a *reverse* reaction network:

$$S \underset{k_1}{\overset{k}{\rightleftarrows}} P$$

has the following canonical form:

$$S \xrightarrow{k} P,\ P \xrightarrow{k_1} S.$$

As one more example of a non-canonical familiar reaction network let us mention the enzyme kinetic reaction scheme between an enzyme E with a single active site and a substrate S, forming an enzyme-substrate complex C, which then yields product P, known as Henri-Michaelis-Menten reaction [7]:

$$S + E \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} C \xrightarrow{k_2} P + E.$$

In canonical form the above reaction network should be presented as:

$$\begin{aligned} S + E &\xrightarrow{k_1} C, \\ C &\xrightarrow{k_{-1}} S + E, \\ C &\xrightarrow{k_2} P + E. \end{aligned}$$

As we shall see below canonical forms are useful for an easier transform of a reaction network into a system of differential equations via mass action principle.

Notation. All species (reactants and products) partaking in a reaction are denoted by uppercase letters, such as P, Q, R, S, X, Y. A positive number called "rate parameter" is written over the reaction arrow and indicates the velocity of the reaction.

The reactants on the left side of a reaction arrow either decay or remain constant, whereas the product species on the right side of the arrow are growing or constant. In some cases a species may appear two or more times at one side of the arrow, such as $A + A$, briefly denoted as $2A$.

For example, in the reaction (1) the reactants S, Q on the left side decay with time, whereas the product species P, R on the right side are growing. In a biological context we can say that in this case the product species grow at the expenses of the reactant species, or that the growing species consume the species on the left side of the arrow (as food resources). In population dynamics (some of) the species on the left side could be considered as "parent" species that give birth (reproduce) into the outcome species on the right side of the arrow.

Catalyst species. One more special case should be mentioned, namely when a species X appears on both sides of the arrow, e.g. $S+X \xrightarrow{k} P+X$. In this case species X does not change in time, it is called a *catalyst*. Catalyst species enable a reaction to perform, e. g. in this example without X, the reaction $S \xrightarrow{k} P$ cannot practically happen.

When studying biological growth/decay processes, it is important to identify the species with catalytic action, the *catalysts*. In this work catalysts will be usually denoted by some of the letters X, Y, Z. Once again, by definition a catalyst species appears on both sides of a reaction arrow: on the left side as a reactant and on the right side as a product.

Note also that some species may partake as catalysts in a particular reaction, but can also be involved as reagents in other reaction(s) as part of the same network; there they may change (grow or decay). In such situations a catalyst species may change as result of its total participation in a particular reaction network [20].

In the "logistic" reaction $S + X \xrightarrow{k} 2X$ species X is a catalyst which catalyses the reaction $S \xrightarrow{k} X$, that is X catalyzes its own production (growing). Such species are called auto-catalysts. As a (total) result of the logistic reaction, the catalyst species X is growing in time.

B. Differential systems induced by reaction networks via mass action kinetics

Law of Mass action: The rate of a reaction is proportional to the (mathematical) product of the concentrations of the reactants.

Using *mass action kinetics principle* every particular reaction network can be uniquely transformed (translated) into a system of ordinary differential equations (ODE's), briefly: system of rate equations, or dynamical system [20], [23]. Such a transformation ("translation") is performed in the following way.

Firstly, we assume homogenous distribution of the species involved, say P, Q, S, in a certain volume/area/compartment. Then the quantitative (numeric) values assigned to species P, Q, S, such as masses, concentrations, densities, number of entities (individuals, molecules, cells, etc.), are considered as smooth functions of time denoted respectively: $p = p(t), q = q(t), s = s(t)$, so that their derivatives, resp. $p' = dp(t)/dt, q' = dq(t)/dt, s' = ds(t)/dt$, exist up to a certain order. Functions p, q, s are briefly called concentrations or masses, and the first derivatives of the masses p', q', s' are called rates of change (growth or decay or both) of the respective species. Under these assumptions, the mass action principle says that the rate of change of each species is proportional to the product of the masses of the reacting species, thereby the coefficient of proportionality is negative if the species decays (which is the case when it appears on the left hand-side of the reaction arrow) and is positive if the species grows (when appearing on the right hand-side of the arrow). The proportionality coefficient is called the *rate parameter* and is usually written over the reaction arrow. This procedure is performed for every elementary reaction of the system of reactions, that is the reaction network.

The "translation" of a reaction network into a system of ODE's via mass action kinetics is illustrated on the following examples.

Example 1. Consider the reaction network

$$S + R \xrightarrow{k} P, \quad k > 0. \tag{2}$$

Under mass action kinetics principle, reaction (2)

induces a system of three differential equations, one for each of the three species, also known as reaction equations or rate equations:

$$s' = -ksr, \;\; r' = -ksr, \;\; p' = ksr, \;\; k > 0. \quad (3)$$

System (3) demonstrates the application of the mass action law when two reacting species S, R produce a new species P. In this reaction species S, R decay, whereas species P grows; so the signs of the rate parameters for S and R are negative, and the sign of the rate parameter for P is positive. The rates (of change) of all three species are proportional to the product of the masses of the reacting species S and R, so the absolute values of all rates are of the form ksr, with $k > 0$.

Dynamical system (3) implies the identities $s' + r' = 0$, $s'+p' = 0$, resp. $s+r = c_1 = \text{const}$, $s+p = c_2 = \text{const}$. Such identities are often known as conservation relations (laws).

Example 2. Consider the reaction network:

$$S + X \xrightarrow{k} P + X, \;\; k > 0. \quad (4)$$

The induced system of ODEs is:

$$s' = -ksx, \;\; x' = 0, \;\; p' = ksx, \;\; k > 0. \quad (5)$$

Note that equation $x' = 0$ is obtained as $x' = -ksx + ksx = 0$. Species X is a catalyst. The masses of species S and P satisfy the identity $s + p = \text{const}$.

Example 3. Consider the following reaction network involving two reactions and three species:

$$S + X \xrightarrow{k} P + X, \;\; X \xrightarrow{\alpha} P, \quad (6)$$

wherein $k > 0, \alpha > 0$.

The first reaction $S + X \xrightarrow{k} P + X$ of reaction network (6) does not cause changes in catalyst species X, whereas the second reaction $X \xrightarrow{\alpha} P$ causes exponential decay of X. The other declining species is S; species P is growing. The induced dynamical system is:

$$s' = -ksx, \;\; x' = -\alpha x, \;\; p' = ksx + \alpha x. \quad (7)$$

Note that the rate p' of species P is obtained as the sum $ksx + \alpha x$ of the rates of P from the two reactions involving P. Note also that the catalyst species X changes (decays) due to reaction $x' = -\alpha x$. Dynamical system (7) induces the identity $p + x + s = \text{const}$.

Example 4. For the Henri-Michaelis-Menten reaction network $S + E \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} C \xrightarrow{k_2} P + E$ a correct translation produces the following system of ODE's for the concentrations s, e, c, p of the resp. species S, E, C, P:

$$s' = -k_1es + k_{-1}c, \;\; e' = -k_1es + (k_{-1} + k_2)c,$$
$$c' = k_1es - (k_{-1} + k_2)c, \;\; p' = k_2c.$$

In this last example the "most difficult" rates formulation seem to be the rates $e' = de/dt$ and $c' = dc/dt$ as they correspond to three distinct reaction arrows: e.g. for c' one incoming in species C and two outgoing arrows from C. The example also demonstrates one more practically useful property of reaction networks: they are more obvious than the resp. systems of ODE's and more easy to memorize.

The above examples illustrate the process of translation of a chemical reaction networks into systems of ordinary differential equations. They also illustrate the derivation of an identity relation connecting the state variables in the system of ODE's. We are going next to illustrate how the induced dynamical systems can be further mathematically analysed.

C. Growth-decay models based on reaction networks

Below we present three case studies of familiar growth/decay functions generated by reaction networks. The goal is to demonstrates the use of the reaction networks methodology in several aspects: i) parallel to the growth function other useful functions appear (such as decay and wave-like functions) that should be analysed; ii) the original reaction networks offers meaningful interpretations of the resulting model solutions; iii) in

the process of modelling and numerical simulation of particular data sets the modeler can modify the basic reaction network by introducing meaningful changes in (some of) the elementary reactions. This latter possibility will be demonstrated in Section 4, where we modify the classic Gompertz model.

Case study 1. Consider the reaction (network):

$$S \xrightarrow{k} P, \;\; k > 0, \tag{8}$$

known in chemistry as a "first-order (FO)" reaction and in nuclear physics as "one-step exponential radioactive decay (1-SERD)". This elementary reaction is known under several additional names due to its application to various processes such as radioactive nuclear decay, fluid dynamics, enzyme kinetics, marine ecology, physico-chemistry, etc. By definition, a first-order reaction proceeds at a rate that depends linearly on only one reactant concentration. Indeed, reaction (8) induces the following dynamical system for the change rates of the concentrations $s = s(t)$, $p = p(t)$ of species S, P:

$$s' = -ks, \;\; p' = ks, \;\; k > 0. \tag{9}$$

Dynamical system (9) illustrates how the expression "product of masses (concentrations)" should be interpreted in the definition of the mass action principle when just one species appears on the left hand-side of the reaction arrow. In such a situation the "product" consists of only one state variable, in the case of system (9)—concentration s.

System (9) implies the relation $s' + p' = 0$, which after integration gives the identity (conservation) relation

$$s + p = c = \text{const}. \tag{10}$$

Identity (10) says that at any time moment variable p gains as muuch as s loses. In certain real life situations this could be interpreted either as: i) species P consumes species S as a food resource, or: ii) compartment S migrates (flows, transforms) into compartment X. Thus reaction network (8) exhibits a specific mechanism for the time evolution of the two species S and P. Species P grows for the expense of species S, which proportionally decays.

When equipped with initial conditions

$$s(0) = s_0 > 0, \; p(0) = p_0 \geq 0, \tag{11}$$

such that $s_0 + p_0 = c$, dynamical system (9) turns into an initial value problem (IVP) (9)–(11) and relation (10) becomes $s + p = s_0 + p_0 = c$, hence $s = s_0 + p_0 - p = c - p$.

Let us briefly analyse the IVP for ODEs (9)–(11). Substituting $s = c - p$ in equation $p' = ks$ we obtain an autonomous ordinary differential equation for the growth function p of the form:

$$p' = k(c - p), \tag{12}$$

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

The differential equations (9), (12) for functions s and p under initial conditions (11) admit explicit solutions as functions of $t \geq 0$. The solution for s is the familiar first-order exponential (radioactive) decay:

$$s(t) = s_0 e^{-kt}. \tag{13}$$

Function s has an asymptote $s(\infty) = 0$, that is concentration s vanishes at infinity. Species with such a property are known as "limiting reagents" in chemistry.

The solution for p can be obtained using identity (10) when substituting s by $c - p$ in (13):

$$\begin{array}{rcl} p(t) & = & c - s = c - (c - p_0)e^{-kt}, \\ c & = & s_0 + p_0. \end{array} \tag{14}$$

Function p solving (14) has an upper asymptote $p(\infty) = c$; it is known as exponential (also saturation) growth model.

To obtain the absolute change rates of functions s, p we can differentiate expressions (13), (14), or insert the expression for s, p in the resp. differential equations. For the absolute decay rate of s we obtain:

$$s' = -ks_0 e^{-kt}. \tag{15}$$

For the absolute growth rate of function p we have

$$\begin{aligned} p' &= (c-s)' = ks_0e^{-kt} \\ &= k(c-p_0)e^{-kt}, \ \ c = s_0+p_0. \end{aligned} \tag{16}$$

The logarithmic (relative) decay rate r_s of function s is constant, namely:

$$r_s = (\ln s)' = \frac{s'}{s} = \frac{-ks}{s} = -k. \tag{17}$$

The logarithmic (relative) growth rate r_p of p can be obtained as follows:

$$\begin{aligned} r_p = (\ln p)' &= \tfrac{p'}{p} = \tfrac{ks}{c-s} = k\left(\tfrac{c-p}{p}\right) \\ &= k\left(\tfrac{(c-p_0)e^{-kt}}{c-(c-p_0)e^{-kt}}\right). \end{aligned} \tag{18}$$

The second derivatives of functions s, p are:

$$s'' = (-ks)' = k^2s > 0, \tag{19}$$

resp.:

$$p'' = k(c-p)' = -kp' = -k^2(c-p_0)e^{-kt} < 0. \tag{20}$$

Relations $s'' > 0$ and $p'' < 0$ show that function s is convex, whereas function p is concave for all $t \geq 0$.

Remarks. 1. In numerical simulation studies the upper asymptote c of the growth function p, also known as *environmental capacity*, is usually set to one: $p(\infty) = c = 1$. 2. Reaction (8) is the first chain-link of a multi-step exponential radioactive decay chain. In the field of radioactive decay and some population studies one is only interested in the decay process and ignores the evolution of the growth species. In such situations one often presents reaction (8) in the form $S \xrightarrow{k} \emptyset$, $k > 0$. The symbol $\emptyset$ indicates that the reaction equation for the growth species in dynamical system (9), in our case equation $p' = ks$, is suppressed.

Case study 2. This example is an extension of the previous reaction network (8). An exponential mechanism involving two sequential first order steps in the transformation of three species S, P, Q is given in the reaction network:

$$S \xrightarrow{k_1} P, \ \ P \xrightarrow{k_2} Q, \tag{21}$$

where k_1, k_2 are positive rate parameters. (As already mentioned, reaction network (21) is often written in the concise non-canonical form $S \xrightarrow{k_1} P \xrightarrow{k_2} Q$,).

In nuclear physics reaction (21) is known as rwo-step exponential radioactive decay (2-SERD). Denoting the concentrations (densities, masses) of species S, P, Q as functions of time t by $s = s(t), p = p(t), q = q(t)$ and their derivatives resp. by s', p', q', we arrive at the following dynamical system:

$$\begin{aligned} s' &= -k_1s, \\ p' &= k_1s - k_2p, \\ q' &= k_2p. \end{aligned} \tag{22}$$

Dynamical system (22) induces the following conservation identity:

$$s + p + q = c = \text{const}. \tag{23}$$

System (22) shows that $s' < 0$ and $q' > 0$, so function s decays, whereas function q grows. It can be proved that function p first increases until a certain time moment t^* and then decreases in $[t^*, \infty)$. Such functions are called *unimodal*, their graphs are wave-like; such functions will also be considered as growth-decay functions. In chemistry, species like P, having zero concentration at the beginning and at the end of the process, are called "intermediate".

A detailed discussion of reaction network (21) and the solutions s, p, q to system (22) are given in [5]. For the solution to general n-step exponential radioactive decay system of differential equations the reader may consult [4].

Case study 3. Let us discuss the familiar logistic model as induced by a reaction network. The logistic (Verhulst) growth function is originally introduced in [28] as the solution of a differential equation of the form $x' = kx(c-x)$. The solution of this equation is a sigmoidal growth function $x = x(t), \ t \in R$. One usually ignores the related decay function which is implicitly involved in the right-hand side of the differential equation as $c-x$.

In contrast, the growth-decay presentation of the logistic model based on reaction networks involves simultaneously the two functions—growing and decaying—as a single tuple (pair). The logistic growth-decay pair is generated by the following reaction network involving two reacting species S, X:

$$S + X \xrightarrow{k} 2X, \tag{24}$$

wherein k is a positive rate parameter. As already mentioned, the symbol $2X$ in (24) is an abbreviation for $X + X$.

Reaction network (24) shows that S is a decaying species, and X is a growing species that catalyses the 1-SERD reaction $S \xrightarrow{k} X$, hence, X is an auto-catalyst species.

Under the assumption of mass action kinetics reaction network (24) induces the following dynamical system of two differential reaction equations for the masses (concentrations, densities) $s = s(t)$, $x = x(t)$ of species S, X, resp.:

$$s' = -ksx, \;\; x' = kxs, \; k > 0. \tag{25}$$

Due to $s' + x' = 0$, after integration, system (25) induces the conservation identity relation:

$$s + x = \text{const} = c. \tag{26}$$

Assume initial value conditions

$$s(0) = s_0 > 0, \; x(0) = x_0 > 0, \tag{27}$$

satisfying relation (26), so that

$$s_0 + x_0 = c. \tag{28}$$

The initial value problem (25)–(27) implies the following autonomous differential equations for the growth function x and the decay function s:

$$\begin{aligned} x' &= kx(c - x), \; x(0) = x_0, \\ s' &= -ks(c - s), \; s(0) = s_0 = c - x_0. \end{aligned} \tag{29}$$

Differential equations (29) show that function x is monotonically increasing and bounded in R^+ with values the interval $[x_0, c)$, where the value $c = s_0 + x_0$ is known as (environmental) *carrying capacity*. More specifically, function x approaches asymptotically c: $x(\infty) = x_\infty = c$. Function s is monotonically decreases approaching zero: $s(\infty) = s_\infty = 0$. As traditionally accepted in the literature, we shall assume $c = 1$, thus relation (26) becomes

$$s + x = 1. \tag{30}$$

Equations (29) posses explicit algebraic solutions for $t \in R$. To find solution x we have to solve:

$$\frac{x'}{x(1 - x)} = k,$$

which can be written as

$$\frac{x'}{x} + \frac{x'}{1 - x} = k. \tag{31}$$

Integrating (31) we obtain

$$\ln x - \ln (1 - x) = kt + \ln C,$$

or

$$\frac{x}{1 - x} = Ce^{kt}, \;\; C = \frac{x_0}{1 - x_0},$$

which can be presented as

$$x = \frac{Ce^{kt}}{1 + Ce^{kt}} = \frac{x_0}{(1 - x_0)e^{-kt} + x_0}. \tag{32}$$

For the boundary values of x at $t = 0, \; t = \infty$, expression (32) gives resp. $x(0) = x_0, \; x(\infty) = 1$, as expected.

Using expression (32) for the growth function x, the decay function s is readily obtained from identity relation (30) as follows:

$$\begin{aligned} s &= 1 - x = \tfrac{(1-x_0)e^{-kt}}{(1-x_0)e^{-kt}+x_0} \\ &= \tfrac{s_0 e^{-kt}}{s_0 e^{-kt}+(1-s_0)} = \tfrac{s_0}{s_0+(1-s_0)e^{kt}}. \end{aligned} \tag{33}$$

Absolute and logarithmic (relative) change rates.

To obtain the absolute rate of change of the growing species X, also called absolute growth rate (AGR), we can differentiate expression (32).

Alternatively, we can substitute the obtained expressions for s and x in the equation $x' = ksx$ from (29) to obtain:

$$\begin{aligned} x' &= k\frac{s_0e^{-kt}}{s_0e^{-kt}+(1-s_0)} \cdot \frac{x_0}{(1-x_0)e^{-kt}+x_0} \\ &= \frac{kx_0(1-x_0)e^{-kt}}{[(1-x_0)e^{-kt}+x_0]^2}. \end{aligned} \tag{34}$$

For the boundary values of function x' we have $x'(0) = kx_0s_0 = kx_0(1-x_0)$, $x'(\infty) = 0$.

The logarithmic change rate of function x, known also as relative growth rate (RGR), is defined as:

$$r_x = (lnx)' = d(lnx)/dt = \frac{x'}{x}. \tag{35}$$

The RGR (35) of x can be obtained by substituting expression (33) for function s in differential equation $x'/x = ks$ to get:

$$r_x = \frac{x'}{x} = ks = \frac{k(1-x_0)e^{-kt}}{(1-x_0)e^{-kt}+x_0}. \tag{36}$$

For the boundary values of function $r_x = x'/x$ we have $r_x(0) = ks_0 = k(1-x_0)$, $r_x(\infty) = 0$.

To obtain the absolute change (decay) rate of the species S, we can proceed as follows:

$$\begin{aligned} s' &= (1-x)' = -x' \\ &= -\frac{kx_0(1-x_0)e^{-kt}}{[(1-x_0)e^{-kt}+x_0]^2} = -\frac{ks_0(1-s_0)e^{-kt}}{[s_0e^{-kt}+(1-s_0)]^2}. \end{aligned} \tag{37}$$

The boundary values of function s' are $s'(0) = -ks_0(1-s_0)$, $s'(\infty) = 0$.

The logarithmic change rate (relative decay rate) of species S is:

$$\begin{aligned} r_s &= (lnx)' = d(lnx)/dt = \frac{s'}{s} \\ &= -kx = -k\frac{x_0}{(1-x_0)e^{-kt}+x_0} \\ &= -\frac{k(1-s_0)}{s_0e^{-kt}+(1-s_0)}. \end{aligned} \tag{38}$$

For the boundary values of the relative decay rate we have $r_s(0) = -ks_0$, $r_s(\infty) = 0$.

Inflection point of the growth function. To look for inflection points of growth function x we need an expression for function $x'' = x''(t)$:

$$\begin{aligned} x'' &= (x')' = (kxs)' = k(x's + s'x) \\ &= k\left((kxs)s + (-kxs)x\right) = k^2xs(s-x). \end{aligned} \tag{39}$$

Expression (39) reduces the solution of equation $x''(t^*) = 0$ for an inflection point t^* to equation

$$s(t^*) = x(t^*), \tag{40}$$

showing that the values of the decay function s and the growth function x at t^* are identical.

The two equations (40): $s(t^*) = x(t^*)$, and $s(t^*) + x(t^*) = 1$, due to (30), imply $s(t^*) = x(t^*) = 1/2$. Thus we have:

$$x(t^*) = \frac{x_0}{(1-x_0)e^{-kt^*}+x_0} = \frac{1}{2}, \tag{41}$$

equivalently

$$e^{-kt^*} = \frac{x_0}{1-x_0} = \frac{x_0}{s_0}, \tag{42}$$

or

$$t^* = -\frac{1}{k}\ln\frac{x_0}{1-x_0} = \ln\left(\frac{x_0}{(1-x_0)}\right)^{-\frac{1}{k}}. \tag{43}$$

Expression (43) for t^* shows that for $t^* > 0$, that is for the existence of inflection of the growth function, it is necessary that the logarithm in (43) is positive, that is

$$\frac{x_0}{(1-x_0)} = \frac{x_0}{s_0} < 1,$$

that is $x_0 < s_0$, hence $x_0 < 1/2$.

Consequently, when $x_0 \geq 1/2$ growth function x has no inflection. In this case we have $x''(t) < 0$ for all $t \geq 0$, hence growth function x is concave on R^+.

In the special case $x_0 = s_0 = 1/2$, we obtain the simple expressions:

$$\begin{aligned} x &= 1/(1+e^{-kt}), \\ s &= e^{-kt}/(1+e^{-kt}) = 1/(1+e^{kt}). \end{aligned}$$

Lag time (phase). Let us find an expression for the slope of function x at the inflection point. Using (34) and (42), we obtain

$$\begin{aligned} x'(t^*) &= \frac{kx_0(1-x_0)e^{-kt^*}}{[(1-x_0)e^{-kt^*}+x_0]^2} \\ &= \frac{kx_0{}^2}{(x_0+x_0)^2} = \frac{k}{4}. \end{aligned} \tag{44}$$

Using (44), we can compute the lag time y, which satisfies the relation

$$\frac{x(t^*)}{y} = x'(t^*) = \frac{k}{4},$$

hence $y = 2/k$.

Applications of the logistic and the one-step exponential radioactive decay (1-SERD) models. The logistic model finds numerous applications. A popular application is the Lotka-Volterra "prey-predator" model in population dynamics. Denoting the prey species by S and the predator by X, in its simplest form the Lotka-Volterra model can be written as a reaction network [6]:

$$\begin{array}{lllll} S & + & X & \xrightarrow{k} & 2X, \\ S & \xrightarrow{\nu} & 2S, & X & \xrightarrow{\mu} \emptyset, \end{array} \tag{45}$$

wherein k, ν, μ are positive rate parameters. Reaction network (45) induces the dynamical system:

$$\begin{aligned} s' &= -ksx + \nu s, \\ x' &= ksx - \mu x. \end{aligned} \tag{46}$$

The logistic reaction $S + X \xrightarrow{k} 2X$ describes the natural reproduction of the predator population. Reaction $X \xrightarrow{\mu} \emptyset$ represents the mortality of the predator. Reaction $S \xrightarrow{\nu} 2S$ describes the natural reproduction of the prey population.

The last two reactions vary in different versions of the Lotka-Volterra (45), however, the logistic reaction remains usually the same.

Another familiar application of the logistic model is the epidemiological SI model, where S stays for *susceptible* population and I for *infective* one:

$$S + I \xrightarrow{k} 2I. \tag{47}$$

As we see, the basic epidemiological reaction network (47) coincides with the logistic reaction (24). Again, the epidemiological SI model (47) is the backbone of various modifications, such as the popular SIR model, where R means "removed" (or "recovered") population:

$$\begin{array}{l} S + I \xrightarrow{k} 2I, \\ I \xrightarrow{\nu} R, \end{array} \tag{48}$$

where $k > 0$, $\nu > 0$ are positive rate parameters.

As a further extension to (48), the "vital" SIR model includes additionally newborn (B) and dead (D) population compartments; in the simple case of equal birth and death rates the reaction-network-formulation of the vital SIR model reads:

$$\begin{array}{l} S + I \xrightarrow{k} 2I, \\ I \xrightarrow{\nu} R, \quad D \xrightarrow{\mu} B, \end{array} \tag{49}$$

where $k > 0$, $\nu > 0$, $\mu > 0$ are positive rate parameters. The last reaction: $D \xrightarrow{\mu} B$ looks somewhat strange; however, it describes adequately the situation in stable populations.

Models (45), (48), (49) demonstrate an useful property of the reaction-network-formulation of models. Namely, such a formulation allows a modeller to construct easily various combinations of existing familiar elementary models with already established characteristics. We shall demonstrate this property in Section 4 with a modification of the Gompertz model implementing in it certain features of the 1-SERD and the logistic models.

The two models considered next in the present work—the classic and modified Gompertz models—can serve as further examples for our proposed methodology of treating growth-decay models induced by reaction networks.

III. The classic Gompertz model revisited from the perspective of reaction networks theory

The Gompertz growth function has been initially designed for insurance purposes [9], and later used more generally as a modelling growth function in life sciences, like the logistic one [33]. It is usually presented as the explicit algebraic solution $x = x(t)$ to an autonomous differential equation of the form: $x' = \nu x \ln(1/x)$, $\nu > 0$. In the sequel we deduce the Gompertz function $x = x(t)$ starting from a reaction network using the terminology of CRNT. This allows us to obtain and analyse the Gompertz growth function together with the related decay function, giving

us a general view on the Gompertzian growth-decay process, as well as a meaningful physico-chemical interpretation of the state variables and rate parameters involved. The reaction network approach explanes and unifies the two approaches.

Consider the following reaction network involving three species S, X, Q and two reactions:

$$S \xrightarrow{\nu} Q, \;\; S + X \xrightarrow{k} 2X + S, \qquad (50)$$

wherein ν, k are positive rate parameters [5], [21].

Remarks. Reaction $S + X \xrightarrow{k} 2X + S$ of network (50) says that both species X and S act as catalysts. More specifically species X catalyses the reaction $S \longrightarrow X + S$, turning it into reaction: $S + X \longrightarrow X + X + S$. So, X is a growing species autocatalysing itself. On the other hand, species S is also a catalyst in this reaction, it catalyses the reaction: $X \longrightarrow X + X$. As result in this reaction, species S does not change in time; however, globally S changes (declines) as result of the first-order exponential decay reaction $S \longrightarrow Q$. The latter reaction shows that S *flows (migrates)* into species Q, that is, outside the system of the two compartments of our interest (S, X). As mentioned, species Q can be replaced by the symbol $\emptyset$: $S \xrightarrow{\nu} \emptyset$, meaning that we shall ignore the time evolution of species Q.

Assuming homogeneity, denoting the mass-related numerical characteristics (such as concentrations, masses, densities, etc.) of species S, X, resp., by lowercase letters s, x, reaction network (50) induces the following system of two ODE's for the state variables $s = s(t)$, $x = x(t)$, $t \in R^+ = [0, \infty)$ [21]:

$$s' = -\nu s, \;\; x' = kxs, \qquad (51)$$

where $\nu > 0, \; k > 0$ are rate parameters.

System (51) belongs to the class of biochemical systems (S-systems), cf. [25], [27] [26], [29], [31]. From system (51) we see that function s satisfies the uncoupled autonomous first order differential equation: $s' = -\nu s, \;\; \nu > 0$. As mentioned in Section 2, Case study 1., solution $s = s(t)$ is given by:

$$s(t) = s_0 e^{-\nu t}, \; t \in R^+, \qquad (52)$$

for any initial value $s(0) = s_0 > 0$. Hence, function s is monotone decreasing, exponentially approaching zero at $t \longrightarrow \infty$.

Proposition 1. *Let functions $s = s(t)$, $x = x(t)$ satisfy the system of ODE's (51) for $t \in R^+$. Then the following identity relation holds true in R^+:*

$$\gamma s + \ln x = \ln x(\infty), \;\; \gamma = k/\nu. \qquad (53)$$

wherein $x(\infty) = x_\infty = x(t)|_{t \longrightarrow \infty}$ is the ordinate of the horizontal asymptote of growth function x.

Proof: Dynamical system (51) implies the identity: $x' = kxs = -kx(s'/\nu)$, which can be written as:

$$\gamma s' + x'/x = 0, \;\; \gamma = k/\nu. \qquad (54)$$

The integration of (54) yields $\gamma s + \ln x = \text{const} = c$. This equation shows that, while function s decreases with time, function x increases, however, the latter increase is bounded by the constant c in the equation.

The constant c has an important geometric meaning. Indeed, boundary values $s(\infty), x(\infty)$ satisfy identity (53), so that

$$\gamma s(\infty) + \ln x(\infty) = c, \;\; \gamma = k/\nu. \qquad (55)$$

Using that for $t \longrightarrow \infty$ function $s = s_0 e^{-\nu t}$ approaches zero for any positive $s_0, \; \nu$, symbolically $s(\infty) = s_\infty = s|_{t \longrightarrow \infty} = 0$, expression (52) implies $\ln x(\infty) = c$. This proves identity (53). ■

The asymptote of the growth function. The constant $c = \ln x(\infty)$ from identity (53) determines the value of the horizontal asymptote $x = x(\infty)$ of growth function $x(t)$. As traditionally done in the literature on Gompertz model, we fix the value for the asymptote as $x(\infty) = x|_{t \longrightarrow \infty} = 1$. This choice of the asymptote leads to the value of c in expression (53) as

$$c = \ln x(\infty) = \ln 1 = 0. \qquad (56)$$

Fixing $c = 0$, identity (53) becomes:

$$\gamma s + \ln x = 0, \;\; \gamma = k/\nu. \tag{57}$$

In what follows we shall consider the solution to (51) as an ordered 2-tuple (pair) (s, x), satisfying identity (57) in R^+. Under the choice $c = 0$ relation (57) guarantees that the growth solution x approaches the asymptote $x = 1$ at $t \longrightarrow \infty$.

Initial value problem. We shall next consider the system of ODE's (51) as initial value problem involving an initial tuple $(s(0), x(0)) = (s_0, x_0)$ for the solutions. Identity (57) is satisfied by solution (s, x) for all $t \geq 0$ including $t = 0$ and $t = \infty$. Hence, when considering system (51) as an initial value problem, we shall naturally assume that the initial tuple (s_0, x_0) satisfies identity (57), i.e.:

$$\gamma s_0 + \ln x_0 = 0, \;\; \gamma = k/\nu. \tag{58}$$

Relation (58) restricts the range of x_0 in the interval $x_0 \in (0, 1)$. Indeed, if $x_0 \geq 1$, then (58) implies $s_0 \leq 0$, which makes no practical sense. So, the choice $c = 0$ scales the total evolution of the (monotonically increasing) growth function x in the range $x \in [x_0, 1)$. In contrast, the monotonically decreasing decay function s ranges in the interval $(0, s_0]$, thereby the value s_0 can be greater than one, $s_0 > 1$.

Identity (57) implies the following practically useful relations:

$$ks + \nu \ln x = 0, \tag{59}$$

or, equivalently, using notation $\delta = 1/\gamma = \nu/k$:

$$\begin{aligned} s &= -\delta \ln x = \ln x^{-\delta}, \\ x &= e^{-\gamma s}, \end{aligned} \tag{60}$$

in particular. at $t = 0$;

$$\begin{aligned} s_0 &= -\delta \ln x_0 = \ln {x_0}^{-\delta}, \\ x_0 &= e^{-\gamma s_0}, \end{aligned} \tag{61}$$

to be used in the calculations to follow. In particular, for $s_0 = 1$ we need to have, according to (61): $x_0 = e^{-\gamma}$.

We now formulate the following:

Proposition 2. *Let initial value pair (s_0, x_0) satisfy*

$$0 < x_0 < 1, \;\; s_0 = -\delta \ln x_0, \;\; \delta = \nu/k, \tag{62}$$

then:

1) solution (s, x) to initial value problem (51)–(62) satisfies in $R^+ = [0, \infty)$ relation (57): $\gamma s + \ln x = 0$;

2) solution x to system (51) satisfies the autonomous differential equation:

$$x' = \nu x(-\ln x); \tag{63}$$

3) solution x to initial value problem (51)–(62), can be presented in the form

$$x = {x_0}^{e^{-\nu t}}. \tag{64}$$

Proof:

1) Using initial values (62) the integration of relation (54) under the choice $c = 0$ yields (57) together with $x_\infty = 1$.

2) Substituting (59): $ks = -\nu \ln x$, in differential equation $x' = kxs$ yields:

$$\begin{aligned} x' &= kxs = x(ks) = x(-\nu \ln x) \\ &= \nu x(-\ln x), = \nu x \ln(1/x), \end{aligned} \tag{65}$$

which is the familiar Gompertz differential equation (63).

3) Using expressions (60), (52), solution $x = x(t)$ can be obtained from relation (57), as follows:

$$\begin{aligned} \ln x &= -\gamma s = -\gamma(s_0 e^{-\nu t}) \\ &= (-\gamma s_0)e^{-\nu t} = (\ln x_0)e^{-\nu t} \\ &= \ln {x_0}^{e^{-\nu t}}, \end{aligned} \tag{66}$$

resp. for x we obtain (64). This proves the proposition. ■

Using part 3 of Proposition 2 we can present the solution tuple (s, x) to initial value problem (51)–(62) in the form

$$(s, x) = \left(s_0 e^{-\nu t}, \;\; {x_0}^{e^{-\nu t}}\right). \tag{67}$$

Change rates. To obtain an explicit algebraic expression for the absolute growth rate of species X we write:

$$\begin{aligned} x' &= kxs = (ks)x = (-\nu \ln x)x \\ &= -\nu \ln x_0 \; e^{-\nu t} \; exp(\ln x_0 \; e^{-\nu t}), \end{aligned} \tag{68}$$

which is positive due to $\ln x_0 < 0$.

For the boundary values of function x' we have:

$$\begin{aligned} x'(0) &= kx_0 s_0 = x_0(-\nu \ln x_0) > 0, \\ x'(\infty) &= kx(\infty)s(\infty) = 0. \end{aligned}$$

For the logarithmic (relative) growth rate $r_x = r_x(t)$ of Gompertz growth function x we obtain:

$$\begin{aligned} r_x &= (\ln x)' = x'/x \\ &= -\nu \; \ln x_0 \; e^{-\nu t} = \ln {x_0}^{-\nu e^{-\nu t}}. \end{aligned} \tag{69}$$

For the boundary values of $r_x = x'/x$ we have:

$$\begin{aligned} r_x(0) &= -\nu \ln x_0 \; e^0 = \ln(1/x_0)^{\nu}, \\ r_x(\infty) &= -\nu \ln x_\infty \; e^{-\infty} = 0. \end{aligned} \tag{70}$$

To obtain the absolute change (decay) rate of species S we write

$$s' = -\nu s = -\nu s_0 e^{-\nu t}. \tag{71}$$

The boundary values of function s' are $s'(0) = -\nu s_0$, $s'(\infty) = 0$.

The logarithmic (relative) change rate $r_s = r_s(t)$ of species S is constant (and so are the boundary values of r_s):

$$r_s = \frac{s'}{s} = -\nu. \tag{72}$$

Inflection points. Consider next the existence of a possible inflection point t^* for the Gompertz growth function x.

For the second derivative $x'' = x''(t)$ of growth function x we have:

$$\begin{aligned} x'' &= (x')' = (kxs)' = k(x's + s'x) \\ &= k\left((kxs)s + (-\nu s)x\right) \\ &= kxs(ks - \nu) = k^2 xs(s - \nu/k). \end{aligned} \tag{73}$$

Expression (73) reduces the solution of equation $x''(t^*) = 0$ for t^* to equation

$$s(t^*) = \nu/k = \delta, \tag{74}$$

showing that the value of the decay function s at the inflection point t^* is equal to the rate parameter ratio $\delta = \nu/k$.

Using (52), equation (74) reads: $s(t^*) = s_0 e^{-\nu t^*} = \delta$, hence

$$e^{-\nu t^*} = \delta/s_0 = 1/(\gamma s_0), \tag{75}$$

thus we obtain

$$t^* = (1/\nu)\ln(\gamma s_0) = \ln(\gamma s_0)^{\frac{1}{\nu}}. \tag{76}$$

Expressed via x_0, the inflection time moment t^* can be obtained when substituting γs_0 in (76) by $\ln(1/x_0)$:

$$t^* = \ln(\ln \frac{1}{x_0})^{\frac{1}{\nu}}. \tag{77}$$

To compute the value $x(t^*)$ we can use relations (74):

$$x(t^*) = e^{-\gamma s(t^*)} = e^{-\gamma\delta} = e^{-1} = 1/e. \tag{78}$$

Expression (76) implies: in order to have $t^* > 0$, that is to exist an inflection point for growth function x on R^+, it is necessary relation $1 < \gamma s_0$ to take place. In terms of x_0 this reads (using $\gamma s_0 = -\ln x_0$): $1 < \ln(1/x_0)$, equivalently:

$$x_0 < 1/e. \tag{79}$$

The condition for existence of inflection point $s(t^*) = \delta < s_0$ is equivalent to $0 < x_0 < 1/e = x(t^*)$.

Lag time (phase). To compute the so-called *lag* time interval of growth function x for the classic Gompertz model, we need the slope of function x at the inflection point, that is $x'(t^*)$. Denote the intersection of the tangent line to the graph of x through the inflection point $t^*, x(t^*)$ with the abscissa and the asymptote $x = x_\infty = 1$, resp. by $(t_a, 0)$ and $(t_b, 1)$. The length of interval $[t_a, t^*]$ on the abscissa is the lag time, whereas the length of the interval $[t^*, t_b]$ is the log time.

Substituting $x(t^*) = 1/e$, resp. $\ln x'(t^*) = -1$, in expression $x' = ksx = -\nu x \ln x$, we obtain

$$x'(t^*) = \nu/e. \tag{80}$$

The *lag* time $L = t^* - t_a$ is equal to the ratio

$$L = x(t^*)/x'(t^*) = 1/\nu, \tag{81}$$

observing the triangle below its vertex point $(t^*, x(t^*))$.

We summarize the results obtained on the expressions for solution rates, inflection points and lag/log times in the following

Proposition 3. *1. Solution tuple (s, x) to Gompertz initial value problem (51)–(62) is characterized by the following properties:*

1a. Solution (s, x) is given by (67):

$$(s, x) = \left(s_0 e^{-\nu t},\ \ {x_0}^{e^{-\nu t}}\right),$$

thereby $\gamma s = -\ln x$, in particular: $\gamma s_0 = -\ln x_0$, $\gamma = k/\nu = 1/\delta$.

The boundary values of Gompertz growth/decay functions s, x are:

$s(0) = \ln {x_0}^{-\delta}$, $s(\infty) = 0$;

$x(0) = e^{-\gamma s_0}$, $x(\infty) = 1$.

1b. The absolute change rates of species S, X are given by expressions (71), (68):

$$\begin{aligned} s' &= -\nu s_0 e^{-\nu t}; \\ x' &= -\nu \ln x_0 \ e^{-\nu t} \ {x_0}^{e^{-\nu t}}. \end{aligned}$$

The boundary values of functions s', x', are:

$s'(0) = -\nu s_0$, $s'(\infty) = 0$;

$x'(0) = -\nu x_0 \ln x_0 > 0$, $x'(\infty) = 0$.

1c. The logarithmic change rates of functions s, x are given by (72), (69):

$$\begin{aligned} r_s &= (\ln s)' = \tfrac{s'}{s} = -\nu, \\ r_x &= (\ln x)' = x'/x = \ln {x_0}^{-\nu e^{-\nu t}}. \end{aligned}$$

For the boundary values of the logarithmic change rates of Gompertz growth/decay functions s, x we have:

$$\begin{aligned} r_s(0) &= r_s(\infty) = -\nu; \\ r_x(0) &= \ln(1/x_0)^{\nu},\ \ r_x(\infty) == 0. \end{aligned}$$

2a. The inflection point t^* of Gompertz growth function x is given by (77):

$$t^* = \ln\left(\ln \frac{1}{x_0}\right)^{\frac{1}{\nu}}.$$

The values of the growth/decay functions at inflection point t^* are, cf. (74), (78):

$$s(t^*) = \delta = \nu/k,\ \ x(t^*) = e^{-1}.$$

For the existence of inflection point in $[0, \infty)$, the necessary and sufficient condition is $s_0 > \delta$, resp.: $0 < x_0 < 1/e$.

2b. The lag time L is given by the ratio (81):

$$L = x(t^*)/x'(t^*) = 1/\nu.$$

Remarks on the logistic and Gompertz models. 1) The inflection point of the growing species X in the Gompertz model is lower than those in the logistic model, $1/e < 1/2$. As a consequence, the Gompertzian growth curve has a shorter lag time, resp. longer lag (ageing, mortality) time, than the logistic growth curve. In both models the growing species X reproduces by a doubling mechanism, being constrained by species S which declines with time until vanishing. The inhibiting decay mechanism of species S is different in the two growth-decay models. In the logistic case species S is consumed by X as nutritional (food) resource (S charges X); thereby X is the solely species using S. In contrast, in the Gompertz model species S serves as a catalyst for X; thereby S charges some "other" species as well. The catalytic vs. the resource-charging role of species S turns out to be decisive in the distinction of the two models. 2) Both the logistic and the Gompertz models make use of just one rate parameter, which is not so obvious in the Gompertz model. The parameter k in the Gompertz model participates only in the identity relation and its role there is to determine the value of s_0, resp. the limit value (one) of the upper asymptote of the growth function. Without loss of generality the parameter k can be set to one, se e.g. [32]. The decisive role of the rate parameter ν is noticed by many authors,

using for ν names such as "relative maturity rate", "mortality rate", etc.

IV. A NEW MODEL BASED ON A MODIFIED (HYBRID) GOMPERTZ-LIKE REACTION NETWORK

In this section we propose and mathematically analyse a growth-decay model induced by a reaction network that is close to Gompertz network (50) but borrows some features of the one-step exponential decay 1-SERD model.

Consider the following reaction network involving two species S and X:

$$S \xrightarrow{\nu} X, \quad S + X \xrightarrow{k} 2X + S, \tag{82}$$

wherein ν, k are positive rate parameters.

Denoting the mass-related quantitative (numerical) characteristics of species S, X, resp. by s, x, under the assumption of mass action kinetics, reaction network (82) induces the following dynamical system of two reaction equations:

$$s' = -\nu s, \quad x' = kxs + \nu s, \tag{83}$$

where ν, k are positive rate parameters.

Proposition 4. *If functions $s = s(t)$, $x = x(t)$ satisfy the system of ODE's (83) on $R^+ = [0, \infty)$, then the following identity relation holds true on R^+:*

$$\gamma s + \ln(x + 1/\gamma) = \ln(x_\infty + 1/\gamma), \tag{84}$$

wherein $\gamma = k/\nu$ and $x_\infty = x(\infty) = x(t)|_{t \longrightarrow \infty}$.

Proof: System (83) implies the relation:

$$\frac{s'}{\nu} + \frac{x'}{kx + \nu} = 0,$$

or

$$\gamma s' + \frac{x'}{x + \nu/k} = 0.$$

After integration, the above relation leads to the following identity

$$\gamma s + \ln(x + 1/\gamma) = \text{const} = c, \quad \gamma = k/\nu. \tag{85}$$

As in the classic Gompertz model, solution s to system (83) satisfies the autonomous ordinary differential equation $s' = -\nu s$, with solution (13) (or (52)). Hence function s is monotone decreasing, approaching zero: $s(\infty) = s_\infty = 0$. Passing to limit $t \longrightarrow \infty$ in identity (85), using $s(\infty) = 0$, we obtain const $= c = \ln(x(\infty) + 1/\gamma)$, hence (84). ■

Identity (84) suggests that while function s monotonically decays, function x monotonically grows remaining bounded from above by $x(\infty)$, so the line $x = x(\infty)$ is a horizontal asymptote for the growth function $x = x(t)$.

We have the freedom to choose the boundary value $x(\infty)$ for x at $t = \infty$; so, as done traditionally, we set

$$x_\infty = x(\infty) = 1.$$

Using boundary values $s_\infty = 0$, $x_\infty = 1$, we obtain relation (84) in the form

$$\gamma s + \ln(x + 1/\gamma) = \ln(1 + 1/\gamma),$$

or, using notation $\delta == 1/\gamma = \nu/k$:

$$\gamma s + \ln(x + \delta) = \ln(1 + \delta),$$

equivalently

$$\gamma s + \ln \frac{x + \delta}{1 + \delta} = 0. \tag{86}$$

Remark. Introducing the "deviated" growth function x_δ:

$$x_\delta = \frac{x + \delta}{1 + \delta},$$

in relation (86), we obtain $\gamma s + \ln x_\delta = 0$, which formally matches the corresponding identity (57) for the classic Gompertz model: $\gamma s + \ln x = 0$. This similarity takes place for a number of results to follow. In fact it is possible to rewrite most of the classical Gompertz results from Section 3 replacing function x by x_δ, then performing a reverse transformation: $x = x_\delta(1 + \delta) - \delta$.

From relation (86) we can obtain expressions for s in terms of x and for x in terms of s. Here are given some practically useful relations:

$$s = \delta \ln \frac{1 + \delta}{x + \delta} = \ln \left(\frac{x + \delta}{1 + \delta} \right)^{-\delta}, \tag{87}$$

$$\gamma s = \ln\left(\frac{1+\delta}{x+\delta}\right), \tag{88}$$

$$e^{\gamma s} = \frac{1+\delta}{x+\delta}, \tag{89}$$

$$x = (1+\delta)e^{-\gamma s} - \delta. \tag{90}$$

In the special case $t = 0$ we have the following relations for the initial pair (s_0, x_0), assuring the limit condition $x_\infty = 1$:

$$s_0 = \ln\left(\frac{1+\delta}{x_0+\delta}\right)^{\delta} = \ln\left(\frac{x_0+\delta}{1+\delta}\right)^{-\delta}; \tag{91}$$

$$\gamma s_0 = \ln\left(\frac{1+\delta}{x_0+\delta}\right); \tag{92}$$

$$e^{\gamma s_0} = \frac{1+\delta}{x_0+\delta}; \tag{93}$$

$$x_0 = (1+\delta)e^{-\gamma s_0} - \delta. \tag{94}$$

Substituting s from (87) in the differential equation for growth function x in dynamical system (83), leads to the following autonomous differential equation:

$$\begin{aligned} x' &= kxs + \nu s = k(x+\delta)s \\ &= k(x+\delta)\ln\left(\tfrac{1+\delta}{x+\delta}\right)^{\delta}. \end{aligned} \tag{95}$$

To deduce an explicit solution for growth function x, we first use relation (89) to write:

$$\frac{1+\delta}{x+\delta} = e^{\gamma s} = e^{\gamma s_0 e^{-\nu t}} = (e^{\gamma s_0})^{e^{-\nu t}}. \tag{96}$$

We then substitute the term $e^{\gamma s_0}$ in (96), using the expression (93), to get

$$\frac{1+\delta}{x+\delta} = (e^{\gamma s_0})^{e^{-\nu t}} = \left(\frac{1+\delta}{x_0+\delta}\right)^{e^{-\nu t}}. \tag{97}$$

Relation (97) implies an explicit expression for growth function $x = x(t)$:

$$x(t) = (1+\delta)\left(\frac{x_0+\delta}{1+\delta}\right)^{e^{-\nu t}} - \delta. \tag{98}$$

Based on the above considerations, we formulate the following

Proposition 5. *Let initial value tuple (s_0, x_0) be such that*

$$\begin{aligned} &0 < x_0 < 1, \;\; s_0 = \ln\left(\tfrac{1+\delta}{x_0+\delta}\right)^{\delta} > 0, \\ &\delta = 1/\gamma = \nu/k, \end{aligned} \tag{99}$$

then

i) solution (s, x) to initial value problem (83)–(99) satisfy on $R^+ = [0, \infty)$ relation (84); in particular relations (87), (90):

$$s = \ln\left(\frac{x+\delta}{1+\delta}\right)^{-\delta};$$
$$x = (1+\delta)e^{-\gamma s} - \delta.$$

ii) the growth function x satisfies the autonomous ordinary differential equation (95);

$$x' = k(x+\delta)\ln\left(\frac{1+\delta}{x+\delta}\right)^{\delta};$$

iii) the solution x to equation (95) with initial value $x(0) = x_0$, resp. system (83)–(99) can be presented in the explicit form (98):

$$x(t) = (1+\delta)\left(\frac{x_0+\delta}{1+\delta}\right)^{e^{-\nu t}} - \delta.$$

Change rates. To obtain an explicit algebraic expression for the absolute growth rate of species X we use expressions (95) and (98) to obtain:

$$\begin{aligned} x' &= k(x+\delta)\ln\left(\tfrac{1+\delta}{x+\delta}\right)^{\delta} \\ &= k(1+\delta)\left(\tfrac{x_0+\delta}{1+\delta}\right)^{e^{-\nu t}} \ln\left(\tfrac{1+\delta}{x_0+\delta}\right)^{e^{-\nu t}}. \end{aligned} \tag{100}$$

For the boundary values of function x' we have:

$$\begin{aligned} x'(0) &= kx_0s_0 = x_0(-\nu\ln x_0) > 0 \\ x'(\infty) &= kx(\infty)s(\infty) = 0. \end{aligned} \tag{101}$$

For the relative (logarithmic) growth rate $r_x = r_x(t)$ of growth function x we obtain:

$$\begin{aligned} r_x &= (\ln x)' = x'/x \\ &= -\nu\ \ln x_0\ e^{-\nu t} = \ln {x_0}^{-\nu e^{-\nu t}}. \end{aligned} \tag{102}$$

For the boundary values of $r_x = x'/x$ we have:

$$\begin{aligned} r_x(0) &= -\nu \ln x_0\ e^0 = \ln(1/x_0)^\nu, \\ r_x(\infty) &= -\nu \ln x_\infty\ e^{-\infty} = 0. \end{aligned} \tag{103}$$

The expressions for the absolute and logarithmic change (decay) rates of decay species S are the same as those for the classic Gompertz model, cf. (71), (72).

Inflection points. To calculate the inflection points of the growth function x (if any) we need to obtain an expression for the second derivative x'' of x:

$$\begin{aligned} x'' &= (x')' = (ksx + \nu s)' = (ksx)' + (\nu s)' \\ &= k(s'x + sx') + \nu s' \\ &= k(-\nu sx + s(ksx + \nu s)) - \nu^2 s \\ &= ks(-\nu x + ksx + \nu s - \nu^2/k) \\ &= ks\left(ks(x + \nu/k) - \nu(x + \nu/k)\right) \\ &= ks(x + \delta)(ks - \nu) \\ &= k^2 s(x + \delta)(s - \delta). \end{aligned} \tag{104}$$

According to expression (104) equation $x''(t) = 0$ is equivalent to equation $s(t) - \delta = 0$, or $s(t) = \delta$. Let time instant t^* solve the latter equations, then

$$s_0 > s(t^*) = \delta \tag{105}$$

is a necessary condition for the existence of an inflection point. Indeed, if (105): $s_0 > \delta$, then the monotone decreasing function $s(t)$ equals to δ at time instant t^*: $s(t^*) = \delta$. In other words, for $s_0 > \delta$ then there exists time moment t^*, such that the pair $t^*, x(t^*)$ is an inflection point for growth function x, such that $s(t^*) = \delta$, resp. $x''(t^*) = 0$.

Expression (104) reduces the solution of equation $x''(t^*) = 0$ for t^* to equation

$$s(t^*) = \nu/k = \delta, \tag{106}$$

saying that the value of the decay function s at inflection time instant t^* is equal to the rate parameter ratio $\delta = \nu/k$.

Using (52), we have $s(t^*) = s_0 e^{-\nu t^*} = \delta$, hence

$$e^{-\nu t^*} = \delta/s_0 = 1/(\gamma s_0), \tag{107}$$

thus we obtain

$$t^* = (1/\nu)\ln(\gamma s_0) = \ln(\gamma s_0)^{\frac{1}{\nu}}. \tag{108}$$

Let us now "translate" formulae (105), (108) in terms of growth function x. Expressed via x_0, the inflection time instant (108) can be obtained when substituting γs_0 in (108) by $\ln((1+\delta)/(x_0+\delta))$:

$$t^* = \ln(\ln \frac{1+\delta}{x_0+\delta})^{\frac{1}{\nu}}. \tag{109}$$

Knowing the s-value $s(t^*) = \delta$, we compute the x-value $x(t^*)$ using expression (90):

$$\begin{aligned} x(t^*) &= (1+\delta)e^{-\gamma s(t^*)} - \delta \\ &= (1+\delta)e^{-\gamma\delta} - \delta \\ &= (1+\delta)e^{-1} - \delta \\ &= (1 - (e-1)\delta)/e, \end{aligned}$$

thus finally we have:

$$x(t^*) = \frac{1 - (e-1)\delta}{e}. \tag{110}$$

From (110) we obtain a necessary and sufficient condition for the existence of inflection:

$$\frac{1}{e} > x(t^*) = \frac{1 - (e-1)\delta}{e} > x_0 > 0. \tag{111}$$

Relation (111) implies a necessary condition for the existence of inflection: $x(t^*) > 0$, namely:

$$\delta < \frac{1}{e-1} = \overline{e} \approx 0.58197671, \tag{112}$$

resp.

$$\nu < \overline{e}\ k. \tag{113}$$

Using (111) we obtain a second necessary condition for the existence of inflection: $1/e > x(t^*) > x_0$, namely:

$$1 - (e-1)\delta > e x_0, \tag{114}$$

resp.

$$\delta < \frac{1-ex_0}{e-1} = \overline{e}(1-ex_0), \qquad (115)$$

resp.

$$\nu < \overline{e}(1-ex_0)k. \qquad (116)$$

Practically, the necessary and sufficient condition (111) for the existence of inflection point can be tested by verifying the two necessary conditions (112), (115), resp. (113), (116).

Inequality (112) implies the following restriction on the initial value x_0 for existence of inflection point:

$$x_0 < 1/e. \qquad (117)$$

Remarks. i) Restriction (117) says that for the existence of inflection initial value x_0 should be below the inflection value for the classical Gompertz model, i.e. $1/e$.

ii) Note that in the classic Gompertz case the growth function may have no inflection only when $x_0 > 1/e$. In contrast, the hybrid Gompertz growth function may have no inflection for any initial values $x_0 \in (0,1)$, even for initial values satisfying (117).

iii) Depending on the values of the rate parameters ν, k, the inflection point can be arbitrarily close to the classic Gompertz value $1/e$, as well as to initial value x_0 no matter how small x_0 is. In the latter case the inflection point can be arbitrarily close to zero (providing x_0 itself is sufficiently small). This possibility makes the shape of the graph of x extremely flexible, which makes a considerable difference with the classic Gompertz case. Under suitable choice of the initial conditions and rate parameters the hybrid model can be close to the one-step exponential decal model.

iv) Inequality (112) implies

$$\delta < \frac{1-ex_0}{e-1} < \frac{1}{e-1}. \qquad (118)$$

The "rough" inequality (118) can be used when x_0 is close to 0.

Lag time (lag phase). To compute the lag time of growth function x for the hybrid Gompertz model, we need the value of slope of function x at inflection time moment t^*, that is $x'(t^*)$. Denote the intersection of the tangent line through the inflection point $(t^*, x(t^*))$ with the abscissa and the asymptote $x = x_\infty$, resp. by $(t_a, 0)$ and $(t_b, 1)$. The width (length) of interval $[t_a, t^*]$ is by definition the lag time.

To compute the slope $x'(x^*)$ of growth function x at inflection time moment t^*, we substitute the value: $x^* = x(t^*)$ from (110), resp. $x^* + \delta = (1+\delta)/e$, in the expression for the slope x' to obtain:

$$\begin{aligned} x'(t^*) &= k(x^*+\delta)\ln\left(\tfrac{1+\delta}{x^*+\delta}\right)^{\delta} \\ &= \tfrac{k\delta}{e}(1-\delta)\ln\left(e\tfrac{1+\delta}{1+\delta}\right) \\ &= \tfrac{\nu}{e}(1-\delta). \end{aligned} \qquad (119)$$

As in the classical Gompertz case, we define the lag time (phase) L as the length of the segment on the abscissa between inflection moment t^* and the intersection point of the abscissa and the tangent with slope $x'(t*)$. Hence, for the lag time L we obtain:

$$L = \frac{x^*}{x'(t*)} = \frac{1}{\nu}\left(1 - \frac{e\delta}{1+\delta}\right). \qquad (120)$$

We summarize the obtained results as follows.

Proposition 6. *1. Solution pair (s,x) to initial value hybrid Gompertz problem (83), $(s(0) = s_0, x(0) = x_0)$, is characterized by the following properties:*

1a. The absolute change rate of species X is given by: (100):

$$x' = k(1+\delta)\left(\frac{x_0+\delta}{1+\delta}\right)^{e^{-\nu t}} \ln\left(\frac{1+\delta}{x_0+\delta}\right)^{e^{-\nu t}}.$$

1b. For the boundary values of function x' we have expression (101):

$$\begin{aligned} x'(0) &= kx_0s_0 = x_0(-\nu\ln x_0) > 0 \\ x'(\infty) &= kx(\infty)s(\infty) = 0. \end{aligned}$$

1c. The logarithmic change rate $r_x = r_x(t)$ of the hybrid Gompertz growth function x is given by expression (102):

$$r_x = (\ln x)' = x'/x = -\nu\ \ln x_0\ e^{-\nu t}.$$

For the boundary values of the logarithmic change rates of the hybrid Gompertz growth function x we have (103):

$$\begin{aligned} r_x(0) &= -\nu \ln x_0 \; e^0 = \ln(1/x_0)^\nu, \\ r_x(\infty) &= -\nu \ln x_\infty \; e^{-\infty} = 0. \end{aligned} \tag{121}$$

2a. The inflection time moment t^* of the hybrid Gompertz growth function x is given by (109):

$$t^* = \ln(\ln \frac{1+\delta}{x_0+\delta})^{\frac{1}{\nu}}.$$

The values of the growth/decay functions at inflection point t^* are (74): $s(t^*) = \delta = \nu/k$, resp. (110):

$$x(t^*) = \frac{1-(e-1)\delta}{e}.$$

The slope of the tangent line through the inflection point is given by (119):

$$x'(t^*) = \frac{\nu}{e}(1-\delta).$$

For the existence of inflection point in $[0,\infty)$, the necessary and sufficient condition is (111):

$$\frac{1}{e} > x(t^*) = \frac{1-(e-1)\delta}{e} > x_0 > 0.$$

2b. The lag time L is given by the ratio (120):

$$L = \frac{x^*}{x'(t*)} = \frac{1}{\nu}\left(1 - \frac{e\delta}{1+\delta}\right).$$

Finally, the following proposition holds true:

Proposition 7. *The hybrid Gompertz function (98) is a generalization of the classical Gompertz function (64).*

Proof: The classical Gompertz function (64) is obtained from the hybrid Gompertz function (98) for the special case $k \longrightarrow \infty$, resp. $\delta = \nu/k \longrightarrow 0$, while keeping the rate parameter ν fixed. ■

V. Concluding remarks

Biological growth functions are usually presented in the mathematical literature by means of their explicit expressions or as solutions to differential equations [11]–[18]. However, biological growth models are usually related to decay processes/functions, which becomes especially transparent when the models are based on reaction equations. Using chemical reaction network theory, one can easily observe close relations between various growth/decay processes, as well as between existing growth-decay models, e.g. classes of biochemical systems [25]–[27], [29]–[31].

In the present work we propose an elementary introduction in the reaction network approach based on mass action kinetics. To this end we discuss in some detail several familiar examples, such as the one- and two-step exponential (radioactive) decay, the logistic and the Gompertz models.

We focus on the simultaneous analysis of the growth and the decay functions using the identity relation between the two functions naturally induced by the reaction equations.

The power of the reaction network approach is fully revealed in Section 3 when applied to the analysis of the classical Gompertz model. There we propose a revision of the model based on the reaction network inducing the original Gompertz model, which we call "Gompertz reaction network" in honour of the author of the well-known growth model and his seminal paper [9].

Our final goal in this work is the modification of the Gompertz reaction network in a natural way, using fully the dynamical features of the one-step (first-order) exponential decay reaction. In this way we obtain a hybrid of the one-step exponential and the classic Gompertz model in a natural way, performing a small modification in the Gompertz reaction network. The growth function of the obtained new hybrid Gompertz-like model possesses one additional degree of freedom (one more rate parameter) and is thus more flexible when applied to modelling and numerical simulation of measurement and experimental

data sets. More specifically, the ordinate (height) of the inflection point of the hybrid model can largely vary, whereas the resp. height of the classic Gompertz model is fixed (at $1/e$). The presented generalization of the Gompertz model possesses some common features with the Richards model in direction of improved flexibility when simulating measurement data sets [24], [34].

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