



A note on the n -stage growth model. Overview

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Abstract. In this paper we study the one-sided Hausdorff approximation of the generalized cut function by sigmoidal general n -stage growth model. We show that under some conditions the model is useful insofar as the theory of sigmoidal functions is well developed. The estimates of the value of the best Hausdorff approximation obtained in this article can be used in practice as one possible additional

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criteria in "saturation" and "lag-time" study. As an illustrative example we consider the modelling of the growth of red abalone (*Haliotis Rufescens*) in Northern California. Numerical examples are presented using *CAS MATHEMATICA*.

Keywords: modified n -stage growth model, generalized cut function associated to the model, Hausdorff distance, upper and lower bounds

1 Introduction

Let us examine the following three-stage growth model



with two steps (k_1 and k_2) depending on the ratio of the growth parameters $\frac{k_1}{k_2}$.

For the mechanism the following system of ODEs is known [1]:

$$\begin{aligned} \frac{dA(t)}{dt} &= -k_1A(t), \\ \frac{dB(t)}{dt} &= k_1A(t) - k_2B(t), \\ \frac{dC(t)}{dt} &= k_2B(t), \\ A(0) &= A_0, \quad B(0) = 0, \quad C(0) = 0. \end{aligned} \tag{2}$$

Noticing that

$$\frac{dA(t)}{dt} + \frac{dB(t)}{dt} + \frac{dC(t)}{dt} = 0,$$

hence $A + B + C = A_0$, and at any time, we find

$$C(t) = A_0 - B(t) - A(t). \tag{3}$$

From the first equation of the system (2) we find

$$A(t) = A_0e^{-k_1t}. \tag{4}$$

The equation

$$\frac{dB(t)}{dt} + k_2 B(t) = k_1 A_0 e^{-k_1 t} \quad (5)$$

is Leibnitz's differential equation with the solution:

$$\begin{aligned} B(t) &= e^{-\int k_2 dt} \int_0^t k_1 A_0 e^{-k_1 t} e^{\int k_2 dt} dt + R e^{-\int k_2 dt} \\ &= e^{-k_2 t} k_1 A_0 \int_0^t e^{-k_1 t} e^{k_2 t} dt + R e^{-k_2 t} \\ &= e^{-k_2 t} k_1 A_0 \frac{1}{k_2 - k_1} \int_0^t d e^{(k_2 - k_1)t} + R e^{-k_2 t} \\ &= e^{-k_2 t} \frac{k_1 A_0}{k_2 - k_1} (e^{(k_2 - k_1)t} - 1) + R e^{-k_2 t} \\ &= \frac{k_1 A_0}{k_2 - k_1} (e^{-k_1 t} - e^{-k_2 t}) + R e^{-k_2 t}. \end{aligned}$$

For $t = 0$ we have $B(t = 0) = 0 = R$ and

$$B(t) = \frac{k_1 A_0}{k_2 - k_1} (e^{-k_1 t} - e^{-k_2 t}). \quad (6)$$

Hence we obtain the model

$$C(t) = A_0 \left(1 - \frac{k_1}{k_2 - k_1} (e^{-k_1 t} - e^{-k_2 t}) - e^{-k_1 t} \right) \quad (7)$$

For some details, see [2], [3].

We note that the equation (6) is the general expression for the decay of a radionuclide, formed another radionuclide [2] (Chapter 5).

In [4], the authors debated to the following modified model for the individual growth of marine invertebrates:

$$\tilde{C}(t) = A_0 \left(1 - \frac{k_1}{n} (e^{-k_1 t} - e^{-k_2 t}) - e^{-k_2 t} \right)$$

where $n = k_2 - k_1$, and $\frac{k_1}{k_2}$ is close to 1.

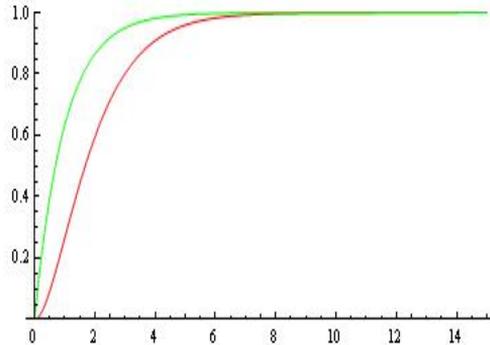


Figure 1: Three-stage growth model $\tilde{C}(t)$ (sigmoidal; red) for $n = k_2 - k_1$, $k_1 = 1$, $k_2 = 1.001$ and three-stage model $C(t)$ (first order; green) for $n = k_1 - k_2$, $k_1 = 1$, $k_2 = 2500$.

The model \tilde{C} predicts sigmoidal growth (see, Fig. 1), i.e. in a three-stage growth model, the shape is controlled by the ratio $\frac{k_1}{k_2}$ [5].

For 3D-surface plot for the three-stage mechanism in the range $n = k_2 - k_1$, or $n = k_1 - k_2$, see, Fig. 2 [5].

Without loosing of generality, for $A_0 = 1$ and $n = k_2 - k_1 > 0$, $\frac{k_1}{k_2} \rightarrow 1$ we consider the following family:

$$\tilde{C}(t) = 1 - \frac{k_1}{n} (e^{-k_1 t} - e^{-k_2 t}) - e^{-k_2 t}. \quad (8)$$

We find that the sigmoid (8) has an inflection at point:

$$t^* = \frac{1}{n} \ln \left(\frac{\left(-k_2^2 + \frac{k_1 k_2^2}{n} \right) n}{k_1^3} \right).$$

Definition 1. *The associate to the (8) cut function \tilde{C}^* is defined by*

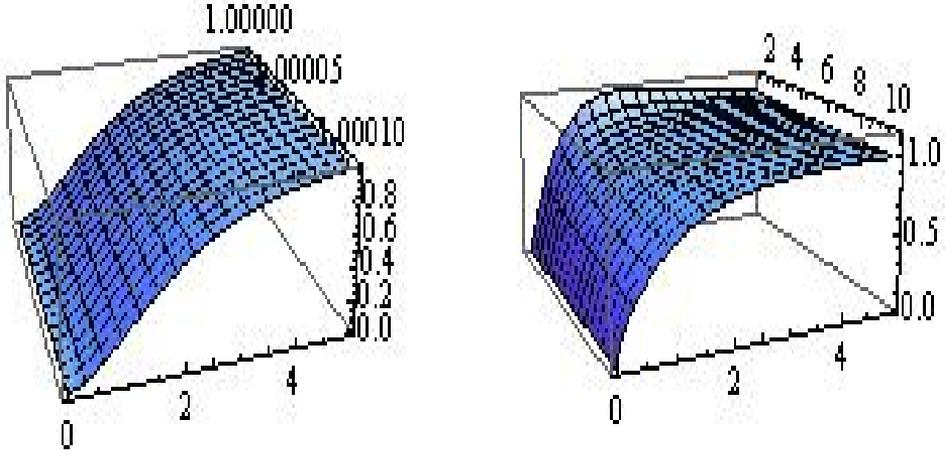


Figure 2: 3D–surface plot for the three–stage mechanism in the range $n = k_2 - k_1$, or $n = k_1 - k_2$ [5].

[5]

$$\tilde{C}^*(t) = \begin{cases} 0, & \text{if } t < t_1, \\ \tilde{C}'(t^*)(t - t^*) + \tilde{C}(t^*), & \text{if } t_1 \leq t < t_2, \\ 1, & \text{if } t \geq t_2. \end{cases} \quad (9)$$

The straight line $y = \tilde{C}'(t^*)(t - t^*) + \tilde{C}(t^*)$ crosses the lines $y = 0$ and $y = 1$ at the points t_1 and t_2 .

Definition 2. [6] *The one–sided Hausdorff distance $\vec{\rho}(f, g)$ between two interval functions f, g on $\Omega \subseteq \mathbb{R}$, is the one–sided Hausdorff distance between their completed graphs $\mathcal{F}(f)$ and $\mathcal{F}(g)$ considered as closed subsets of $\Omega \times \mathbb{R}$. More precisely,*

$$\vec{\rho}(f, g) = \sup_{B \in \mathcal{F}(g)} \inf_{A \in \mathcal{F}(f)} \|A - B\|,$$

where $\|\cdot\|$ is a norm in \mathbb{R}^2 .

We recall that completed graph of f is the closure of the graph of f as a subset of $\Omega \times \mathbb{R}$. If the graph of an interval function f equals $\mathcal{F}(f)$, then the f is called S-continuous.

The Hausdorff distance $\rho(f, g) = \max\{\vec{\rho}(f, g), \vec{\rho}(g, f)\}$ defines a metric in the set of the S-continuous interval functions [7]–[10].

The one-sided Hausdorff distance d between the functions (8) and (9) satisfies the relation

$$\tilde{C}(t_2 + d) = 1 - d. \quad (10)$$

The following theorem gives upper and lower bounds for d

Theorem A [5]. *Let*

$$\begin{aligned} p &= -e^{-k_2 t_2} - \frac{k_1}{n} e^{-k_1 t_2} + \frac{k_1}{n} e^{-k_2 t_2}, \\ q &= 1 + k_2 e^{-k_2 t_2} + \frac{k_1^2}{n} e^{-k_1 t_2} - \frac{k_1 k_2}{n} e^{-k_2 t_2}, \\ r &= -2 \frac{q}{p}; \quad n = k_2 - k_1 > 0; \quad \frac{k_1}{k_2} \rightarrow 1; \quad \frac{2k_1 - k_2}{k_1} < e^{t_2(k_2 - k_1)}. \end{aligned}$$

For the one-sided Hausdorff distance d between $\tilde{C}^(t)$ and the sigmoidal function (8) the following inequalities hold for: $r > e^2$*

$$d_l = \frac{1}{r} < d < \frac{\ln r}{r} = d_r. \quad (11)$$

The model (8) for $k_1 = 1$, $k_2 = 1.01$, $t^* = 0.985033$, $t_1 = 0.27045$, $t_2 = 2.97525$ is visualized on Fig. 3.

From the nonlinear equation (10) and inequalities (11) we have: $d = 0.174444$, $d_l = 0.0865764$, $d_r = 0.211829$.

The estimates of the value of the best Hausdorff approximation can be used in practice as one possible additional criterion in "saturation" study.

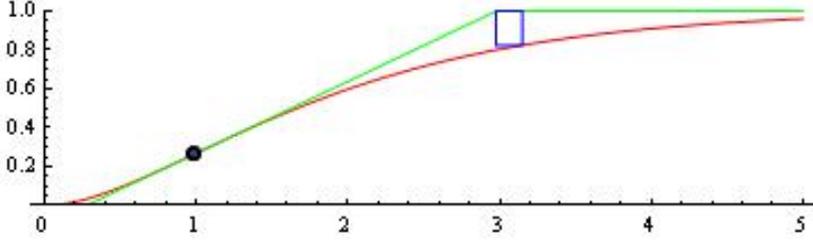


Figure 3: The cut function $\tilde{C}^*(t)$ and the sigmoidal function $\tilde{C}(t)$ with $k_1 = 1$, $k_2 = 1.01$, $t^* = 0.985033$, $t_1 = 0.27045$, $t_2 = 2.97525$; H-distance $d = 0.174444$, $d_l = 0.0865764$, $d_r = 0.211829$.

2 Main Results

2.1 The four-stage growth model

Let us examine the following four-stage growth model



For the mechanism the following system of ODEs is known:

$$\begin{aligned} \frac{dA(t)}{dt} &= -k_1 A(t), \\ \frac{dB(t)}{dt} &= k_1 A(t) - k_2 B(t), \\ \frac{dC(t)}{dt} &= k_2 B(t) - k_3 C(t), \\ \frac{dD(t)}{dt} &= k_3 C(t), \\ A(0) &= A_0, \quad B(0) = 0, \quad C(0) = 0, \quad D(0) = 0. \end{aligned} \quad (13)$$

Noticing that

$$\frac{dA(t)}{dt} + \frac{dB(t)}{dt} + \frac{dC(t)}{dt} + \frac{dD(t)}{dt} = 0,$$

hence $A + B + C + D = A_0$, and at any time, we find

$$D(t) = A_0 - C(t) - B(t) - A(t). \quad (14)$$

Calculate $C(t)$, assuming that $C(0) = 0$

$$\begin{aligned} C(t) &= e^{-\int k_3 dt} \int_0^t \frac{k_1 k_2 A_0}{k_2 - k_1} (e^{-k_1 t} - e^{-k_2 t}) e^{\int k_3 dt} dt \\ &= e^{-k_3 t} \frac{k_1 k_2 A_0}{k_2 - k_1} \int_0^t (e^{-k_1 t} - e^{-k_2 t}) e^{k_3 t} dt \\ &= e^{-k_3 t} \frac{k_1 k_2 A_0}{k_2 - k_1} \left(\int_0^t e^{(k_3 - k_1)t} dt - \int_0^t e^{(k_3 - k_2)t} dt \right) \\ &= e^{-k_3 t} \frac{k_1 k_2 A_0}{k_2 - k_1} \left(\frac{1}{k_3 - k_1} \int_0^t de^{(k_3 - k_1)t} - \frac{1}{k_3 - k_2} \int_0^t de^{(k_3 - k_2)t} \right) \quad (15) \\ &= e^{-k_3 t} \frac{k_1 k_2 A_0}{k_2 - k_1} \left(\frac{e^{(k_3 - k_1)t}}{k_3 - k_1} - \frac{1}{k_3 - k_1} - \frac{e^{(k_3 - k_2)t}}{k_3 - k_2} + \frac{1}{k_3 - k_2} \right) \\ &= k_1 k_2 A_0 \left(\frac{e^{-k_1 t}}{(k_2 - k_1)(k_3 - k_1)} + \frac{e^{-k_2 t}}{(k_1 - k_2)(k_3 - k_2)} + \frac{e^{-k_3 t}}{(k_1 - k_3)(k_2 - k_3)} \right). \end{aligned}$$

From (4), (6) and (15) we find

$$\begin{aligned} D(t) &= A_0 \left(1 - \frac{k_1}{k_2 - k_1} (e^{-k_1 t} - e^{-k_2 t}) - \right. \\ &\quad \left. k_1 k_2 \left(\frac{e^{-k_1 t}}{(k_2 - k_1)(k_3 - k_1)} + \frac{e^{-k_2 t}}{(k_1 - k_2)(k_3 - k_2)} + \frac{e^{-k_3 t}}{(k_1 - k_3)(k_2 - k_3)} \right) - e^{-k_1 t} \right). \quad (16) \end{aligned}$$

Without loosing of generality, for $A_0 = 1$ and $k_3 > k_2 > k_1 > 0$, $\frac{k_3}{k_1} \rightarrow 1$, $\frac{k_3}{k_2} \rightarrow 1$ we consider the following family:

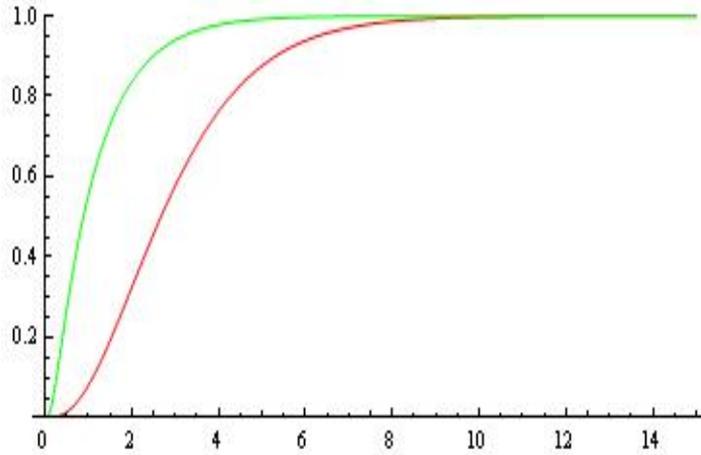


Figure 4: Four-stage growth model $\tilde{D}(t)$ (sigmoidal; red) for $k_1 = 1$, $k_2 = 1.001$, $k_3 = 1.002$ and $\tilde{D}(t)$ (first order; green) for $k_1 = 1$, $k_2 = 10$, $k_3 = 12$.

$$\tilde{D}(t) = 1 - \frac{k_1}{k_2 - k_1} (e^{-k_1 t} - e^{-k_2 t}) - k_1 k_2 \left(\frac{e^{-k_1 t}}{(k_2 - k_1)(k_3 - k_1)} + \frac{e^{-k_2 t}}{(k_1 - k_2)(k_3 - k_2)} + \frac{e^{-k_3 t}}{(k_1 - k_3)(k_2 - k_3)} \right) - e^{-k_1 t}. \quad (17)$$

The model \tilde{D} predicts sigmoidal growth (see, Fig. 4), i.e. in a four-stage growth model, the shape is controlled by the ratio $\frac{k_3}{k_1}$ and ratio $\frac{k_3}{k_2}$.

Let the sigmoid (17) has an inflection point t^* .

Consider the following associate to the (17) cut function \tilde{D}^*

$$\tilde{D}^*(t) = \begin{cases} 0, & \text{if } t < t_1, \\ \tilde{D}'(t^*)(t - t^*) + \tilde{D}(t^*), & \text{if } t_1 \leq t < t_2, \\ 1, & \text{if } t \geq t_2. \end{cases} \quad (18)$$

The straight line $y = \tilde{D}'(t^*)(t - t^*) + \tilde{D}(t^*)$ crosses the lines $y = 0$ and $y = 1$ at the points t_1 and t_2 .

The one-sided Hausdorff distance d between the functions (17) and (18) satisfies the relation

$$\tilde{D}(t_2 + d) = 1 - d. \quad (19)$$

The following theorem gives upper and lower bounds for d

Theorem B. Let

$$\begin{aligned} p &= -e^{-k_1 t_2} - \frac{k_1}{k_2 - k_1} (e^{-k_1 t_2} - e^{-k_2 t_2}) - \\ &\quad k_1 k_2 \left(\frac{e^{-k_1 t_2}}{(k_2 - k_1)(k_3 - k_1)} + \frac{e^{-k_2 t_2}}{(k_1 - k_2)(k_3 - k_2)} + \frac{e^{-k_3 t_2}}{(k_1 - k_3)(k_2 - k_3)} \right), \\ q &= 1 + e^{-k_1 t_2} k_1 + \frac{k_1^2}{k_2 - k_1} e^{-k_1 t_2} - \frac{k_1 k_2}{k_2 - k_1} e^{-k_2 t_2} + \\ &\quad k_1 k_2 \left(\frac{e^{-k_1 t_2} k_1}{(k_2 - k_1)(k_3 - k_1)} + \frac{e^{-k_2 t_2} k_2}{(k_1 - k_2)(k_3 - k_2)} + \frac{e^{-k_3 t_2} k_3}{(k_1 - k_3)(k_2 - k_3)} \right), \\ r &= -2\frac{q}{p}; \quad k_3 > k_2 > k_1 > 0, \quad \frac{k_3}{k_1} \rightarrow 1, \quad \frac{k_3}{k_2} \rightarrow 1. \end{aligned} \quad (20)$$

For the one-sided Hausdorff distance d between $\tilde{D}^*(t)$ and the sigmoidal function (17) the following inequalities hold for: $r > e^2$

$$d_l = \frac{1}{r} < d < \frac{\ln r}{r} = d_r. \quad (21)$$

Proof. Let us examine the function:

$$F(d) = \tilde{D}(t_2 + d) - 1 + d. \quad (22)$$

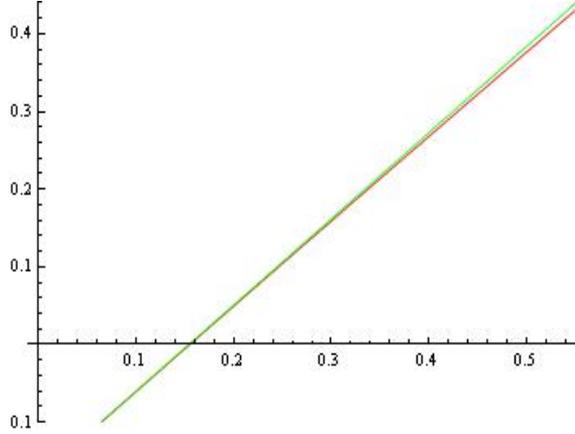


Figure 5: The functions $F(d)$ and $G(d)$ for $k_1 = 1; k_2 = 1.001; k_3 = 1.002$.

From $F'(d) > 0$ we conclude that function F is increasing.

Consider the function

$$G(d) = p + qd. \quad (23)$$

From Taylor expansion we obtain $G(d) - F(d) = O(d^2)$.

Hence $G(d)$ approximates $F(d)$ with $d \rightarrow 0$ as $O(d^2)$ (see Fig. 5).

In addition $G'(d) > 0$.

From the conditions of the theorem, we see that $p < 0$ and $q > 0$ (for some details, see [5]) and $G(d_l) < 0$, $G(d_r) > 0$.

This completes the proof of the theorem.

The model (17) for $k_1 = 1$, $k_2 = 1.001$, $k_3 = 1.002$, $t^* = 1.998$, $t_1 = 0.80467$, $t_2 = 4.4955$ is visualized on Fig. 5.

From the nonlinear equation (19) and inequalities (21) we have: $d = 0.15669$, $d_l = 0.0772965$, $d_r = 0.197887$.

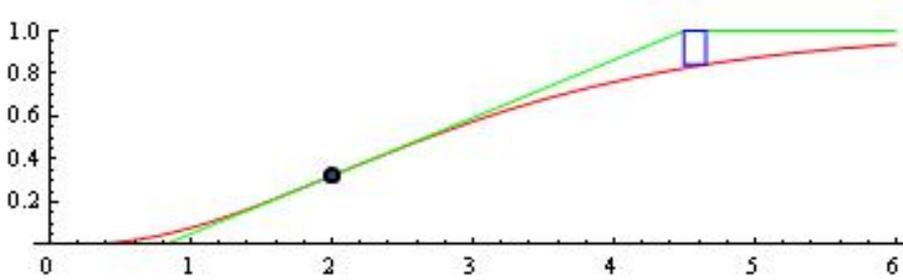


Figure 6: The cut function $\tilde{D}^*(t)$ and the sigmoidal function $\tilde{D}(t)$ with $k_1 = 1$, $k_2 = 1.001$, $k_3 = 1.002$, $t^* = 1.998$, $t_1 = 0.80467$, $t_2 = 4.4955$; H- distance $d = 0.15669$, $d_l = 0.0772965$, $d_r = 0.197887$.

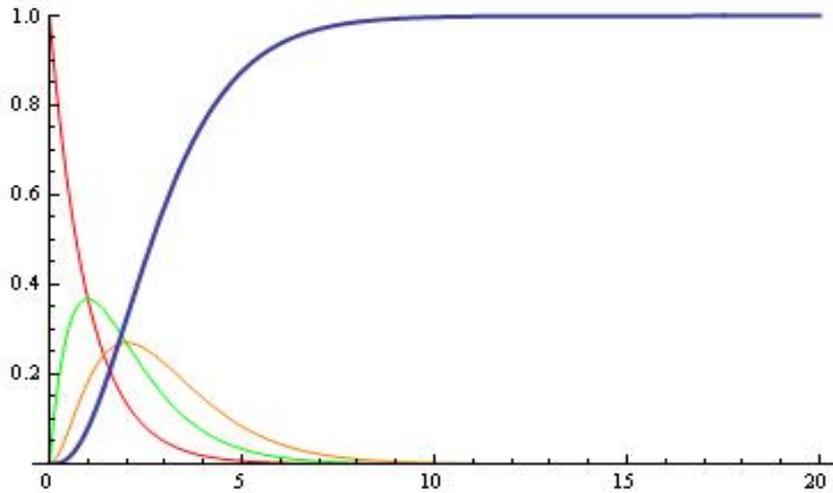


Figure 7: The solution of the system of ODEs (13): $A(t)$ (red), $B(t)$ (green), $C(t)$ (orange) and $D(t)$ (sigmoid; thick) for $k_1 = 1$, $k_2 = 1.001$, $k_3 = 1.002$.

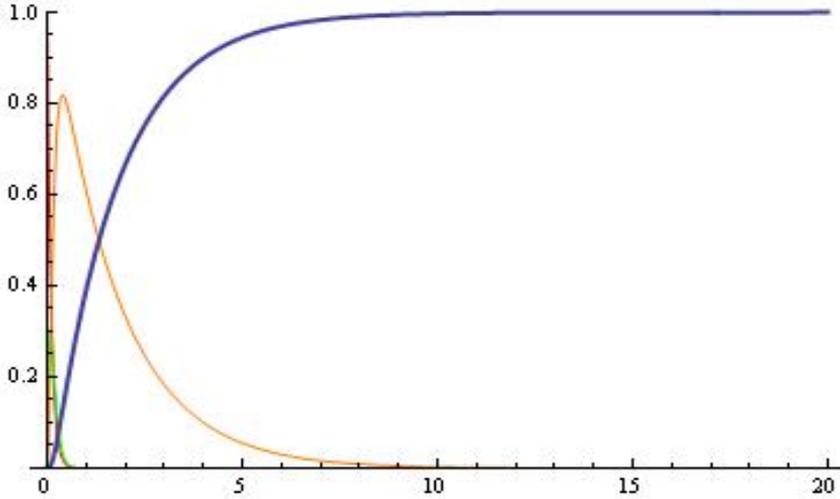


Figure 8: The solution of the system of ODEs (13): $A(t)$ (red), $B(t)$ (green), $C(t)$ (orange) and $D(t)$ (first order; inflection point $t^* = 1.00592 \times 10^{-16} \approx 0$; thick) for $k_1 = 10$, $k_2 = 15$, $k_3 = 0.6$.

The solution of the system of ODEs (13) with $k_1 = 1$, $k_2 = 1.001$, $k_3 = 1.002$ and $A(0) = 1$, $B(0) = 0$, $C(0) = 0$, $D(0) = 0$ is plotted on Fig. 7.

In a strongly disturbed order of the reaction constants k_i , for example $k_1 = 10$, $k_2 = 15$, $k_3 = 0.6$, the solution of the ODEs is depicted in Fig. 8.

Growth curves are found in a wide range of disciplines, such as biology, chemistry and medical science.

Estimating the lag time in the growth process is a practically important problem, as it may indicate a successful therapy for a number of diseases.

The curve $\tilde{C}(t)$ is typically divided into the lag phase, the growth phase, and the plateau phase.

The inflection time t^* is when the growth rate reaches its maximum. The lag time is then typically estimated by extending the tangent at

t^* down to the time axis.

Nevertheless, any sigmoid function can be good illustration for the concept of lag time [11].

2.2 The general case

Let us examine the general case



For the mechanism the following system of ODEs is known:

$$\begin{aligned} \frac{dN_1(t)}{dt} &= -k_1 N_1(t), \\ \frac{dN_2(t)}{dt} &= k_1 N_1(t) - k_2 N_2(t), \\ \cdots & \\ \frac{dN_{n-1}(t)}{dt} &= k_{n-2} N_{n-2}(t) - k_{n-1} N_{n-1}(t), \\ \frac{dN_n(t)}{dt} &= k_{n-1} N_{n-1}(t). \end{aligned} \quad (25)$$

Let $N_1(0) = A_0 = 1$; $N_2(0) = \cdots = N_{n-1}(0) = N_n(0) = 0$.

Noticing that

$$\frac{dN_1(t)}{dt} + \frac{dN_2(t)}{dt} + \cdots + \frac{dN_{n-1}(t)}{dt} + \frac{dN_n(t)}{dt} = 0,$$

hence $N_1 + N_2 + \cdots + N_{n-1} + N_n = A_0 = 1$, and at any time, we find

$$N_n(t) = 1 - \sum_{i=1}^{n-1} N_i(t)$$

or

$$N_n(t) = 1 - \sum_{i=2}^{n-1} N_i(t) - e^{-k_1 t}. \quad (26)$$

The solutions $N_i(t)$; $i = 2, 3, \dots, n - 1$ can be generated by the formula of Bateman [3]:

$$N_l(t) = k_1 k_2 \dots k_{l-1} \sum_{i=1}^l W_i e^{-k_i t}; \quad l = 2, 3, \dots, n - 1 \quad (27)$$

where

$$W_i = \prod_{\substack{j=1 \\ j \neq i}}^l \frac{1}{k_j - k_i}.$$

3 Numerical example.

We examine the following data. (The small data for modeling the growth of red abalone is shown in Table 1. For more details, see [12]).

The model $\tilde{D}(t)$ (17) based on the data of Table 1 for the estimated parameters:

$$A_0 = 179.6; \quad k_1 = 0.575; \quad k_2 = 0.58; \quad k_3 = 0.593622$$

is plotted on Fig. 9.

4 Concluding Remarks

The model (26) has a certain right of existence insofar as the theory of sigmoidal functions is well developed.

The estimates of the value of the best Hausdorff approximation obtained in this article can be used in practice as one possible additional criterion in "saturation" study.

<i>Age</i>	<i>Length(mm)</i>
1	16.1
2	33.9
3	54.3
4	76.2
5	97.8
6	117.1
7	133.3
8	146.5
9	157.2
10	166
11	173.3
12	179.6

Table 1: Data for modeling the growth of red abalone *Haliotis Rufescens* in Northern California [12]

For some approximation, computational and modelling aspects, see [13]–[40].

The results obtained in this paper can be used when controlling growth in Software Reliability Models, see [41]–[44].

Based on the methodology proposed in the present note, the reader may formulate the corresponding approximation problems for the general model $N_n(t)$ (26) on his/her own.

Acknowledgment

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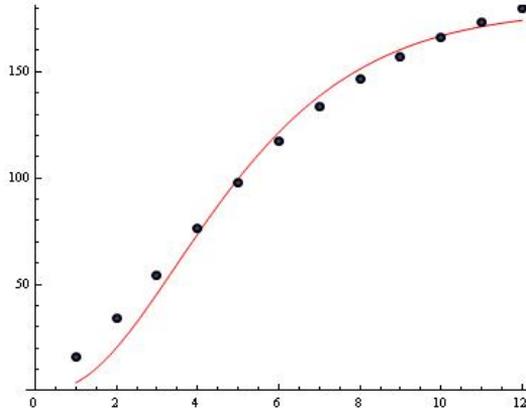


Figure 9: The model $\tilde{D}(t)$

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