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Sigmoidal Functions: Some Computational and Modelling Aspects [1]

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Dedicated to the 210th anniversary of the birth of P.-F. Verhulst

Abstract

We focus on some computational, modelling and approximation issues related to the logistic sigmoidal function and to Heaviside step function. The Hausdorff approximation of the Heaviside interval step function by sigmoidal functions is discussed from various computational and modelling aspects. Some relations between Verhulst model and certain biochemical reaction equations are discussed and analyzed. Numerical examples are presented using CAS *Mathematica*.

Keywords. Interval functions, Heaviside step function, Approximation, Sigmoidal functions.

1 Introduction

Many biological dynamic processes, such as certain enzyme kinetic and population growth processes, develop almost step-wise [9], [13]. Such processes are usually described or approximated by smooth sigmoidal functions; such functions are widely used in the theory of neural networks [3], [4]. Step-wise interval functions are a special class of sigmoidal functions; such functions

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are "almost" continuous, or Hausdorff continuous (H-continuous) [2]. Depending on the particular modelling situation one may decide to use either continuous or H-continous (step-wise) functions. Moreover, in many cases both types of modelling tools can be used interchangeably. This motivates us to study the closeness of both classes of functions. To substitute a sigmoidal function by a step function (or conversely) we need to know the approximation error between the two functions. A natural metric used in such a situation is the Hausdorff metric between the graphs of the functions. To this end we recall some basic results concerning the class of interval Hausdorff continuous functions and the related concept of Hausdorff approximation. We then focus on classes of logistic sigmoidal functions which are solutions of the Verhulst population model. We demonstrate that Verhulst model arises from simple autocatalytic (bio)chemical reactions and thus can be considered as special case of a biochemical reproduction reaction mechanism. The latter implies a more general model that permits the formulation of some important modelling and computational problems including nonautonomous, impulsive and delay DE.

In section 2 we consider sigmoidal and step functions arising from biological applications. The Hausdorff distance between the Heaviside step function and the sigmoidal Verhulst function is discussed. In section 3 we discuss certain kinetic mechanisms yielding Verhulst model via the mass action law. We show that the Verhulst model arises from some simple autocatalytic (bio)chemical reactions.

2 Sigmoidal and step functions

2.1 Hausdorff continuity

The concept of Hausdorff continuity (H-continuity) generalizes the familiar concept of continuity so that essential properties of the usual continuous real functions remain present. It is possible to extend the algebraic operations on the set of continuous real functions $C(\Omega)$ to the set $\mathbb{H}(\Omega)$ of H-continuous functions in such a way that the set $\mathbb{H}(\Omega)$ becomes a commutative ring and a linear space with respect to the extended operations [2]. In this work we restrict ourselves to functions of one real variable, that is real functions defined on a subset $\Omega \subseteq \mathbb{R}$.

2.2 Step functions

For $r \in \mathbb{R}$ denote by $h_r \in \mathbb{H}(\mathbb{R})$ the (interval) Heaviside step function given by

$$h_r(t) = \begin{cases} 0, & \text{if} \quad t < r, \\ [0,1], & \text{if} \quad t = r, \\ 1, & \text{if} \quad t > r, \end{cases} \tag{1}$$

cf. Fig. 1. For $r = 0$ we obtain the basic Heaviside step function

$$h_0(t) = \begin{cases} 0, & \text{if} \quad t < 0, \\ [0,1], & \text{if} \quad t = 0, \\ 1, & \text{if} \quad t > 0. \end{cases} \tag{2}$$

Functions (1)–(2) are examples sigmoidal functions. A sigmoidal function on $\mathbb{R}$ with a range $[a, b]$ is defined as a monotone function $s(t) : \mathbb{R} \to [a, b]$ such that $\lim_{t\to-\infty} s(t) = a$, $\lim_{t\to\infty} s(t) = b$.

2.3 Sigmoidal cut functions

One may consider continuous (or even smooth) or discontinous sigmoidal functions. Within the class of H-continuous interval functions, the Heaviside step function is a particular case of sigmoidal function. An example of a continuous sigmoidal function is the "cut function" defined as

$$c_{[a,b]}(t) = \begin{cases} 0, & \text{if} \quad t \le a, \\ (t-a)/(b-a), & \text{if} \quad a < t < b, \\ 1, & \text{if} \quad t \ge b. \end{cases} \tag{3}$$

The cut function (3) is visualized on Fig. 2.

2.4 Sums of sigmoidal functions

For a given vector $r = (r_1, r_2, ..., r_k) \in \mathbb{R}^k$, such that $r_1 < r_2 < ... < r_k$, and a vector $\alpha = (\alpha_1, \alpha_2, ..., \alpha_k) \in \mathbb{R}^k$ denote

$$H(r, \alpha; t) = \Sigma_{i=1}^{k} \alpha_i h_{r_i}(t). \tag{4}$$

Function (4) is a step function with k steps (jumps). Using suitable values for r_k and α_k one can represent a histogram, such as the one of Fig.

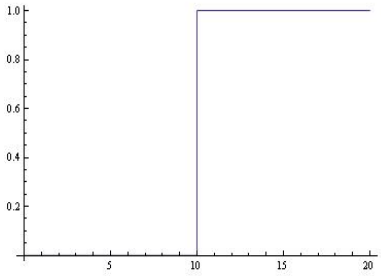

Figure 1: A step function (1) with jump at $r = 10$

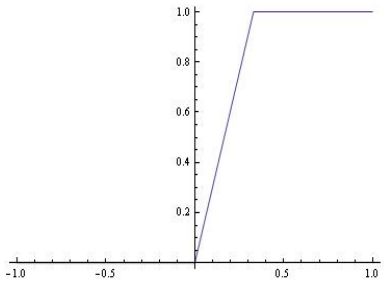

Figure 2: Cut function

3, as a sum of step functions of the form (4); in that case we usually have $r_k = r_1 + hi, i = 1, ..., k$ and $\Sigma_{i=1}^{k} \alpha_i = 0$. Similarly, one can construct sums of other suitably shifted sigmoidal functions.

2.5 Hausdorff distance

Let us recall that the Hausdorff distance (H-distance) $\rho(f, g)$ between two functions $f, g \in \mathbb{H}(\Omega)$ for $\Omega \subseteq \mathbb{R}$ is defined as the distance between their completed graphs $F(f)$ and $F(g)$ considered as closed subsets of $\mathbb{R}^2$ [7], [14]. More precisely,

$$\rho(f, g) = \max\{ \sup_{A \in F(f)} \inf_{B \in F(g)} ||A - B||, \sup_{B \in F(g)} \inf_{A \in F(f)} ||A - B|| \}, \quad (5)$$

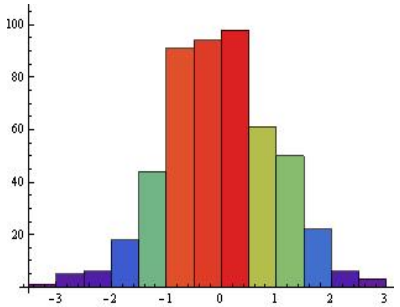

Figure 3: A histogram (from wikipedia)

wherein $||.||$ is a norm in $\mathbb{R}^2$. According to (5) the H-distance $\rho(f,g)$ between two functions $f, g \in \mathbb{H}(\Omega)$ for $\Omega \subseteq \mathbb{R}$ makes use of the maximum norm in $\mathbb{R}^2$ so that the distance between the points $A = (t_A, x_A)$, $B = (t_B, x_B)$ in R^2 is given by $||A - B|| = \max(|t_A - t_B|, |x_A - x_B|)$.

2.6 The logistic sigmoidal function

Sigmoidal functions find multiple applications to neural networks and cell growth population models [4], [9].

Several practically important families of smooth sigmoidal functions arise from population dynamics. A classical example is the Verhulst population growth model to be discussed below. Verhulst model makes an extensive use of the "logistic" sigmoidal function

$$s_0(t) = \frac{a}{1 + e^{-kt}}, \tag{6}$$

see Fig. 4. We next focus on the approximation of the Heaviside step function (2) by logistic functions of the form (6) in Hausdorff distance.

2.7 Approximation issues

In what follows we shall estimate the H-distance (5) between a step function and a logistic sigmoidal function. W. l. g. we can consider the Heaviside step function $f = ah_0$ and the logistic sigmoidal function (6): $g = s_0$. As visualized on Fig. 5, the H-distance $d = \rho(f,g) = \rho(ah_0, s_0)$ between

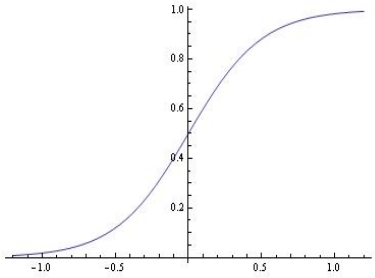

Figure 4: Logistic sigmoidal function (6)

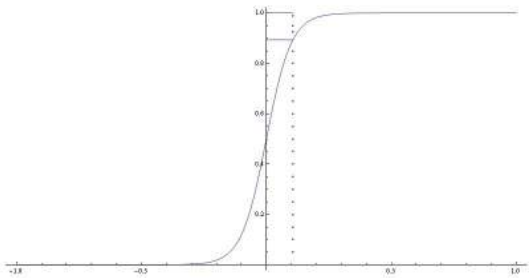

Figure 5: Reaction rate $k = 20$; Hausdorff distance $d = 0.106402$

the step function ah_0 and the sigmoidal function s_0 satisfies the relations $0 < d < a/2$ and $a - s_0(d) = d$, that is

$$(a - d)/d = e^{kd}, \quad (0 < d < a/2). \tag{7}$$

Obviously $d \to 0$ implies $k \to \infty$ (and vice versa). From (7) we obtain a straightforward expression for the rate parameter k as a function of d:

Proposition 1. *The rate parameter k can be expressed in terms of the H-distance d as follows:*

$$k = k(d) = \frac{1}{d} \ln \frac{a - d}{d} = O(d^{-1} \ln(d^{-1})). \tag{8}$$

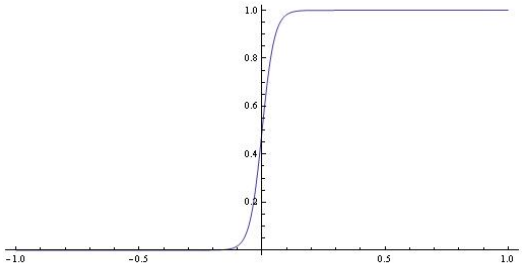

Figure 6: Reaction rate $k = 40$; Hausdorff distance $d = 0.0661748$

Relation (8) gives the rate k in terms of the H-distance d, a few examples are computed in Table 1.

Dist. d	10^{-1}	10^{-2}	10^{-3}	10^{-4}	10^{-5}	10^{-6}
Rate k	0.22×10^2	0.46×10^3	0.69×10^4	0.92×10^5	0.12×10^7	0.14×10^8

Table 1: Values of the rate k as function of the H-distance d according to (8)

Conversely, a relation for the H-distance d in terms of the rate parameter k is given in the next proposition. For simplicity we assume below $a = 1$, considering thus the basic logistic function as depending only on the rate k: $s_0(t) = (1 + e^{-kt})^{-1}$.

Proposition 2. *[2] The Hausdorff distance $d = \rho(h_0, s_0)$ between the Heaviside step function h_0 and the sigmoidal Verhulst function s_0 can be expressed in terms of the the reaction rate k for any real $k \geq 2$ as follows:*

$$d_l(k) = \frac{\ln(k+1)}{k+1} - \frac{\ln\ln(k+1)}{k+1} < d(k) < \frac{\ln(k+1)}{k+1} = d_r(k), \qquad (9)$$

or

$$d(k) = \frac{\ln(k+1)}{k+1}\left(1 + O\left(\varepsilon(k)\right)\right), \;\; \varepsilon(k) = \frac{\ln\ln(k+1)}{\ln(k+1)}. \qquad (10)$$

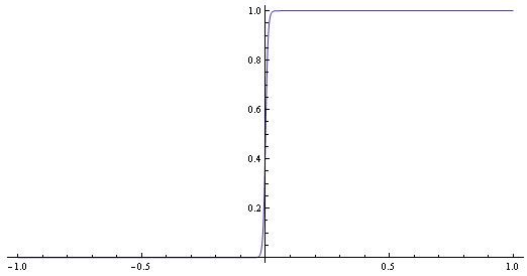

Figure 7: Reaction rate $k = 200$; Hausdorff distance $d = 0.01957$.

A proof of relations (9)–(10) is given in [2]. Some computational examples using relations (9)–(10) are presented in Table 2, see also Figures 6, 7, resp. Appendix 1. The last column of Table 2 contains the values of d for prescribed values of k computed by solving the nonlinear equation (7).

k	$d_l(k)$	$d_r(k)$	$\Delta = d_r - d_l$	$\varepsilon(k)$	$d(k)$ by (7)
2	0.334	0.366	0.032	0.0856	0.337416
100	0.0305	0.0456	0.015	0.3313	0.033592
1000	0.00497	0.00691	0.0019	0.2797	0.005245
10000	0.000698	0.000921	0.00022	0.2410	0.000723

Table 2: Bounds for $d(k)$ computed by (9)–(10) for various rates k

Remarks. a) For the general case $a \neq 1$ one should substitute everywhere in formulae (9)–(10) the expression $k+1$ by $k+a^{-1}$. b) An estimate similar to (10) in integral metric has been obtained in [6].

2.8 Shifted logistic functions

Here we are interested in arbitrary shifted (horizontally translated) logistic functions. Both the step function and the logistic function preserve their form under horizontal translation—note that Verhulst equation possess constant isoclines. Hence the shifted step function h_r is approximated by the shifted logistic function s_r in the same way as function h_0 is approx-

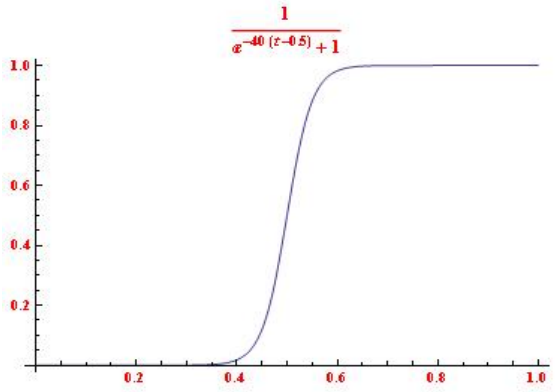

Figure 8: A logistic function shifted with $r = 0.5$.

imated by the basic logistic function s_0, that is for the H-distance we have $\rho(h_r, s_r) = \rho(h_0, s_0)$. Focusing on the shifted logistic function we have

$$s_r(t) = s_0(t - r) = \frac{a}{1 + e^{-k(t-r)}}. \tag{11}$$

The value of the (basic) logistic function (6) at the point $-r$ is

$$s_0(-r) = \frac{a}{1 + e^{kr}}.$$

Figure 8 visualizes a logistic function shifted with $r = 0.5$.

3 Kinetic mechanisms yielding Verhulst model

In this section we demostrate that Verhulst model can be derived from certain (bio)chemical reaction equatiosn using mass action kinetics. It is worth noting that Verhulst model was invented some 30-40 years before the invention of the Mass Action Law. Let us recall the mass action law in its kinetic aspect.

The Law of Mass Action states that the rate of change in concentration of each reactant in a chemical reaction is proportional to the product of the

concentrations of the reactants in that reaction. If a particular reactant is involved in several reactions, then the rate of change of this reactant is made by adding up all positive rates and subtracting all negative ones [12].

3.1 A simple autocatalytic reaction

Consider the following autocatalytic reversible reaction mechanism:

$$X \underset{k_{-1}}{\overset{k}{\rightleftarrows}} X + X, \tag{12}$$

which can be also written as $X \underset{k_{-1}}{\overset{k}{\rightleftarrows}} 2X$.

Applying the mass action law we obtain the Verhulst model:

$$x' = kx - k_{-1}x^2 = kx(1 - (k_{-1}/k)x). \tag{13}$$

The stationary point is $x^* = k/k_{-1}$.

Another kinetic mechanism inducing Verhulst model that seems theoretically possible and better practically justified follows.

3.2 Autocatalytic reaction involving nutrient substrate

Consider the following autocatalytic reaction equation:

$$S + X \xrightarrow{k'} X + X, \tag{14}$$

(or $S + X \xrightarrow{k'} 2X$), where S is a nutrient substance, X is a population and k' is the specific growth rate of the particular population. The biological (biochemical) interpretation of reaction equation (14) is that the substrate S is utilized by the population X leading to the reproduction of the population (simple binary fusion reproduction in the case of bacterial cells population). Denoting the biomass (or density) of X by x and the mass (concentration) of S by s and applying the mass action law, one obtains the following dynamical system for functions $s(t), x(t)$:

$$\begin{array}{rcl} ds/dt & = & -k'xs, \\ dx/dt & = & k'xs, \ s(0) = s_0, \ x(0) = x_0. \end{array} \tag{15}$$

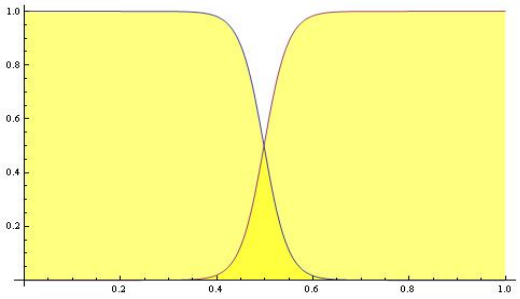

Figure 9: Reaction rate $k = 40$; $s_0 = 1$, $x_0 = 1. \times 10^{-9}$

The solutions s, x of (15) for reaction rate $k = 40$ and initial conditions $s_0 = 1$, $x_0 = 1. \times 10^{-9}$ are iluustrated on Fig. 9, see Appendix 2. Noticing that $ds/dt + dx/dt = 0$, hence $s + x = \text{const} = x_0 + s_0 = a$, we can substitute $s = a - x$ in the differential equation for x to obtain the differential equation $dx/dt = k'sx = k'x(a - x)$ also known as Verhulst model [15]–[17].

$$\frac{dx}{dt} = k'x(a - x). \tag{16}$$

Clearly, the solution x of the initial problem (15) coincides with the solution x of problem (16) with initial condition $x(0) = x_0$:

$$\frac{dx}{dt} = k'x(a - x). \;\; x(0) = x_0. \tag{17}$$

Conversely, the solution of (17) coincides with the solution x of the inital problem (15) whenever $s_0 = a - x_0$. The above can be summarized in the following:

Proposition 3. *The autocatalytic reaction (14) via mass action kinetic induces the dynamic model (15). Models (15) and (17) are equivalent in the sense that their solutions x coincide (for $x_0 + s_0 = a$).*

We see that the underlying mechanism in Verhulst model (17) is a biochemical reproduction reaction (14) based on the utilization of a nutrient

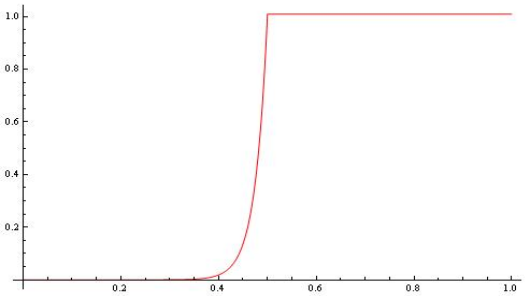

Figure 10: Reaction rate $k = 40$, $r = 0.5$, $x_0 = 1.85 \times 10^{-9}$

substrate. This explains the important versatile applications of Verhulst model.

The Verhulst model is usually written with a normalized rate constant $k = k'/a$ as

$$\frac{dx}{dt} = \frac{k}{a}x(a-x) = kx\left(1 - \frac{x}{a}\right). \tag{18}$$

The solution x to equation (19) with initial condition $x_0 = a/2$, is the (basic) logistic sigmoidal function:

$$s_0(t) = \frac{a}{1+be^{-kt}}; \;\; b = \frac{a-x_0}{x_0} = 1,$$

that is (6).

3.3 Nutrient supply as input function

The Verhulst model can be considered as a prototype of models used in bioreactor modelling. There, especially in the case of continuous bioreactore, the nutrient supply is considered as an input function $s(t)$ as follows:

$$\frac{dx}{dt} = kx(t)s(t), \tag{19}$$

where s is additionally specified.

The solution x for the input nutrient function $s(t) = (Sign(r-t)+1)/2$ obtained by a *Mathematica* module is given in Appendix 4, see Fig. 10.

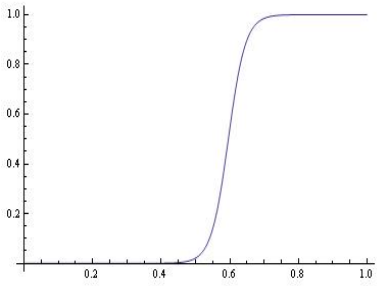

Figure 11: Reaction rate $k = 40$; $r = 0.6$

3.4 Computational issues

The shifted logistic function (11) can be computed as a solution of the Verhulst model (16); in that case we need to know a suitable initial condition for equation (16). The shifted (by r) logistic function (11) can be considered as solution of the initial problem:

$$\frac{dx}{dt} = \frac{k}{a}x(a-x),\ x(0) = x_0 = a/(1+e^{kr}). \tag{20}$$

As r increases the computational time for solving problem (20) increases rapidly if large values of k have been used (in order to achieve good approximation of the step function). As an example, on CAS *Mathematica* for $kr > 30$ the computations fails, whenever using formula (20) for the computation of the shifted logistic function, see Fig. 11 corresponding to a case $kr \leq 30$ and Fig. 12 for the case $kr > 30$, cf. Appendix 3. We note that within such an approach very small values (for the distance d) and very large values (for the rate k) are simultaneously involved in the computation.

In order to reduce the computational problems in CAS *Mathematica* the user should take care with specifying facilities such as AccuracyGoal, PrecisionGoal, and WorkingPrecision.

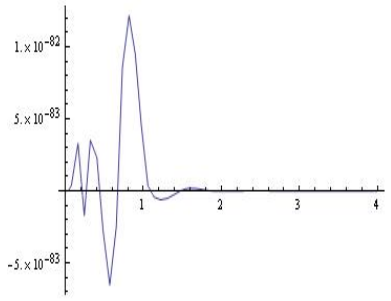

Figure 12: Solution of (20) fails for $kr > 30$

4 Conclusions

H-continuous step functions and smooth sigmoidal functions are used to model biological dynamic processes, in particular certain enzyme kinetic and population growth processes which develop almost step-wise [9]. Such processes are usually described or approximated by smooth sigmoidal functions (especially in the theory of neural networks), however, H-continuous step-wise functions can be also conveniently used. To substitute a sigmoidal function by a step function (or conversely) we need to know the approximation error as given in Proposition 2. Biological processes are often very sensitive and can be effectively studied within the frames of interval analysis [8]. Verhulst model is an important classical example involving a simple logistic sigmoidal function as solution. We demonstrate that this model is induced by simple autocatalytic reactions that describe certain reproduction biochemical mechanisms. On a number of computational examples we demonstrate the applicability of the logistic function to approximate the Heaviside step function and consequently to be emploit in fitting time course experimental data related to population dynamics.

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Appendix 1. Calculation of the value of the Hausdorff distance d between the Heaviside step function h and the sigmoidal Verhulst function s in terms of the reaction rate k

```
Print["Calculation of the value of the Hausdorff distance d between the Heaviside step function h
and the sigmoidal Verhulst function s in terms of the reaction rate k "];
k = Input["  k"];(*100 *)
Print["The reaction rate -  k = ", k];
Print["The following nonlinear equation is used to determination of the Hausdorff distance d: "];

m = 1 / (1 + Exp[-d * k]) - 1 + d;

Print[m, " = 0"];
Print["The roots of this equation are: "];
NSolve[m == 0, ϵ];
Print[TableForm[%]];
Print["The unique positive root of the equation is the searched value of d: "];

positiveReals = Solve[Reduce[{m == 0, d > 0}, d], d];
If[Length[positiveReals] > 0,
  If[Length[positiveReals] == 1,
   Print["There exists an unique ", Length[positiveReals], " positive root: "]
  ];
  Print[TableForm[N[positiveReals]]];
 ];
```

```
Calculation of the value of the Hausdorff distance d between the Heaviside step function h
and the sigmoidal Verhulst function s in terms of the reaction rate k
The reaction rate -  k = 1000
The following nonlinear equation is used to determination of the Hausdorff distance d:
```

$$-1 + d + \frac{1}{1 + e^{-1000\,d}} = 0$$

```
The roots of this equation are:
{}
The unique positive root of the equation is the searched value of d:
There exists an unique 1 positive root:
d → 0.00524519
```

Appendix 2. A kinetic mechanism yielding Verhulst model

```
Print["The reaction equation:"];

Print["S + X -k->  X + X "];

Print["The Law of Mass Action applied to the above reaction leads to the following system
 of differential equations: "];

Print["s'[t] ==-k*s[t]*x[t]"];
Print["x'[t] ==k*s[t]*x[t]"];

k = Input["Input Rate constant -  k"]; (* 40 *)
Print["Rate constant -  k = ", k];

s0 = Input["Input initial condition - s[0]"]; (* 0.999999999 *)
Print["Initial condition s0 = ", s0];

x0 = Input["Input initial condition - x[0]"]; (* 0.000000001 *)
Print["Initial condition x0 = ", x0];

t0 = Input["Input t0"];
Print["t0 = ", t0];

t1 = Input["Input t1"];
Print["t1 = ", t1];

Print["The solutions of the above reaction equation are visualized on the next figure"];

NDSolve[{s'[t] == -k * s[t] * x[t], x'[t] == k * s[t] * x[t],
   s[0] == s0, x[0] == x0}, {s, x}, {t, t0, t1}];

Plot[Evaluate[{s[t], x[t]} /. First[%]], {t, t0, t1}, Filling → Axis,
 FillingStyle -> Directive[Opacity[0.5], Yellow]]
```

Appendix 3. The general case

```
Print["x'[t] ==k*x*(1-x)"];
k = Input["Input -  k"];(* 40 *)
Print[" k = ", k];
r = Input["Input -  r"];(* 0.6 *)
Print[" r = ", r];
t0 = Input["Input t0"];
Print["t0 = ", t0];
t1 = Input["Input t1"];
Print["t1 = ", t1];

s = NDSolve[{x'[t] == k * x[t] * (1 - x[t]), x[0] == 1 / (1 + Exp[k * r])}, x, {t, t0, t1}];
Plot[Evaluate[x[t] /. s], {t, t0, t1}, PlotRange → All]
```

Appendix 4. Nutrient supply as input function

```
Print["x'[t] ==k*x[t]*S[t]"];
Print["S[t] ==(Sign[r-t]+1)/2"];
k = Input["Input -  k"];(* 40 *)
Print[" k = ", k];
r = Input["Input -  r"];(* 0.5 *)
Print[" r = ", r];
x0 = Input["Input initial condition - x[0]"]; (* 0.00000000185 *)
Print["Initial condition x0 = ", x0];
t0 = Input["Input t0"];
Print["t0 = ", t0];
t1 = Input["Input t1"];
Print["t1 = ", t1];

sol1 = NDSolve[{x'[t] == k * x[t] * (Sign[r - t] + 1) / 2, x[0] == x0}, x, {t, t0, t1}];
Plot[Evaluate[x[t] /. sol1], {t, t0, t1}, PlotRange → All, PlotStyle → {Red}]
```