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A robust estimation of the exponent function in the Gompertz law

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Abstract

The estimation of the solution of a system of two differential equations introduced by Norton et al. [Predicting the course of Gompertzian growth, Nature 264 (1976) 542–544] that is equivalent to the famous Gompertz growth law is performed by means of the recent adaptive scheme of Besançon and collaborators [High gain observer based state and parameter estimation in nonlinear systems, paper 204, the sixth IFAC Symposium, Stuttgart Symposium on Nonlinear Control Systems (NOLCOS), 2004, available at ⟨http://www.nolcos2004.uni-stuttgart.de⟩]. Results of computer simulations illustrate the robustness of the approach.

Keywords: Gompertz law; Adaptive scheme; Diffeomorphism

1. Gompertz growth functions

Mathematically speaking, the Gompertz law refers to the class of functions having exponentially decreasing logarithmic derivatives. It has been introduced in 1825 by B. Gompertz in a paper on the law of human mortality [1]. He noted that for people between 40 and 100 years "the rate of mortality variable with age measures a force of death which grows each year by a fraction, always the same, of its present value". According to Winsor [2], the possible application of the Gompertz curve in biology was first spelled out in 1926 by Sewall Wright in a few remarkable statements: " In organisms, on the other hand, the damping off of growth depends more on internal changes in the cells themselves ... The average growth power as measured by the percentage rate of increase tends to fall at a more or less uniform percentage rate, leading to asymmetrical types of s-shaped curves ...".

If the size $z(t)$ of a growing structure evolves according to the equation [3]

$$\dot{z} = z \ln\left(\frac{S}{z}\right), \tag{1}$$

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we say that its growth is of Gompertz type. The evolution is continuous from a given initial stage to a plateau value S. In a Nature letter on the growth of tumours, Norton et al. [4] wrote the Gompertz law as the system of the following two first-order differential equations:

$$\dot{Z}_1 = K_1 Z_1 Z_2, \tag{2}$$

$$\dot{Z}_2 = -K_2 Z_2, \tag{3}$$

where $Z = (Z_1, Z_2) \in \mathbb{R}^2$, $K_i > 0$, Z_1 is the volume of the tumour at time t, and Z_2 is a function entirely described by the second equation (3) that gives the difference in growth with respect to a pure exponential law. According to Norton, $K_2 Z_2$ gives the fraction of the volume that doubles in size during the instant dt. Thus, Z_2 that we call for obvious reasons the *Gompertzian exponent function* is of special interest and we would like to determine it with high accuracy even though we know neither the initial conditions for Z_1 and Z_2 nor K_2. Norton et al. wrote the solution of the system in the following form:

$$Z_1(t) = Z_1(0) \exp\left[\left(\frac{K_1}{K_2}\right) Z_2(0)\{1 - \exp(-K_2 t)\}\right], \tag{4}$$

$$Z_2(t) = \left(\frac{K_2}{K_1}\right) \ln\left[\frac{S}{Z_1(t)}\right]. \tag{5}$$

We will treat Z_1 and Z_2 as states of a dynamical system that in our case is the evolution of a tumour. The fundamental concept of state of a system or process could have many different empirical meanings in biology, and in our case the first state Z_1 is just the size of the tumour, whereas Z_2 is the deviation of the growth rate from the pure exponential growth. In general terms, a potentially useful tool in biology is the reconstruction of some specific states under conditions of limited information. For animal tumours, it is not trivial to know their state Z_1 at the initial moment and most often we do not know the instant of nucleation that can be determined only by extrapolation of the fitting to the analytic solutions of growth models, such as Eqs. (4) and (5). In this paper, the main goal is to show an excellent alternative procedure for estimating the phenomenological quantities of the tumour growing process in the frequent case in which we do not know the initial conditions and the parameter K_2 is the recent adaptive scheme for state estimation proposed by Besançon and collaborators [5]. In addition, what is generally measured, i.e., the output y, is a function of states that we denote by $h(Z)$ and in the particular case of tumours one usually measures their volume. Then,

$$y = h(Z) = Z_1. \tag{6}$$

The mathematical formalism of the adaptive scheme that follows relies entirely on the Lie derivatives of the function $h(Z)$ that are defined in the next section. By a Lie mapping, we are able to write the Gompertz–Norton system in Besançon's matrix form (system F below) that allows to write the corresponding adaptive algorithm (the dynamical system $\hat{\mathsf{F}}$ and its explicit Gompertz form $\hat{\mathsf{F}}_G$ below).

2. The adaptive scheme

Taking into account the fact that rarely one can have a sensor on every state variable, and some form of reconstruction from the available measured output data is needed, an algorithm can be constructed using the mathematical model of the process to obtain an estimate, say $\hat{X}$ of the true state X. This estimate can then be used as a substitute for the unknown state X. Ever since the original work by Luenberger [6], the use of state "observers" has proven useful in process monitoring and for many other tasks. The engineering concept of observer means an algorithm capable of giving a reasonable estimation of the unmeasured variables of a process using only the measurable output. Even more useful are the so-called *adaptive* schemes that mean observers that are able to provide an estimate of the state despite uncertainties in the parameters. The so-called high-gain techniques proved to be very efficient for state estimation, leading in control theory to the well-known concept of *high-gain observer* [7]. The gain is the amount of increase in error in the observer's structure. This amount is directly related to the velocity with which the observer recovers the unknown signal. The high-gain observer is an algorithm in which the amount of increase in error is *constant* and usually of high values in