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Evolution of Density of States for Delay Blood Cell Production Model

Pawel J. Mitkowski† and Maciej J. Ogorzalek‡

†PhD student Faculty of EAIiE, AGH
al. Mickiewicza 30, 30-059, Krakow, Poland
‡Department for Information Technology,
Faculty of Physics, Astronomy and Applied Computer Science,
Jagiellonian University, Krakow, Poland
ul. Golebia 24, 31-007 Krakow
Email: pawel.mitkowski@agh.edu.pl, Maciej.Ogorzalek@uj.edu.pl

Abstract—In the paper we analyse delay model for the blood cell production (The Lasota equation). The main goal is to study the evolution of the density of states. Frobenius-Perron operator describing the density transformation is presented. Numerical calculations are constructed to analyse the approximation of evolving density functions. Initial density functions are determined using inverse cumulative distribution functions. For selected parameters of the equation simulations shows that chosen different initial densities converge to the same invariant density, what indicates the possibility of existence of an invariant measure.

1. Introduction

We are considering the following delay model for blood cells production:

$$\frac{dN(t)}{dt} = -\alpha \cdot N(t) + (\rho \cdot N(t-\tau))^s \cdot e^{-\gamma N(t-\tau)}. \quad (1)$$

Equation (1) was formulated by A. Lasota in [5]. Its biological interpretations are related with earlier model for red blood cells system called the Lasota-Wazewska equation, which is age structured equation with delay feedback [23]. $N(t)$ represents amount of red blood cells (erythrocytes) in blood circulation, α, ρ, γ are constants that have biological meaning (for details see [23] or [22]), τ is a delay time interpreting as a time of maturation of erythrocytes and s is a power in nonlinearity describing the production rate of blood cells. Some informations about the power dependence of production rate of blood cells can be found e.g. in [22], [13]. Because of the non-monotone character of this nonlinearity equation (1) exibits complicated dynamics. The influence of such nonlinearities on dynamics were studied by many authors e.g. [21], [6], [10], [19], [3], [11]. The nonlinearities with non-monotone character were used in some other delay models in biology and medicine e.g. in Nicholson's blowflies equation [16], [5], [4] or Mackey-Glass delay model for white blood cell production [14].

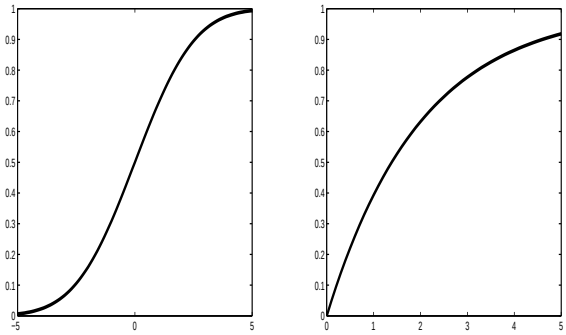
In [5] A. Lasota was analysing chaotic behaviour of biological systems, using approach of ergodic theory. The goal was to investigate existence of continous invariant and ergodic measures in theoretical models of biological systems. From the Birkhoff indyvidual ergodic theorem it follows, that almost all trajectories are complicated if such measure exists see [7]. With reference to eq. (1) the following conjecture were formulated [5, p. 248]:
Let C_h be the space of continous functions $v : [-\tau, 0] \to R$ with the supremum norm topology.
For some positive values of parameters ρ, τ, s and α there exists on C_h a continuous measure which is ergodic and invariant with respect to equation (1).
Searching of an invariant measures is a very difficult problem, requiering advance mathematical knowledge especially in the measure theory, ergodic theory and the stochastic approach to dynamical systems [8], [17], [20]. One of the methods consist in analysis of the convergence of the Frobenius-Perron operator for given transformation. In the section 2.1 we will briefly describe Frobenius-Perron operator. Other methods have also been reported (see e.g. [9], [18], [2], [1]).

For some parameters numerical simulations of eq. (1) indicates that system exibits ergodic properties and suggest that continous invariant measure could exists on some subspaces of the space C_h (see [15]). Here we want to study preliminarily evolution of density of distribution of initial states of the system (1). If there exists invariant and ergodic measure numerical simulations should indicate that the initial density of any distibution converges to some invariant limiting density. The goal will be to prepare numerical simulations for eq. (1) in order to be able to set distribution of initial states and later to observe the evolution of initial density.

2. Evolution of Densities

2.1. The Frobenius-Perron operator

Let $(X, \mathcal{A}, \mu)$ be a measure space. Let $S : X \to X$ be a measurable and nonsingular transformation. The evolution of the density function $f(x)$ for the initial states under the action of S is given by the Frobenius-Perron operator P (see [8], [20]) corresponding to the transformation S and



(a) (b)

Figure 1: Cumulative distribution functions of the (a) normal distribution with $\mu = 0, \sigma = 2$ (b) exponential distribution with $\mu = 2$

defined by the equation

$$\int_A Pf(x)\mu(dx) = \int_{S^{-1}(A)} f(x)\mu(dx), \quad \text{for } A \in \mathcal{A}. \quad (2)$$

2.2. Numerical simulations

The space C_h is an infinite dimesional space, thus we can only investigate the evolution of densities on some subspaces of C_h.

We will analyse the set of trajectories of eq. (1) for constant initial functions, with values distributed with some initial density. We determine the initial density using inverse cumulative distribution functions. Let us take the ensemble $X_1, X_2, \ldots, X_n$ with density f, that is with the cumulative distribution function F. Now we take $Y_1, Y_2, \ldots, Y_n$ uniformly distributed on $(0, 1)$ and we have

$$X_i = F^{-1}(Y_i) \quad (3)$$

Let us then determine some distributions for the ensemble of values of constant initial functions. For example the normal distribution with mean $\mu = 0$ and standard deviation $\sigma = 2$ and the exponential distribution with mean $\mu = 2$. The cumulative distribution functions of the normal distribution is

$$F(x) = \frac{1}{2}(1 + \mathrm{erf}(\frac{x-\mu}{\sigma\sqrt{2}})), \quad (4)$$

(see Fig. 1 (a)), where erf is the so-called "error function". For the exponential distribution we have

$$F(x) = \begin{cases} 1 - e^{-\frac{x}{\mu}}, & x \geq 0 \\ 0, & x < 0 \end{cases} \quad (5)$$

(see Fig. 1 (b)). Applying formula (3) we can obtain ensemble with given distribution. The result can be observed by displaying the histograms of the locations of the values

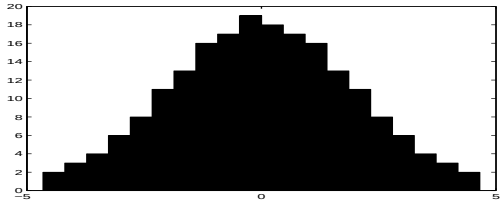


Figure 2: Histogram for the normal distribution of an ensable of 197 values of constant initial functions

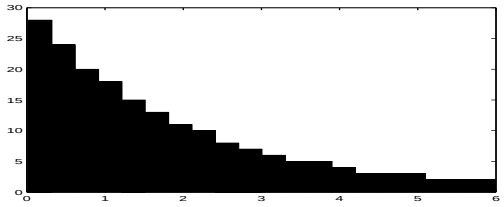


Figure 3: Histogram for the exponential distribution of an ensable of 189 values of constant initial functions

of constant initial functions (Fig. 2 - normal distribution, of the set of 197 values, $\mu = 0$ and $\sigma = 2$, Fig. 3 - exponential distribution, of the set of 189 values, $\mu = 2$).

Now we can approximate the density function by dividing the number of values in each bin of the histograms by $\epsilon \cdot N$, where ϵ is the width of the bin and N is the total number of the values in all bins. Fig. 4 (a) shows approximation of initial density for normal distribution and Fig. 5 (a) for exponential distribution. To study the evolution of this initial densities we calculate the numerical solution of eq. (1) for all initial functions. For obtained ensambles of solutions we construct the histograms of the locations of values for the increasing time of simulation. The histograms are normalized like before to get the approximation of the evolving density functions. The evolution of initial density of normal distribution is presented in Fig. 4 (a)-(g) and the exponential distribution in Fig. 5 (a)-(g). We can see that both initial densities converge to some invariant densities, which additionaly seem to be identical. This results indicate possibility of existence of invariant measure, for eq. (1), because the system independently on initial density converge always to the same invariant density. Numerical solutions of eq. (1) were obtained here for $\alpha = 0.8$, $\rho = 0.46$, $\gamma = 1$, $s = 8$ and delay $\tau = 10$. Calculations were done using MATLAB's solver `dde23`.

3. Final Remarks

Discused measure related with the eq. (1) can be invariant and ergodic (see [15]) what is connected with the chaotic behaviour. In Fig. 6 we have the example of irregular (chaotic) trajectory obtained for eq. (1) with the values

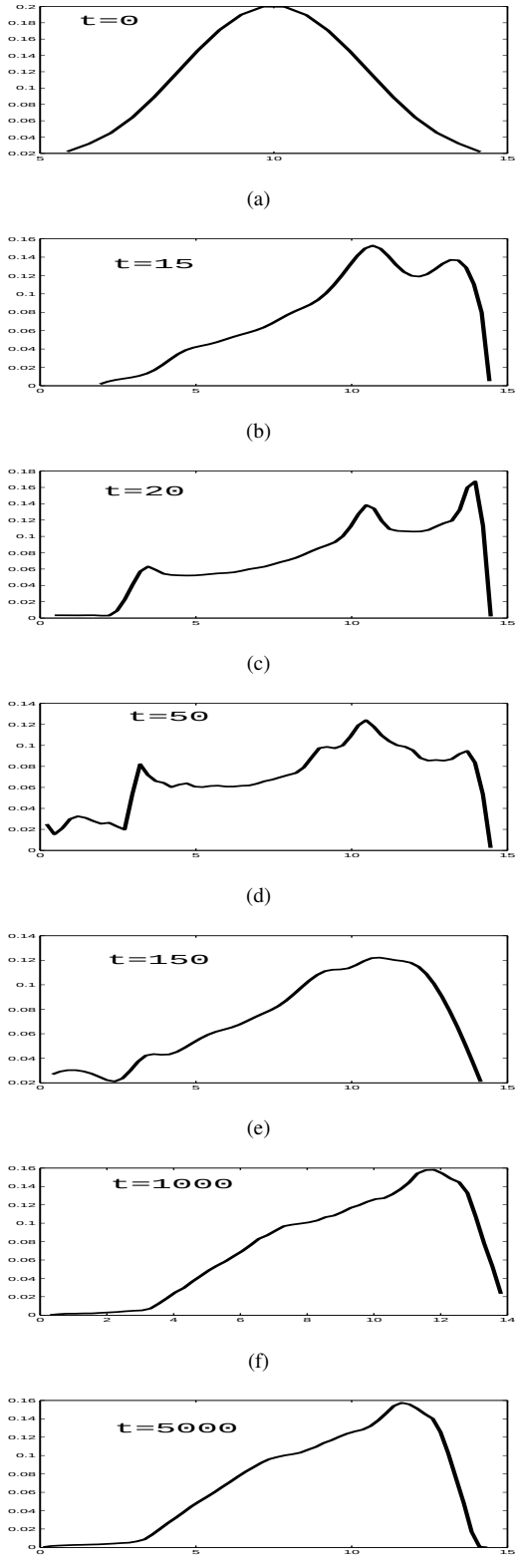


Figure 4: Evolution of initial density of normal distribution ($\mu = 0,\ \sigma = 2$). 197 constant initial functions

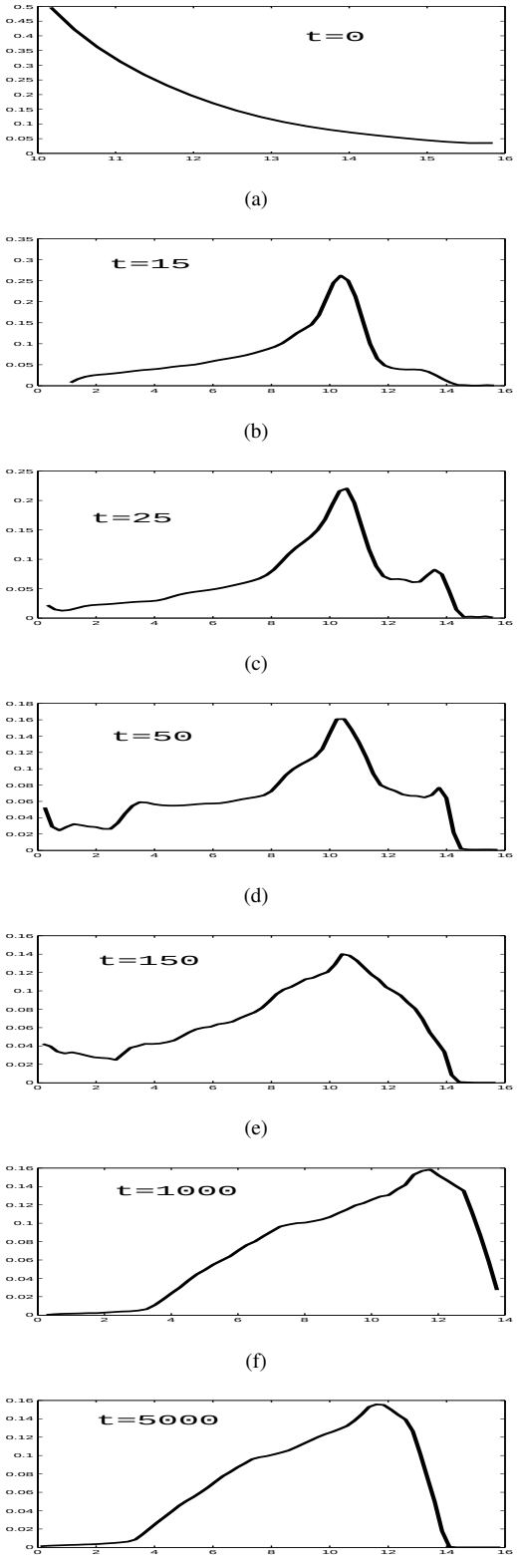


Figure 5: Evolution of initial density of exponential distribution ($\mu = 2$). 189 constant initial functions

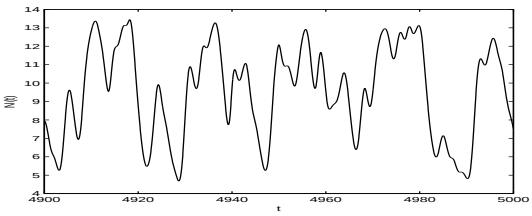


Figure 6: Chaotic trajectory of eq. (1)

of parameters the same as for the simulations of evolution of densities from Fig. 4 and Fig. 5.

Approach to chaotic dynamics, concerning evolution of densities and existence of invariant and ergodic measures brings interesting interpretations of behaviour of biological systems. It shows that chaos in biological systems can be related with their properties and not only the with the difficulties in measuring of very complicated biological parameters [5].

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