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MODEL OF SICKLEMIA NO AUTONOMOUS WITH THE COEFFICIENT PERIODIC IN GENERAL

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ABSTRACT

In that article is proved the theorem that reduces general periodic coefficient system to a system with the matrix of the constant lineal part and nonlinear part a function with coefficient periodic. It has given enough conditions for stability of the null solution of the system and is given a specific example in which the stability of system has to be obtained through polymerization function.

Keywords: ***Sickle cell; anemia; mathematical model; polymers.***

1. INTRODUCTION

The study of polymers and glasses formation has been divulged enough, have been done investigations from the molecular point view, where is modeled the process through the chemistry equations, applying magnetic resonance, applying computational and statistic methods. Also that process just has been modeled applying ordinary differential equations no autonomous; all that is indicated as following, where is done reference to the main works, where the results are proved.

Making use of the following no autonomous differential equations system, that simulate the formation of polymers in the hemoglobin.

$$\begin{cases} \dot{x} = -(c-d+l)x + rw - nP(x) + nR(y) \\ \dot{y} = -(e-f+k)y + sw + P(x) - R(y) \\ \dot{z} = \left[\frac{c-d}{n}\right]x + (e-f)y \\ \dot{w} = lx + nky - (r+ns)w \end{cases} \quad (1)$$

Among other woks of Cabal, C and Ruiz, A.I. [3, 4], can be indicated, that did a qualitative analysis of process simulated here, also to treat the problem of the extremely absent cases of crystallization and advanced crystallization.

The problem of polymers formation was treated, making use of the nuclear magnetic resonance by different authors, among we must cite Fernández A et. al. [6] and Lores M. A; Cabal C. [7].

Aimee M. and others [1] study the mechanism and kinetic of the aggregation of proteins, making emphasis in polymerization´s process. Chraska T. and others [5] make a technic process study by differential equations of first order.

Zenghui Liu [10], in that work is made a Biochemistry analysis of the hemoglobin structure, where study between other aspects, the polymerization, purification, as well as the polymers formation and growth.

In the present work was obtained a model that simulates the formation of polymers in the blood through a periodic system in general, due to in majority of the cases the crisis of patients appear in periodic form , so it allow more accurate approach in that process.

2. METHODOLOGY

Been the system of the differential equations

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$$\begin{cases} x' = a_1(t)x + d_1(t)w + P_1(t,x,y) \\ y' = b_2(t)y + d_2(t)w + P_2(t,x,y) \\ z' = a_3(t)x + b_3(t)y \\ w' = a_4(t)x + b_4(t)y + d_4(t)w \end{cases} \quad (2)$$

With the Law of conservation of mass

$$N = x(t) + n\,y(t) + n\,z(t) + w(t,p)$$

In that case the coefficients and nonlinear functions satisfies the following equivalent conditions to the mass conservation:

1) $a_1(t) + na_2(t) + na_3(t) = 0$

2) $nb_2(t) + nb_3(t) + b_4(t) = 0$

3) $d_1(t) + nd_2(t) + d_4(t) = 0$

4) $P_1(t,x,y) + nP_2(t,x,y) = 0$

Unknown functions represent following magnitudes:

$x(t)$: concentration of hemoglobin deoxidized in form of monomers or in defectives polymers.

$ny(t)$: concentration of hemoglobin deoxidized in form in polymers.

$nz\,(z)$: concentration of hemoglobin deoxidized in form of crystals.

$w(p,t)$ concentration of hemoglobin oxygenated.

The system (2) must be written as following:

$$x' = A(t)x + X(x,t) \quad (3)$$

Where $x = col(x_1, x_2, x_3, x_4) = col(x, y, z, w)$, $X = col(P_1, P_2, 0, 0)$ and $A(t)$ is the matrix of the linear part, and the polymerization´s function has the form,

$$P_i(x,t) = \sum_{|P|\geq 2} P_i^{(P)}(t) x_1^{(P_1)} x_2^{(P_2)} x_3^{(P_3)} x_4^{(P_4)}$$

$(i = 1,2)$

Sánchez S., Fernández A. and Casas F. (2011, pages 1741-1758) treat the problem of numerical integration of linear system;

$$x' = A(t)x \quad (4)$$

where the matrix *A(t)* no necessarily has to be periodic. For the periodic case that system will correspond to indicate system when there isn´t the polymerization function.

For the case in which the nonlinear part is periodic concerning to the time and the matrix A is constant, comes to determine conclusions in relation to behavior of the disease.

Take into account the system of equations (3), where,

$$X_s(x,t) = \sum_{|P|\geq 2} X_s^{(P)}(t) x_1^{(P_1)} x_2^{(P_2)} x_3^{(P_3)} x_4^{(P_4)}$$

$(s = 1,2)$

For which,

$$A(t+\omega) = A(t)$$

and

$$X_i^{(p)}(t+\omega) = X_i^{(p)}(t).$$

it means, suppose that the coefficients of the system are functions ω- periodic, where ω is *a* positive constant.

The study of systems (3) with variable coefficients, but periodic, must be reduce, at least theoretically, in a case of a system where the matrix´s coefficients *A* are constants, Bounonov M. [2] carry out to those results applying Floket´s theory for a system of type (4).

It will be denote for ø to the fundamental matrix of system (4), e by B a matrix thus, that $\phi(t+\omega) = \phi(t)B$, and will insert a constant matrix R thus, that $R = \omega^{-1}\ln B$, also the

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function is defined $G(t)=\phi(t)e^{-Rt}$.Those expressions will be used as following in the demonstration of the fundamental results of that work.

Theorem 1: The transformation of coordinates

$$x = G(t)y \tag{5}$$

reduces the system (3) to system

$$y' = Ry + Y(t,y) \tag{6}$$

Proof:

Deriving the transformation (5) along the system´s trajectory (3) and (6) and has to

$$x' = \phi'(t)e^{-Rt} - R\phi(t)e^{-Rt}y + \phi(t)e^{-Rt}y'.$$

As x is a solution of (3) and $\phi(t)$ is a fundamental matrix of the system (4), if the corresponding expressions are substituted, must be to write,

$$A(t)\phi(t)e^{-Rt}y + X(t,\phi(t)e^{-Rt}y) = A(t)\phi(t)e^{-Rt}y - R\phi(t)e^{-Rt}y + \phi(t)e^{-Rt}y'$$

.

Reducing the similar terms is carried out to,

$$X(t,\phi(t)e^{-Rt}y) = -R\phi(t)e^{-Rt}y + \phi(t)e^{-Rt}y'$$

Discovering the unknown y' in previous expression, is obtained

$$y' = Ry + \phi(t)^{-1}e^{Rt}X(t,\phi(t)e^{-Rt}y)$$

Making

$$\phi(t)^{-1}e^{Rt}X(t,\phi(t)e^{-Rt}y) = Y(t,y)$$

Is concluded that

$$y' = Ry + Y(t,y)$$

Stay thus theorem demonstrated (1)

The own values $\mu_1,\ldots,\mu_4$ of the matrix B represent multipliers of the system (4), being those values in general complex numbers, and the eigenvalues $\lambda_1,\ldots,\lambda_4$ of the matrix R from the system *(6)* are called characteristic index of the system (4).

From the definition of matrix R, is obtained the

$$\lambda_i = \omega^{-1}\ln\mu_i,\ (i=1,2,3,4).$$

By the definition of logarithm of a complex number, is obtained that,

$$\ln\mu_i = \ln|\mu_i| + i(\arg\mu_i + 2k\pi)$$
$$(i=1,2,3,4).$$

Theorem 2: If $0<|\mu_i|<1\quad(i=1,2,3,4)$, so $\operatorname{Re}\lambda_i<0\quad(i=1,2,3,4)$ and therefore the position of system´s equilibrium (4) is asymptotically steady.

Proof:

As consequence of theorem 1, the system (3) is equivalent to system (6), and is have that the own values of the matrix R are $\lambda_1,\ldots,\lambda_4$, where,

$$\lambda_i = \omega^{-1}\ln|\mu_i| \qquad (i=1,2,3,4),$$

As consequence of the condition, $0<|\mu_i|<1$ is have that $\operatorname{Re}\lambda_i<0\ (i=1,2,3,4)$, whatever complete the demonstration of theorem 2

Observations:

1) Can´t include nothing if $|\mu_i|=1$ for some $(i=1,2,3,4)$, and the remainder were such as $0<|\mu_j|<1\ (i\neq j)$ will obtain that there are some λ_i such as $\operatorname{Re}\lambda_i=0$ and the remainder by real negative part, so that constitutes a doubtful case and the stability of the null solution is have to determine doing use of the polymerization of the function.

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2) It doesn't have any real sense if $|\mu_i| = 0$ for some $(i = 1,2,3,4)$.

3) If $1 < |\mu_i| < \infty$ for some $(i = 1,2,3,4)$, the system (5) is unstable, so in that case $\operatorname{Re} \lambda_i > 0$ for some $(i = 1,2,3,4)$.

As follows is given an example of the system as a system´s form (7) where are indicate the different elements demonstrated before.

Example: Being the system,

$$\begin{cases} x' = -n(\cos t + 1)x + P_1(t, x, y) \\ y' = sent y + P_2(t, x, y) \\ z' = (\cos t + 1)x - sent y \end{cases}$$

In that system is have that,

$$A(t) = \begin{bmatrix} -n(\cos t + 1) & 0 & 0 \\ 0 & sent & 0 \\ \cos t + 1 & -sent & 0 \end{bmatrix}$$

That matrix satisfies the relation,

$$A(t + 2\pi) = A(t)$$

It means, it is a periodic matrix of period 2π. In this case is had that the fundamental matrix of homogeneous system corresponding is,

$$\phi(t) = \begin{bmatrix} e^{-n(sent + t)} & 0 & 0 \\ 0 & e^{-\cos t} & 0 \\ -n^{-1} e^{-n(sent + t)} & e^{-\cos t} & 0 \end{bmatrix}$$

That matrix is thus $\phi(t + 2\pi) = \phi(t)B$

Being B a following matrix

Consider that in a system (1) the oxygenated hemoglobin depends only of the arterial pressure and no of the time, is had that the system adopts the form:

$$\begin{cases} x' = a_1(t)x + P_1(t, x, y) \\ y' = b_2(t)y + P_2(t, x, y) \\ z' = a_3(t)x + b_3(t)y \end{cases} \quad (7)$$

$$B = \begin{bmatrix} e^{-2\pi n} & 0 & 0 \\ 0 & 1 & 0 \\ e^{-2\pi n} & 1 & 0 \end{bmatrix}$$

In that example the multipliers are $\mu_1 = 0$, $\mu_2 = 1$ and $\mu_3 = e^{-2\pi n}$ from this form, that example falls on the second case, then there aren´t the values of λ_1, this result is logic, due to the characteristics of the system; the determinant of the matrix is equal zero.

3. CONCLUSIONS

1. If $0 < |\mu_j| < 1$ $(j = 1,2,3,4)$ in a period of the time no to big the disease will have a stable behavior.

2. If there is i such as $1 < |\mu_i| < \infty$ the patient will enter in crisis in whichever moment.

3. If $|\mu_i| = 1$ for some $(i = 1,2,3,4)$, and the remainders are such, that $0 < |\mu_j| < 1$ $(i \neq j)$ May happen whatever, from a stationary steady of the disease, until enter in sharp crisis.

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