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Influence of physical exercise on the strengthening of immunity. Mathematical model.

Influencia del ejercicio físico en el fortalecimiento de la inmunidad. Modelo matemático.

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Abstract

In the present work we analyze how physical exercises can influence the increase of a person's immunity; a study of the different types of pathogens is carried out, in particular the characteristics of viruses, their manifestations and appearance are investigated; the characteristics of the immune system as well as immunity, either innate or acquired, are studied. The relationship between viruses and a person's immune system is investigated, as well as how the immune system can react to the presence of a virus.

The dynamics of the interaction of the virus vs the immune system is simulated by means of a system of ordinary differential equations, the equilibrium points and the behavior of the trajectories in a neighborhood of the equilibrium points are determined, additionally the critical case of a zero and negative one eigenvalue, giving conclusions about the process in the different cases.

Key words and phrases: Mathematical model, epidemic, physical exercises, immunity.

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Resumen

En el presente trabajo se analiza cómo los ejercicios físicos pueden influir en el aumento de la inmunidad de una persona; se realiza un estudio de los diferentes tipos de patógenos, en particular se investigan las características de los virus, sus manifestaciones y apariencia; se estudian las características del sistema inmunológico así como la inmunidad, ya sea innata o adquirida. Se investiga la relación entre los virus y el sistema inmunológico de una persona, así como el sistema inmunológico puede reaccionar ante la presencia de un virus.

La dinámica de la interacción del virus vs el sistema inmunológico se simula mediante un sistema de ecuaciones diferenciales ordinarias, se determinan los puntos de equilibrio y el comportamiento de las trayectorias en una vecindad de las posiciones de equilibrio, adicionalmente se estudia el caso crítico de un autovalor cero y uno negativo, dando conclusiones sobre el proceso en los diferentes casos.

Palabras y frases clave: Modelo matemático, epidemia, ejercicios físicos, immunidad.

1 Introduction

The immune system is a set of elements that exist in the human body. These elements interact with each other and are intended to defend the body from diseases, viruses, bacteria, microbes, among others. The human immune system serves as a protection, shield or barrier that protects us from undesirable beings, antigens, that try to invade our body. Therefore, it represents the defense of the human body.

There are confessions of patients who, due to the doctor's suggestions, permanently started to perform physical exercises to strengthen their immune system, in the face of infectious diseases, perceiving a low immunity; gradually obtaining a change in your organism. The fitness coach stated that he was not the only case, as he had others with similar situations. This problem is addressed further in specialized bibliographies (cf. [1, 2, 14]).

When the immune system does not function properly, it decreases its ability to defend our body. Thus, we are more vulnerable to diseases such as tonsillitis or stomatitis, candidiasis, skin infections, ear infections, herpes, colds and flu. To strengthen the immune system and avoid problems with low immunity, special attention is needed with food. Some fruits help increase immunity, such as apples, oranges and kiwis, which are citrus fruits. The intake of omega 3 is also an ally for the immune system.

The immune system is made up of a complex of different cells that receive and emit different signals directed at white blood cells, thus regulating the body's defense mechanisms. The mediators of this interaction are proteins, peptides and other substances that for their activity are called immunomodulators. Biological immunomodulators are made up of a group of molecules with specific properties, many of them chemically and biologically very well characterized and others to be discovered. (cf. [16, 18]).

In the human organism there are own cells and inappropriate cells, among the inappropriate are pathogens; These inappropriate cells can cause changes in the body, which can turn into diseases and even cause the death of the person; pathogens can include viruses, bacteria, fungi, and parasites; these can be intracellular or extracellular.

Viruses are simple structures, they are considered mandatory intracellular parasites, because they depend on cells to multiply. Outside the intracellular environment, viruses are inert. However, once inside the cell, the replication capacity of viruses is surprising: a single virus is capable of multiplying, in a few hours, thousands of new viruses. Viruses are capable of infecting living beings from all domains. In this way, represent the greatest biological diversity on the planet, being more diverse than bacteria, plants, fungi and animals combined (cf. [17]).

When the human body is attacked by a virus, a reaction from the immune system to the person quickly occurs to prevent this aggression; there are occasions when this reaction is sufficient to free the organism from any infection, but in many cases this is not enough and it is necessary to supply medication and other artificial substances capable of adding immunity such as interferons, among others.

Immunity can be innate or acquired, acquired immunity is adaptive and is made up of lymphocytes; On the other hand, innate immunity is made up of cells and molecules with the great function of defending the body from any aggressor, these have the ability to kill, this is an instantaneous process, this being the first defense of the body.

Interferons are glycoproteins that have several biological actions, including complex antiviral, immunomodulatory and antiproliferative effects. Its production and endogenous release occurs in response to viruses and other inducers, with the exception of bacterial exotoxins, polyanions, some low molecular weight compounds and microorganisms with intracellular growth (cf. [22]).

There are many diseases that are transmitted from person to person directly, and different forms of contagion are used for this purpose, often through speech or breathing or in some other way; but in many other cases this transmission can be carried out by means of a vector being the mosquito the most common. It is said that the cases of maximum risk are adults of the third age and especially those who suffer from some chronic disease; but practice has shown that in the face of this disease, there is no one safe, and it can have a slow evolution that acts in a fulminating way.

Today the most worrying situation is COVID-19, caused by the SARS-CoV-2 coronavirus, a respiratory disease that has claimed so many lives, there are many ideas on how to combat this disease; but the method that most researchers agree with is the method of isolating those infected to avoid possible transmission to other people [19, 20]. In [21] this process of contagion of the coronavirus is simulated by means of a generalization of the logistic method to characterize the process when it grows and when it decreases; indicating the moment of change of concavity of the curve.

One of the treatments that has already given results is interferon alpha-2b, in addition to others already tested in the treatment of other diseases such as AIDS, hepatitis, among others. Interferon alpha-2b, was developed by the Cuban Genetic Engineering and Biotechnology Center and has already been used in different parts of the world with highly reliable results (cf. [5]).

In [3] different real-life problems are dealt with using autonomous differential equations and systems of equations, where examples are developed and other problems and exercises are presented for the reader to develop. The authors of [4] indicate a set of articles that form a collection of several problems that model different processes, using in their study the qualitative and analytical theory of differential equations for both autonomous and non-autonomous cases, in both books the authors address the problem of epidemic development.

In [17], the probabilistic model is used to simulate population growth, which are applied to the development of epidemics. There are multiple works devoted to the study of the causes and the conditions under which an epidemic may develop, among which we can indicate (cf. [12]).

The problem of epidemic modeling has always been of great interest to researchers, such as [6–11, 13] and [15]. In this work we will apply the generalized logistic model, where the case of the growth and decrease of the infected are applied in the same equation; to model the development of epidemics, a model that allows forecasts of future behavior.

2 Model formulation

The human body works like a prefect machine, producing enzymes, hormones and substances that will be used, according to the needs; but there are occasions that this is not enough due to the causes of those needs, for example in the case of the appearance of a virus situation in which in general artificial supplies are necessary to achieve an effective coping with the situation.

In order to formulate the model using a system of differential equations, the following variables will be introduced:
x_1 is the total concentration of the healthy cells at the moment t
x_2 is the total virus concentration at the time t.

In addition, $\bar{x}_1$ and $\bar{x}_2$ the values of the allowable concentrations of the healthy cells and the virus respectively.

In this way the model will be given by the following system of differential equations.

$$\begin{cases} x_1' = x_1 f(x_1, x_2) \\ x_2' = x_2 g(x_1, x_2) \end{cases} \tag{1}$$

The main objective of this work is to determine the equilibrium positions and to study the trajectories of the system in the vicinity of the equilibrium positions. Suppose that the and functions can be expressed by the following development, which is in correspondence with the relationship between the virus and the home immune system, because between them there is a coping relationship, fighting for survival.

$$f(x_1, x_2) = a_1 - a_2 x_2 - a_3 x_1 + f_1(x_1, x_2)$$
$$g(x_1, x_2) = -b_1 + b_2 x_1 + b_3 x_2 + g_1(x_1, x_2)$$

Remark 1. *Here are considering that the initial encounter is favorable to viruses, otherwise there would be no viral process. The signs of the coefficients of the previous development correspond to the characteristics of the problem addressed.*

The functions $f_1(x_1, x_2)$ and $g_1(x_1, x_2)$ from a physiological point of view represent external influences, in particular the effect of physical exercise, these disturbances from a mathematical point of view are infinitesimal of order superior in a neighborhood of the origin (0,0), that is to say in its development only terms of superior degree appear.

Therefore, the system (1) takes the form:

$$\begin{cases} x_1' = a_1 x_1 - a_2 x_1 x_2 - a_3 x_1^2 + x_1 f_1(x_1, x_2) \\ x_2' = -b_1 x_2 + b_2 x_1 x_2 + b_3 x_2^2 + x_2 g_2(x_1, x_2) \end{cases} \tag{2}$$

If the functions $f_1(x_1, x_2)$ and $g_1(x_1, x_2)$ are identically null, then system (2) takes the form,

$$\begin{cases} x_1' = a_1 x_1 - a_2 x_1 x_2 - a_3 x_1^2 \\ x_2' = -b_1 x_2 + b_2 x_1 x_2 + b_3 x_2^2 \end{cases} \tag{3}$$

The equilibrium positions of the system (3) are the points, $P_1(0,0)$, $P_2\Big(0, \dfrac{b_1}{b_3}\Big)$, $P_3\Big(\dfrac{a_1}{a_3}, 0\Big)$ and $P_4\Big(\dfrac{a_2 b_1 - a_1 b_3}{a_2 b_2 - a_3 b_3}, \dfrac{a_1 b_2 - a_3 b_1}{a_2 b_2 - a_3 b_3}\Big)$.

Analysis at point P_1

To the point P_1, if you have that the characteristic equation of the matrix of the linear part of the system has the form, $\lambda^2 + (b_1 - a_1)\lambda - a_1 b_1 = 0$. Here there is a positive eigenvalue, and therefore the equilibrium position P_1 is unstable.

Example 1. *Be the system*

$$\begin{cases} x_1' = 2x_1 - x_1x_2 - 3x_1^2 \\ x_2' = -x_2 + 2x_1x_2 + 2x_2^2 \end{cases}$$

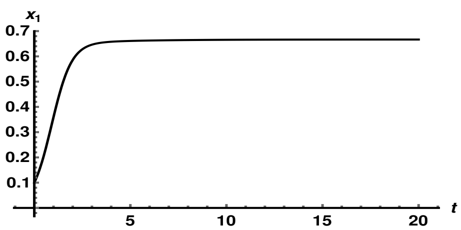

Figure 1: Graph of $y_1(t)$ in the **Example 1**

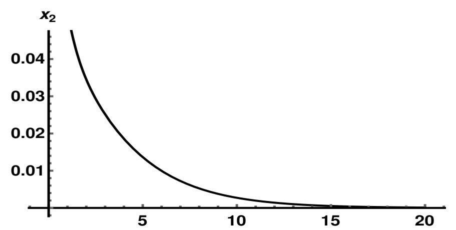

Figure 2: Graph of $y_2(t)$ in the **Example 1**

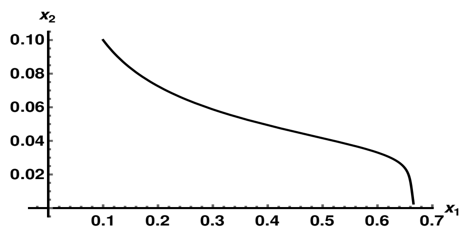

Figure 3: Graph of $y_1(t)$ vs $y_2(t)$ in the **Example 1**

Here we see that in spite of the origin of coordinates both the solution in $x_1(t)$ how in $x_2(t)$ remain in tune, but this position of equilibrium is unstable as it changes in the graph of $x_1(t)$ against $x_2(t)$. This is in correspondence with the results obtained from the theoretical point of view.

It is not important to study the point P_2 because it is made explicit here that the concentrations of healthy cells would disappear, and therefore the person will die.

Analysis at point P_3

To the point P_3 it is necessary to make a change of variables to analyze the behavior of trajectories in a neighborhood at that point. The transformation of coordinates,

$$\begin{cases} x_1 = y_1 + \dfrac{a_1}{a_3} \\ x_2 = y_2 \end{cases}$$

Reduces the system (3) in the next system,

$$\begin{cases} y_1' = -a_1 y_1 - \dfrac{a_1 a_2}{a_3} y_2 - a_2 y_1 y_2 - a_3 y_1^2 \\ y_2' = \dfrac{a_1 b_2 - a_3 b_1}{a_3} y_2 + b_2 y_1 y_2 + b_3 y_2^2 \end{cases} \tag{4}$$

The characteristic equation of the matrix of the linear part of the system (4) has the form, $\lambda^2 + \dfrac{a_3(a_1+b_1) - a_1 b_2}{a_3}\lambda + \dfrac{a_1 a_3 b_1 - a_1^2 b_2}{a_3} = 0$

Theorem 1. *The equilibrium position P_3 it is asymptotically stable if and only if $a_1 b_2 < a_3 b_1$ is fulfilled.*

Proof. Like $\dfrac{a_3(a_1+b_1) - a_1 b_2}{a_3} = \dfrac{a_1 b_2 - a_3 b_1}{a_3} - a_1$ and $\dfrac{a_1 a_3 b_1 - a_1^2 b_2}{a_3} = -a_1(\dfrac{a_1 b_2 - a_3 b_1}{a_3})$ then, the eigenvalues associated with the system (4) are $\lambda_1 = \dfrac{a_1 b_2 - a_3 b_1}{a_3}$ and $\lambda_2 = -a_1$, therefore if the condition $a_1 b_2 < a_3 b_1$ therefore if the condition, λ_1 and λ_2 are negative and the system (4) is asymptotically stable. □

Remark 2. *It follows that if the condition of* **Theorem 1** *are satisfied, the virus will disappear, with no consequences for the patient whenever the point coordinates correspond to the optimal concentration values, otherwise it will be necessary to take the necessary prophylactic measures to prevent the patient from falling into a coma.*

Example 2. *Given the following system that satisfies the conditions of* **Theorem 1**

$$\begin{cases} y_1' = -0.3\ y_1 - 0.12\ y_2 - 0.2\ y_1 y_2 - 0.5\ y_1^2 \\ y_2' = -0.64\ y_2 + 0.1\ y_1 y_2 + 0.1\ y_2^2 \end{cases}$$

Where $a_1 b_2 = a_3 b_1$, $\lambda_1 = 0$ so the system (4) constitutes a critical case, then the matrix of the linear part of the system (4) to have a zero eigenvalue and a negative one, in this case the second method of Liapunov will be applied once this system is reduced to the quasi-normal form. By means of a non-degenerate transformation $z = Sy$, the system (4) can be transformed into the system,

$$\begin{cases} y_1' = Y_1(y_1, y_2) \\ y_2' = \lambda_2 y_2 + Y_2(y_1, y_2) \end{cases} \tag{5}$$

when S is the matrix $\begin{pmatrix} -\dfrac{a_2}{a_3} & 1 \\ 0 & 1 \end{pmatrix}$,

$Y_1(y_1, y_2) = \dfrac{a_3 b_3 - a_2 b_2}{a_3} y_1^2 + b_2 y_1 y_2$ and

$Y_2(y_1, y_2) = \dfrac{a_2(a_3 b_3 - a_2 b_2)}{a_3^2} y_1^2 + \dfrac{a_2(a_3 + b_2)}{a_3} y_1 y_2 - a_3 y_2^2$

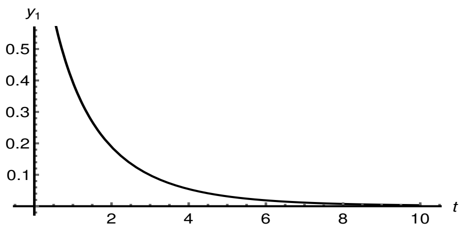

Figure 4: Graph of $y_1(t)$ in the **Example 2**

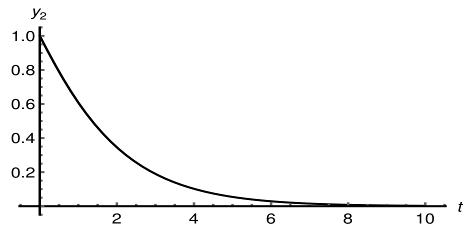

Figure 5: Graph of $y_2(t)$ in the **Example 2**

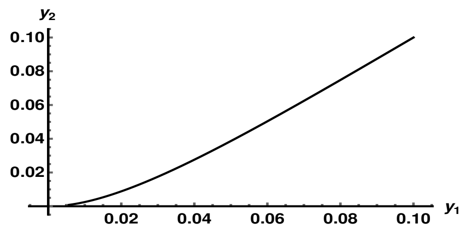

Figure 6: Graph of $y_1(t)$ vs $y_2(t)$ in the **Example 2**

Theorem 2. *The exchange of variables,*

$$\begin{cases} y_1 = z_1 + h_1(z_1) + h^0(z_1, z_2) \\ y_2 = z_2 + h_2(z_1) \end{cases} \tag{6}$$

transforms the system (5) *into almost normal form,*

$$\begin{cases} z_1' = Z_1(z_1) \\ z_2' = \lambda_2 z_2 + Z_2(z_1, z_2) \end{cases} \tag{7}$$

Where h^0 *and* Z_2 *cancel each other out* $z_2 = 0$.

Proof. Deriving the transformation (6) along the trajectories of the systems (5) and (7) the system of equations is obtained,

$$\begin{cases} p_2 \lambda_2 h^0 + Z_1(z_1) = Y_1 - \dfrac{dh_1}{dz_1} Z_1 - \dfrac{\partial h^0}{\partial z_1} Z_1 - \dfrac{\partial h^0}{\partial z_2} Z_2 \\ \lambda_2 h_2 + Z_2 = Y_2 - \dfrac{dh_2}{dz_1} Z_1 \end{cases} \tag{8}$$

To determine the series that intervene in the systems and the transformation, we will separate the coefficients of the powers of degree $p = (p_1, p_2)$ in the following two cases:

Case I): Doing in the system (9) $z_2 = 0$, is to say for the vector $p = (p_1, 0)$ results the system,

$$\begin{cases} Z_1(z_1) = Y_1(z_1 + h_1, h_2) - \dfrac{dh_1}{dz_1} Z_1 \\ \lambda_2 h_2 = Y_2(z_1 + h_1, h_2) - \dfrac{dh_2}{dz_1} Z_1 \end{cases} \tag{9}$$

The system (9) allows determining the series coefficients, Z_1, h_1 and h_2, where for being the resonant case $h_1 = 0$, and the remaining series are determined in a unique way.

$$Z_1(z_1) = \frac{a_3b_3 - a_2b_2}{a_3} z_1^2 - \frac{a_2b_2(a_3b_3 - a_2b_2)}{a_1a_3^2} z_1^3 + \dots$$

$$h_2(z_1) = -\frac{a_2(a_3b_3 - a_2b_2)}{a_1a_3^2} z_1^2 + \frac{2a_2^2(a_3 + b_2)(a_3b_3 - a_2b_2)^2}{a_1a_3^2} z_1^3 + \dots$$

Case II): For the case when $z_2 \neq 0$ of the system (8) it follows that,

$$\begin{cases} p_2\lambda_2 h^0 = Y_1(z_1 + h_1, z_2 + h_2) - \dfrac{\partial h^0}{\partial z_1} Z_1 - \dfrac{\partial h^0}{\partial z_2} Z_2 \\ Z_2 = Y_2(z_1 + h_1, h_2 + z_2) \end{cases} \tag{10}$$

Because the series from system (7) are known expressions, the system (10) allows you to calculate the series h^0 and Z_2.

$$Z_2(z_1, z_2) = \frac{a_2(a_3b_3 - a_2b_2)}{a_3^2} z_1^2 + \frac{a_2(a_3 + b_2)}{a_3} z_1z_2 - a_3z_2^2 + \dots$$

$$h^0(z_1, z_2) = -\frac{b_2}{a_1^2} z_1z_2 + \dots$$

This proves the existence of variable exchange. □

Theorem 3. *When $a_3b_3 < a_2b_2$, the solution of the system* (7) *is stable, otherwise it is inestable.*

Proof. Consider the Lyapunov function defined positive,

$$V(z_1, z_2) = \frac{1}{2}(z_1^2 + z_2^2)$$

The derivative along the trajectories of the system (7) has the following expression,

$$\frac{dV}{dt}(z_1, z_2) = \frac{a_3b_3 - a_2b_2}{a_3} z_1^3 - a_1z_2^2 + R(z_1, z_2).$$

Therefore, taking into account that the point P_3 is in the first quadrant, $\dfrac{dv(z_1, z_2)}{dt}$ is negative definite, because in function R we only have terms of a degree greater than 2 concerning z_1 and higher than the second with respect to z_2, therefore the system (3) is asymptotically stable. □

Remark 3. *In this case, the total concentration of healthy cells converges to the optimal concentration, however, the total concentration of the virus converges to an acceptable concentration; otherwise, the patient would enter a state of crisis at any time, in which case measures would have to be taken to avoid worse consequences. For the convergence of total concentrations to permissible values, the action of external agents is feasible, where the influence of physical exercise is included.*

Example 3. *Given the following system that verifies the conditions of the theorem 3*

$$\begin{cases} z_1' = -z_1 - z_2 - z_1 z_2 - 2z_1^2 \\ z_2' = 2z_1 z_2 + z_2^2 \end{cases}$$

is obtained:

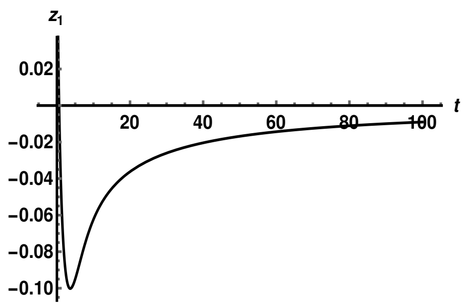

Figure 7: Graph of $z_1(t)$ in the **Example 3**

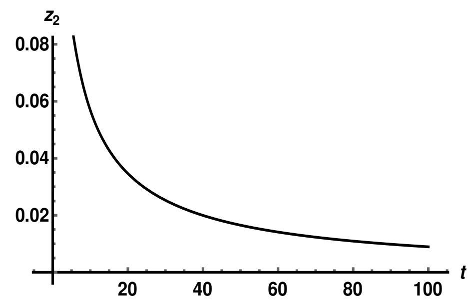

Figure 8: Graph of $z_2(t)$ in the **Example 3**

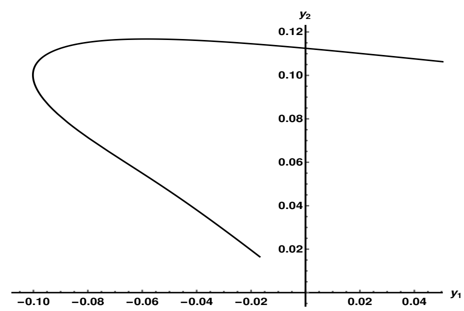

Figure 9: Graph of $z_1(t)$ vs $z_2(t)$ in the **Example 3**

As it is perceived in this system, the conditions of the theorems are fulfilled, and the convergence of the total concentrations to the optical concentrations is graphically demonstrated, this allows to see the reality of the theory developed in this paper.

Analysis at point P_4

For biological interest, let's assume the next conditions of existence $a_2b_1 > a_1b_3$, $a_1b_2 > a_3b_1$ and $a_2b_2 > a_3b_3$, which guarantees that P_4 is in the first quadrant. The transformation of coordinates,

$$\begin{cases} x_1 = u_1 + \dfrac{a_2b_1 - a_1b_3}{a_2b_2 - a_3b_3} \\ x_2 = u_2 + \dfrac{a_1b_2 - a_3b_1}{a_2b_2 - a_3b_3} \end{cases}$$

Reduces the system (3) in the next system,

$$\begin{cases} u_1' = -\dfrac{a_3\left(a_2b_1 - a_1b_3\right)}{a_2b_2 - a_3b_3}u_1 - \dfrac{a_2\left(a_2b_1 - a_1b_3\right)}{a_2b_2 - a_3b_3}u_2 - a_2u_1u_2 - a_3u_1^2 \\ u_2' = \dfrac{b_2\left(a_1b_2 - a_3b_1\right)}{a_2b_2 - a_3b_3}u_1 - \dfrac{b_3\left(a_3b_1 - a_1b_2\right)}{a_2b_2 - a_3b_3}u_2 + b_2u_1u_2 + b_3u_2^2 \end{cases} \tag{11}$$

Whose characteristic equation of the matrix of the linear part of the system (11) has the form,

$$\lambda^2 + \frac{a_3b_1(a_2+b_3) - a_1b_3(a_3+b_2)}{a_2b_2 - a_3b_3}\lambda + \frac{(a_1b_2 - a_3b_1)(a_2b_1 - a_1b_3)}{a_2b_2 - a_3b_3} = 0 \tag{12}$$

Theorem 4. *The equilibrium position P_4 it is asymptotically stable if and only if the condition $a_3b_1(a_2+b_3) > a_1b_3(a_3+b_2)$ is fulfilled.*

Proof. The proof of this theorem is obtained from the conditions of Hurwitz's theorem, by the conditions of existence $(a_1b_2 - a_3b_1) > 0$, $(a_2b_1 - a_1b_3) > 0$ and $(a_2b_2 - a_3b_3) > 0$, therefore $\dfrac{(a_1b_2 - a_3b_1)(a_2b_1 - a_1b_3)}{a_2b_2 - a_3b_3} > 0$, so if $a_3b_1(a_2+b_3) > a_1b_3(a_3+b_2)$ is fulfilled the coefficients of the characteristic equation are positive and the eigenvalues have negative real part. □

Example 4. *Given the following system that verifies the conditions of the theorem 4*

$$\begin{cases} u_1' = -0.0149754u_1 - 2.99507u_2 - 2u_1u_2 - 0.01u_1^2 \\ u_2' = 0.985025u_1 + 0.00492512u_2 + 0u_1u_2 + 0.01u_2^2 \end{cases}$$

is obtained:

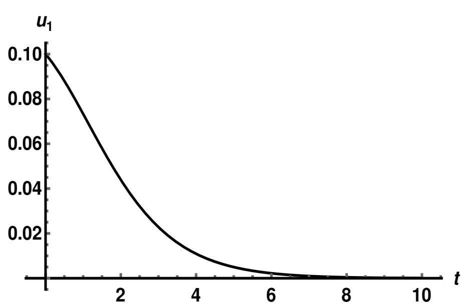

Figure 10: Graph of $u_1(t)$ in the **Example 3**

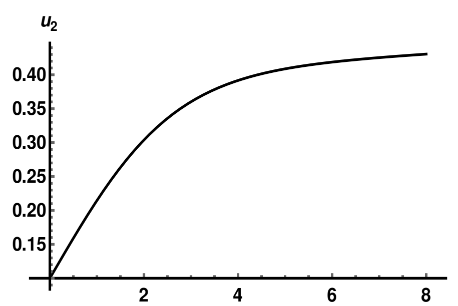

Figure 11: Graph of $u_2(t)$ in the **Example 3**

Remark 4. *It follows that if condition of* **Theorem 4** *are fulfilled, the concentration values of the virus and the cells will remain in the vicinity of the point P_4, and if the coordinates of that point are close to the optimal values of the concentrations, there will be no consequences for the patient, so the concentrations of viruses and cells would be close to the values allowed for the human body, so no there will be consequences, otherwise the necessary prophylactic measures must be taken to avoid a fatal outcome.*

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References

[1] Alak, K., Pilat, Kruger K. *Current Vol. Kanowledge and new chailengesin exercise immunology*, Deutsche Zeitschriftfur Sportmedizin, **70**(10) (2019), 250–260.

[2] Boch. W, *Immunsistem und Sport - E ine wechselhafte Bziehung*, Deutsche Zeitschriftfur Sportmedizin, **70**(10) (2019), 217–218.

[3] Ruiz Chaveco, A. I. et al., *Modelagem matemática de problemas diversos*, Curitiba: Appris, Brazil, 2018.

[4] Ruiz Chaveco, A. I. et al., *Applications of Differential Equations in Mathematical Modeling*, Curitiba: CRV, Brazil, 2016.

[5] Del Sol G. Y, *The interferon that treats covid-19*, `https://www.granma.cu`, 2020.

[6] Earn D. J., Rohani P., Bolker B. M., and Grenfell B. T., *A simple model for complex dynamical transitions in epidemics*, Science, **287** (2000), 667–670.

[7] Esteva L. and Vargas C., *Analysis of a dengue disease transmission model*, Math. Biosci., **150** (1998), 131–151.

[8] Greenhalgh. D and Das. R, *Some threshold and stability results for epidemic models with a density dependent death rate*, Theoret. Population Biol., **42** (1992), 130–151.

[9] Gripenberg. G, *On a nonlinear integral equation modelling an epidemic in an age-structured population*, J. Reine Angew. Math., **341** (1983), 147–158.

[10] Halloran. M. E, Watelet. L and Struchiner. C. J, *Epidemiological e[U+FB00]ects of vaccines with complex direct effects in an age-structured population*, Math. Biosci., **121** (1994), 193–225.

[11] Halloran. M. E, Cochi. S. L, Lieu. T. A, Wharton. M, and Fehrs. L, *Theoretical epidemiologic and morbidity effects of routine varicella immunization of preschool children in the United States*, Am. J. Epidemiol., **140** (1994), 81–104.

[12] Hamer. W. H, *Epidemic disease in England*, Lancet, **1** (1906), 733–739.

[13] Hethcote. H. W, *A thousand and one epidemic models, in Frontiers in Theoretical Biology*, Lecture Notes in Biomath. 100, Springer - Verlag, Berlin, 1994.

[14] Inkabi. S.E, Richter. P and Attakora. K, *Exercise immunology: involved componentes and varieties in diferente types of physical exercise*, Scientect Journal of Life Sciennces, **1**(1) (2017), 31–35.

[15] Hethcote. H. W, *Qualitative analysis of communicable disease models*, Math. Biosci., **28** (1976), 335–356.

[16] Janeway. C.A, Jr., et al., Immunobiology, Garland Science, 2005.

[17] Maitland. H. B and Maitland. M. C, *Cultivation of vaccinia virus without tissue culture*, Lancet., **212** (1928), 596–597. Doi: `10.1016/S0140-6736(00)84169-0`

[18] Mayer. G, *Immunology Chapter Two: Complement. Microbiology and Immunology*, On Line Textbook. USC School of Medicine, 2006.

[19] Montero. C. A, *Covid 19 with science in China*, On `http://www.cubadebate.cu`, 2020.

[20] Rodney. C. B. **Mathematical Modeling**, São Paulo, Brazil, 2004.

[21] Ruiz. A, et al., *Coronavirus, A Challenge For Sciences, Mathematical Modeling*, IOSR Journal of Mathematics (IOSR-JM), **16**(3) (2020), 28–34. Doi:`10.9790/5728-1603012834`

[22] Sen. G, *Viruses and interferons*, Annu. Rev. Microbiol. **55** (2001), 294–300.