Science Research
2023; 11(5): 111-116
http://www.sciencepublishinggroup.com/j/sr
doi: 10.11648/j.sr.20231105.13
ISSN: 2329-0935 (Print); ISSN: 2329-0927 (Online)

Periodic Model in General Toxin Elimination by the Liver and the Kidneys

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To cite this article:

Annia Valiente Monte de Oca, Sandy Sanchez Dominguez, Adolfo Arcenio Fernández García, Antonio Iván Ruiz Chaveco. Periodic Model in General Toxin Elimination by the Liver and the Kidneys. *Science Research*. Vol. 11, No. 5, 2023, pp. 111-116.
doi: 10.11648/j.sr.20231105.13

Received: July 11, 2023; **Accepted**: August 18, 2023; **Published**: October 9, 2023

Abstract: The problem of mathematical modeling has multiple applications, both in other sciences and in Mathematics itself; modeling in Physics and engineering is much more widespread, it is not the same in Medicine and Biology, where there are still few modeled processes; this is the fundamental purpose of this work. This article provides a general study of the kidneys, liver and circulatory system, their characteristics, their main functions, detailing some aspects of the toxin elimination process; the main diseases of these organs are indicated and how to predict these diseases. A compartmental model is created using a system of differential equations with periodic coefficients in general that simulates the toxin elimination process. The system is transformed into a system where the matrix of the linear part has constant coefficients, applying Floket theory; If a qualitative study is carried out, conditions are created that guarantee the stability of the organism's functioning while there is still toxin in our body, an example is given to show in practice what was demonstrated theoretically

Keywords: Liver, Kidneys, Circulatory System, Compartmental Model

1. Introduction

Mathematical modeling has been widely used to characterize different real-life processes, with emphasis here recently on the coexistence of species, disease transmission, development of epidemics, as well as infection processes. Many of these processes are characterized by having a periodic behavior; for this reason, in several cases, it is more effective to carry out this simulation using a system of differential equations with periodic coefficients, which is the objective of this work.

For the case in which only periodic coefficients appear in the perturbation function, the Analytical Theory of Differential Equations is applied to, once simplified, carry out the qualitative study and draw conclusions; in Sánchez S et al’ s study this procedure was applied to the Siklemia model [10, 14] deals with the pollution elimination model, [8] deals with the dynamics between infrared rays and the oxonium layer, and [9] deals with the coexistence between a predator and a mutualistic pair.

In this article, for the model that simulates the elimination of toxin by means of a system of periodic differential equations in general, the Flaquet Theory is applied to reduce this system to a system where the matrix of the linear part of the system has constant coefficients, proceeding similarly to [11] corresponding to the formation of polymers in the Siklemia model; as well as in [4] when simulating the elimination of pollution using two oxidation ponds.

The modeling of the problem of toxin elimination by means of a system of autonomous differential equations has already been treated before [7] where the model that simulates the process by means of a system of compartments in a similar way to how it was done in [1] was indicated, [2] and [3] when the problem of elimination of a drug in the human organism was treated in the autonomous case; as well as in [4, 14] in the non-autonomous case when the pollution elimination problem was researched.

Our objective is to expose a study some characteristics of the blood system, the liver and the kidneys; to make a simulation by means of a system of differential equations of the elimination of toxins by means of these organs; this simulation will be done using a compartmental model.

A compartment system essentially consists of a finite number of interconnected subsystems, called compartments, which exchange with each other and with the environment, amount of concentration of materials or substances, each compartment is defined by its physical properties; in particular, the dynamics of a drug in the human organism was treated; not all drugs have the same route, but in the case ingested in [1] sufficient conditions are given for their elimination; the case of an inhalable drug is treated in [3] and injectables in [2], in all cases, after the qualitative study of the system used in the modeling, the future situation of the process is predicted.

In what follows, some details regarding these compartments will be exposed, which will be used in this model in a similar way to how it was done in [7], but which we consider essential for understanding the work.

The liver is an appendage of the digestive system and is considered one of the largest organs in the human body. This organ is located in the upper region of the abdominal cavity, below the diaphragm and on the right side, has a reddish brown color and weighs, on average, 1.5 kg. In addition, it has a smooth surface and four lobes: direct, left, caudate and square. Each lobe is made up of several cells known as hepatocytes.

One of the important functions of the liver is the excretion of toxic substances. In addition, it is related to the production of red blood cells in the embryo, destroying these cells when they are old, in addition to synthesizing some clotting factors. Despite the various functions of the liver, one of the main and best known is the formation and secretion of bile, a substance formed mainly by bile acids, phospholipids, cholesterol, inorganic salts and bilirubin. This, in turn, is responsible for giving color to the bile and is the result of the destruction of red blood cells.

Bile basically has two primary functions: the excretion of some substances and the emulsion of fats, which helps in the digestion and absorption of lipids. In the bile are mainly eliminated toxins, substances present in drugs and bilirubin. This process is known as liver detoxification. When the liver is suffering from some disease, certain symptoms may arise. A person suffering from liver problems usually has jaundice, fatigue, nausea, vomiting, abdominal pain, bloating, among others. One of the best-known and most specific clinical pictures of liver disease is jaundice, which is characterized by causing yellowing of the skin, sclera of the eyes and mucous membranes as a result of a high concentration of bilirubin in the blood.

Cirrhosis causes fibrosis of the liver and the appearance of nodules. One of the major problems that affect the liver is cirrhosis, a degeneration and inflammation of the organ resulting from various problems. The most common cause of cirrhosis is alcoholism, but viral hepatitis and biliary disease can trigger the problem. It usually causes progressive fibrosis and the appearance of parenchymal nodules. Because it has vital functions, the liver is an extremely important organ for our survival. Therefore, when any symptoms appear, especially yellowish discoloration of the skin and eyes, seek medical attention immediately. Liver problems can be serious and even cause the patient's death [12, 13].

The kidneys are two organs located on either side of the spine, behind the last ribs, and measure approximately 12 centimeters. They weigh about 150 grams each. There are three main functions of the kidneys: eliminating toxins or waste resulting from body metabolism; maintain a constant water balance in the body, eliminating excess water, salts and electrolytes, thus preventing the appearance of edema and increased blood pressure; act as hormone-producing organs, erythropoietin, which participates in the formation of red blood cells, vitamin D, which helps to absorb calcium to strengthen the bones, and renin, which intervenes in the regulation of blood pressure.

Kidney disease can be silent, but there are cases where the individual feels some symptoms. The most known signs and symptoms are: high blood pressure, bloody urine, and foamy urine, presence of protein in the urine, edema, very clear urine output, anemia, pallor, tiredness, chest pain and drowsiness. When the disease is very advanced, there may be loss of appetite, nausea, vomiting, cramps, itching, memory loss, poor concentration, tremors, insomnia or drowsiness. [13].

When the kidneys no longer work properly, dialysis is required. If the patient does not get a kidney transplant, he will possibly have to undergo treatment for the rest of his life. Measures to take care of the kidneys: reduce the consumption of salt in food; drink plenty of water, maintain a healthy diet and exercise regularly; do not smoke and maintain an adequate weight; measure your blood pressure; Be careful when using any medication.

About 70% of the weight of an adult individual is represented by water. Apparently, such an amount of absorbed water would create for the kidneys the main purpose of continuously draining it from the body, as a mere innocuous residue. But, in fact, all this water that enters is necessary for organic functions. In addition to the water ingested with solid foods and liquids, man needs to supplement his needs with the ingestion of pure water, although the body itself produces water as an accidental by-product of biochemical activities. [12, 13].

For this very reason, water plays a fundamental role in the process of osmosis, which is the passage of solvent or other substances through semipermeable membranes that separate two solutions of unequal concentration. The more concentrated solution, which exerts greater pressure, attracts the solvent molecules, thus causing the migration of the latter, until the concentrations are balanced. As the body's cells are surrounded by semipermeable walls, the slag resulting from cellular functioning passes into the interstitial fluid that bathes the cells. In the same way, nutritive substances pass from the interstitial fluid to the interior of the cell.

Almost all of the water in the body is inside the cells. The blood contains only about 10% and the remainder is distributed in other fluids, especially the interstitial. In addition to this function of transporting essential substances to the organism, water also works as a temperature regulating element: perspiration moistens the skin, from where evaporation steals heat and lowers the surrounding temperature. For these reasons, water levels in the body are critical to physiological balance; but the work of the kidneys does not have the sole or main purpose of eliminating excess water, in the urine, water enters once again as a vehicle that allows the excretion of residues resulting from organic activity, and the case of urea "bagasse" final proteins used and reused by the body.

A third function of the kidneys consists in controlling the composition of the blood, with regard to the different inorganic salts, so important due to their osmotic function; this control of saline levels is done through the elimination of excesses, through urine; every minute, about 1/5 of the blood passes through the kidneys for filtering purposes, the filtered product, however, is still much less concentrated than urine. The kidney itself will make this filtrate pass through convoluted tubules, so that water and other compounds are reabsorbed; through this reabsorption, the kidneys help keep water and other necessary substances in the body.

The kidneys control the amount of water and salt in the body, eliminate toxins, help control high blood pressure, produce hormones that prevent anemia and bone decalcification, eliminate some medications and other ingested substances. The main risk factors for kidney diseases are: high blood pressure, diabetes, family history of kidney disease, history of kidney disease in the past [12, 13].

The circulatory or cardiovascular system, formed by the heart and blood vessels, is responsible for transporting nutrients and oxygen to the various parts of the body. Blood circulation corresponds to the entire course of the circulatory system that blood performs in the human body, so that in the complete course, the blood passes twice through the heart. These circuits are called small circulation and large circulation.

The small circulation or pulmonary circulation consists of the path that the blood travels from the heart to the lungs, and from the lungs to the heart; the heart, blood vessels and blood form the cardiovascular or circulatory system. Blood circulation allows the transport and distribution of nutrients, oxygen gas and hormones to the cells of various organs. Blood also carries metabolic waste so that it can be eliminated from the body. The great circulation or systemic circulation is the path of the blood, which leaves the heart to the other cells of the body and vice versa; in the heart, arterial blood from the lungs is pumped from the left atrium to the left ventricle; the ventricle passes to the aorta artery, which is responsible for transporting this blood to the various tissues of the body [6].

The circulatory system consists of the following components: blood, it is the bloodstream that oxygen and nutrients reach the cells; the heart works as a double pump, so that the left side pumps arterial blood to different parts of the body, while the right side pumps venous blood to the lungs; arteries are vessels of the circulatory system, which leave the heart and transport blood to other parts of the body; veins are vessels of the circulatory system, which carry blood back from body tissues to the heart; capillaries are microscopic ramifications of arteries and veins of the circulatory system, their walls have only one layer of cells, which allow the exchange of substances between blood and cells [6, 12].

Several works, books and articles referring to processes in human life are known; Among these books dedicated to mathematical modeling, we recommend the following [5, 6, 8] in which real problems are simulated by means of equations and systems of differential equations, where a certain treatment is also carried out to give conclusions of the processes.

In the research [5] different real-life problems are treated through equations and systems of differential equations, where examples are also developed and other problems and exercises are presented to be developed by the reader. The authors indicate a set of articles forming a collection of different problems that are modeled in different ways, but in general the qualitative and analytical theory of differential equations is used both in the autonomous and non-autonomous case.

2. Model Formulation

For the elaboration of the model we will consider the basic principles that take place in the real phenomenon; it is known that the liver has the function of eliminating certain toxins received directly by the ingested foods or drugs, part of these can pass to the blood system, and from this later to the kidneys where a large part of these can be eliminated through the urine once once the kidneys have been filtered.

To carry out the simulation by means of a system of differential equations, consider the following compartments, compartment one the liver, compartment two the blood system, and compartment three the kidneys; the following notations will be used,

1) $\tilde{x}_1$ the total density of toxins in the compartment I.
2) $\tilde{x}_2$ the total density of toxins in the compartment II.
3) $\tilde{x}_3$ the total density of toxins in the compartment III.

Furthermore, they will be denoted by $\bar{x}_1$, $\bar{x}_2$, and $\bar{x}_3$ the admissible values of toxins in compartments I, II III respectively.

Here the variables will be introduced x_1, x_2, and x_3 defined as follows: $x_1 = \tilde{x}_1 - \bar{x}_1$, $x_2 = \tilde{x}_2 - \bar{x}_2$, and $x_3 = \tilde{x}_3 - \bar{x}_3$, so if $\bar{x}_1 \to 0$, $\bar{x}_2 \to 0$, and $\bar{x}_3 \to 0$ the following conditions would be met, $\tilde{x}_1 \to \bar{x}_1$, $\tilde{x}_2 \to \bar{x}_2$, and $\tilde{x}_3 \to \bar{x}_3$, which would constitute the main objective of this work. It will be denoted by the term $-a_{ij}(t)x_i$ o element step x_i from compartment i to compartment j, and with a positive sign the arrival at compartment j.

Considering the above principles the mathematical modeling of the toxin elimination process has the following form,

$$\begin{cases} x_1' = (a_{11}(t) - a_{12}(t))x_1 + a_{21}(t)x_2 + X_1(t, x_1, x_2, x_3) \\ x_2' = a_{12}x_1 + (a_{22}(t) - a_{21}(t) - a_{23}(t))x_2 + c_{32}(t)x_3 + X_2(t, x_1, x_2, x_3) \\ x_3' = a_{23}(t)x_2 + (a_{33}(t) - a_{32}(t))x_3 + X_3(t, x_1, x_2, x_3) \end{cases} \quad (1)$$

If the coefficient $a_{ii} \neq 0$ indicates that in compartment i there were already toxins before the passage of another compartment; the functions $X_i(t, x_1, x_2, x_3)$, (i=1,2,3) admit the following development,

$$X_i(t, x_1, x_2, x_3) = \sum_{|p|\geq 2} X_i^{(p)}(t) x_1^{p_1} x_2^{p_2} x_3^{p_3}, \text{ (i=1, 2, 3)} \quad (2)$$

System (2) can be written in vector form as follows:

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

Where $x = col(x_1, x_2, x_3)$, $X(t, x) = col(X_1, X_2, X_3)$ and A (t) is the matrix of the linear part

$$A(t) = \begin{bmatrix} a_1(t) & a_2(t) & a_3(t) \\ b_1(t) & b_2(t) & b_3(t) \\ c_1(t) & c_2(t) & c_3(t) \end{bmatrix}$$

Suppose that the matrix $A(t)$ is periodical ω is to say whether they satisfy the relations,

$$A(t + \omega) = A(t) \text{ and } X_i^{(p)}(t + \omega) = X_i^{(p)}(t)$$

Be beyond the linear system,

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

That is to say the coefficients of the system are ω-periodic functions; the study of systems (3) with variable but periodic coefficients should be reduced, at least theoretically, to a system where the coefficients of matrix A are constant, Bounonov M. (1998). Floket's theory provides the theoretical foundations for a type (3) system.

The procedure that will be used from this moment on corresponds to how it was done in [4, 11] when searching for problems with these characteristics will be denotes for Φ to the fundamental matrix of the system (4), and by B a matrix related to the previous one to which is a constant matrix, such that $\varphi(t + \omega) = \varphi(t)B$, such that there is a matrix R for which.

$R = \omega^{-1} \ln B$, define the function $G(t) = \varphi(t)e^{-Rt}$. These expressions will be used below in the demonstration of the fundamental result of this work.

Theorem 1: The transformation of coordinates

$$x = G(t)y \quad (5)$$

Reduces the system (3) in the system

$$y' = Ry + Y(t, y) \quad (6)$$

Proof: Deriving the transformation (5) along the trajectory of systems (3) and (6) we have that,

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

Since x is a solution of (3) and Φ is a fundamental matrix of the system (4), substituting the corresponding expressions, we can write,

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

Reducing like terms, we have

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

Isolating y' in the previous expression, we have:

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

Doing,

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

It is concluded that,

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

Thus, theorem (1) is proved.

The own values $\mu_1, \ldots, \mu_3$ of matrix B represent the multipliers of the system (4), these values being in general complex numbers and the eigenvalues $\lambda_1, \ldots, \lambda_3$ of the matrix R of the system (6) are called the characteristic index of the system (4).

From the matrix R definition, we get:

$$\lambda_i = ln\mu_i, .(i = 1,2,3)$$

By the definition of logarithm of a complex number, we get that,

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

Theorem 2: If $0 < |\mu_i| < 1, (i = 1,2,3)$ if you have to $Re\lambda_i < 0$ $(i = 1,2,3)$ then the equilibrium position of system (4) is asymptotically stable.

Demonstration: As a consequence of theorem 1, system (3) is equivalent to system (6) and the eigenvalues of the matrix R are $\lambda_1, \ldots, \lambda_3$ where,

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

How do we have to, $0 < |\mu_i| < 1$ like this, $Re\lambda_i < 0(i = 1,2,3)$, which completes the proof of theorem 2 using the first approximation method.

Observation:

1) Nothing can be concluded if $|\mu_i| = 1$ for some $(i = 1,2,3)$, and the remainder such that $0 < |\mu_j| < 1 \ (i \neq j)$ because there is some λ_i with $Re\lambda_i = 0$ and the others with a negative real part, this constitutes a doubtful case and the stability of the null solution has to be determined using the polymerization function.

2) It makes no real sense if $|\mu_i| = 0$ for some $(i = 1,2,3)$.

3) If $1 < |\mu_j| < \infty$ for some $(i = 1, 2, 3)$, so in that case $Re\lambda_i > 0$ para algum $(i = 1, 2, 3)$ and so system (5) is unstable.

If the variation of toxin concentrations in each of the compartments only depends on its own concentration, then system (3) would take the form,

$$\begin{cases} x' = a_1(t)x + P_1(t,x,y) \\ y' = b_1(t)y + P_2(t,x,y) \\ z' = a_3(t)x + b_3(t)y \end{cases} \tag{7}$$

Next, an example of the system is given as the form of the system (7) where the different elements previously demonstrated are indicated.

Example: Suppose there is no transfer of toxin from the liver to the blood or from the blood to the liver, as well as from the blood to the kidneys; be the system,

$$\begin{cases} x' = a_1(t)x + P_1(t,x,y) \\ y' = b_1(t)y + P_2(t,x,y) \\ z' = a_3(t)x + b_3(t)y \end{cases}$$

In this system, you have to

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

This matrix satisfies the relation,

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

This means that it is a period periodic matrix. In this case, the fundamental matrix of the corresponding homogeneous system is,

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

Essa matriz é tal que,

$$\phi(t + 2\pi) = \phi(t)B$$

Being B the following matrix,

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

In this example the multipliers are $\mu_1 = 0$, $\mu_2 = 1$ and $\mu_3 = e^{-2n}$ in this way, the example falls into the second case, so the value of is not defined, this result is logical, due to the characteristics of the system; because the determinant of the matrix is equal to zero.

3. Conclusion

1) The problem of eliminating toxins through the kidneys and liver in the human body is a topical problem and of great importance, as this allows us to eliminate impurities from our body and improve its functioning.
2) Diseases of the liver and kidneys must be avoided, as these would impede the proper functioning of these organs and the efficiency of their functions.
3) Theorem 1 gives the technique that allows the transformation of a periodic system in general into a system where the matrix of the linear part has constant coefficients, which allows drawing practical conclusions regarding the model.
4) Theorem 2 gives sufficient conditions for the stability of the system's null solution, which would allow reaching conclusions regarding the presence of toxins in the human body.
5) If $0 < |\mu_i| < 1$, $(i = 1,2,3)$ then the equilibrium position of the system (4) is asymptotically stable, which allows us to state that the concentrations of toxins in the body will decrease continuously to admissible values, otherwise it is not possible to draw conclusions or the concentrations of toxins will have values higher than allowed.

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