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Kinetics of nanoparticles in sanguinean torrent by approximation, Womersley flow

Cinética de nanopartículas en torrente sanguíneo por aproximación, flujo de Womersley

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INFORMACIÓN DEL ARTÍCULO

Historia del artículo:
Enviado: 25/11/2017
Recibido: 12/12/2018
Aceptado: 02/01/2019

Keywords:
Blood flow
Nanoparticles
Numeric

ABSTRACT

Nowadays, cancer is one of the most important morbidity and mortality factors in the world. For these reasons, efforts have been made to optimize the treatments that are used by specialists in the oncology area. One of the main difficulties is the lack of mathematical and statistical models that allow to characterize the performance of the treatments; one of these innovative treatment trends consists of the use of magnetic nanoparticles which are incorporated into the bloodstream either in order to diagnose or transport medications to the affected areas. This paper presents the process of estimating local minimums for a particular case of a function in R^3 –defined by parameters r and t– which allows modeling the kinetics of nanoparticles.

Palabras clave:
Flujo sanguíneo
Nanopartículas
Numérico

RESUMEN

En la actualidad el cáncer es uno de los factores de mayor morbilidad y mortalidad a nivel mundial, por tal razón se han aunado esfuerzos con el fin de optimizar los tratamientos que son usados por especialistas en el área oncológica. Una de las principales dificultades radica en la carencia de modelos matemáticos y estadísticos que permitan caracterizar el desempeño de los tratamientos; en este sentido, una de las tendencias innovadoras de tratamiento consiste en emplear nanopartículas magnéticas que se incorporan al torrente sanguíneo ya sea con el fin de diagnosticar o transportar medicamentos a las zonas afectadas. En este artículo se presenta el proceso de estimación de mínimos locales para un caso particular de una función en R^3 –definida por parámetros r y t– que permite modelar la cinética de las nanopartículas.

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Cite this article as: L. H. Camargo-Casallas; J. F. Pantoja-Benavides; D. J. Rodríguez-Patarroyo, “Kinetics of nanoparticles in sanguinean torrent by approximation, Womersley flow”, *Visión electrónica, algo más que un estado sólido*, vol. 13, no. 1, january-june 2019, pp. 33-38 DOI: *https://doi.org/10.14483/22484728.14409*

1. Introduction

One of the promising techniques for the treatment of cancer are magnetic nanoparticles [1], [2], [3], in order to deliver medication in a targeted manner [4] and reduce the side effects of treatment [5]. To optimize the number of nanoparticles that effectively reach the cancerous tumor, it is necessary to understand the kinetics of the nanoparticles within the bloodstream.

In this article, the general flow model proposed by Womersley is presented, then the conditions and parameters that were determined for the optimization process are described, in order to simplify the equation in terms of the parameters *u (r, t)* it permits The Newton-Rapson method estimating local extreme values finally results and conclusions are shown.

The kinetics that follow the displacement of the nanoparticles is determined by a set of parameters and variables that are involved according to the conditions of the blood flow. In this sense, numerical models have been developed that solve the equations that govern the dynamics [1], [2], [3].

According to Calvo [6], the flow of Womersley (John Ronald Womersley (1907-1958)) is a case with analytical solution for Stokes flow is applicable since the blood flow is pulsatile. This allows checking the operation of the pressure, considering that the element used in the pressure is a degree of internal freedom that condenses and the comparison of the results obtained with the analytical is correct. What is done is to impose a normal tension, but in a fluid in motion the normal tensions are practically equal to the pressure and in a flow at rest coincide [6].

The initial conditions for analyzing the system as a Womersley flow are as follows: the pressure is assumed to be uniform with a sinusoidal variation *P=10cos(w t)*, with values P0=10, the frequency w is left as a variable to modulate the different cases, at the output no pressure is imposed. The geometric characteristics are L=10, and, R=1 the density is Pf=1.05 and the viscosity u=0.04 [2].

Given the initial values, the pressure gradient in the axial direction is:

$$\frac{\partial p}{\partial z} = \frac{0 - P_0 \cos(\omega t)}{L} = \frac{0 - 10\cos(\omega t)}{10} = -\cos(\omega t) \quad (1)$$

Where, p is the pressure, z the direction of flow. The shape of the velocity profile depends on the Womersley parameter, which is dimensionless, and denoting it with α is defined as:

$$\alpha = R\sqrt{\frac{\rho_f \omega}{\mu}} \quad (2)$$

The solution of the flow of Womersley provides the law of speeds and the flow in time. For the speed of the mentioned law is:

$$u(r,t) = R_e\left\{-\frac{iP_0}{\rho_f \omega}\left(1 - \frac{J_0(i^{3/2}\alpha r / R)}{J_0\left(i^{3/2}\alpha\right)}\right)e^{i\omega t}\right\} \quad (3)$$

Where J_0 is the Bessel function of complex order argument 0, $i = \sqrt{-1}$ is the imaginary unit, *r* is the radial coordinate and R_e means that the real part of the resulting complex number is taken.

The purpose of this is to determine the blood flow profile from the solutions of the Navier Stokes equation in particular the first order solution called Womersley flow.

2. Methodology

The analytical solution has been programmed to obtain the velocity values and thus compare them with the computational solution of the element. To calculate the function of Bessel J_0 in this work we have used:

$$J_0(z) = \sum_{k=0}^{\infty}(-1)^k \frac{\left(\frac{1}{4}z^2\right)^k}{(k!)^2} \quad (4)$$

Taking into account that the flow of Womersley generates an analytical solution, an optimization analysis will be performed for mentioned flow, by using the Newton-Rahpson method for two variables, which in this case are *r* and *t* This method was applied in the resulting system of equations when finding the partial derivative with respect to *r* and *t* of the function *u(r,t).*

To optimize the flow behavior of Womersley it is necessary to perform a polynomial interpolation that allows the optimization process through the Newton-Rapson method.

It consists of finding a function that approximates or interpolates a set of points initially given, or perhaps obtained experimentally, for which it is necessary to find a generic behavior, that is, given n points in the Cartesian plane, you want to find the function that interpolates them or the curve that best suits them, so that the characteristics of the points can be extended to the other elements of a real interval that contain precisely preimages of mentioned points.

There are several methods according to the case, for example, linear, quadratic and cubic interpolation among the most used. In the present work, the cubic approximation by least squares was analyzed. If a set of n points $P(x_i, y_i)$ are next to a cubic curve $f(x) = a_0 + a_1x + a_2x^2 + a_3x^3$, for the point-to-point estimate there is

$$y_i = a_0 + a_1x_i + a_2x_i^2 + a_3x_i^3 + e_i\,, \tag{5}$$

That is to say,

$$e_i = y_i - a_0 - a_1x_i - a_2x_i^2 - a_3x_i^3 \tag{6}$$

And a least squares estimation of errors is made.

$$S = \sum_{i=1}^{n} e_i^2 = \sum_{i=1}^{n} \left(y_i - a_0 - a_1x_i - a_2x_i^2 - a_3x_i^3 \right)^2 \tag{7}$$

If the partial derivatives are equated with respect to each of the polynomial coefficients, a system of equations of four unknowns and four equations are obtained, and the solution of these correspond to the estimates of $a_0, a_1, a_2\ y\ a_3$, [5].

The method of Newton is a method based on quadratic approximations of a function given a λ_k. This quadratic approximation is given by [1]

$$q(\lambda) = \theta(\lambda_k) + \theta'(\lambda_k)(\lambda - \lambda_k) + \frac{1}{2}\theta''(\lambda_k)(\lambda - \lambda_k)^2 \tag{8}$$

The point λ_{k+1} is taken from the point where the derivate q is equal zero. The following step $\theta'(\lambda_k) + \theta''(\lambda_k)(\lambda - \lambda_k) = 0$, so:

$$\lambda_{k+1} = \lambda_k - \frac{\theta'(\lambda_k)}{\theta''(\lambda_k)} \tag{9}$$

The process ends when $|\lambda_{k+1} - \lambda_k| \le \varepsilon$ or when $|\theta'(\lambda_k)| \le \varepsilon$, where ε is a predetermined scalar.

The method of Newton is a numeric method that is generally used to find the zeros of a real function $f: Rn \to R$ continuous and differentiable I all its domain, the method consists of three phases.

Initial phase: select a starting point x_k, that belongs to domain R^n, determine $\varepsilon \ge 0$. In the second *phase* $\nabla f(x_k)$ is calculated, if $\|\nabla f(x_k)\| \le \varepsilon$ ends the process, on the contrary, $\nabla^2 f(x_k)$ is calculated and $(\nabla^2 f(x_k))^{-1}$. In the final phase $x_{k+1} = x_k - (\nabla^2 f(x_k))^{-1} \nabla f(x_k)$ is calculated and $k = k+1$ started to the initial phase to do the iterative process.

3. Results

To simplify $u(r,t)$ in terms of r and t it is proceeded to the analysis of each part that composes it like this:

$$u(r,t) = R_e \left\{ -\frac{iP_0}{\rho_f \omega} \left(1 - \frac{J_0(i^{3/2}\alpha r / R)}{J_0(i^{3/2}\alpha)} \right) e^{i\omega t} \right\} \tag{10}$$

When the base parameters for the optimization process are introduced, equation 10 is transformed:

$$u(r,t) = R_e \left\{ -Ai \left(1 - \frac{J_0(z)}{C} \right) D \right\} \tag{11}$$

In this way the objective function of the optimization process consists of the parameters A, J_0, C, D, for the case of study, the following parameters are set: initial pressure $P_0 = 10$, density $\rho_f = 1.05$, frequency $\omega = 7.54\ rad/seg$ and the viscosity $\mu = 0{,}04\ pois$. In this way the Womersley parameter (equation 2) $\alpha = 14{,}06858202$. For the case $J_0(z)$, the adjustment process is done to a polynomial of order three, to have a function that approximates $J_0 = 10$ for the values of z. This process is done for the values of z between 0 and 2,4. So it is obtained that:

$$J_0[(-9{,}9480 + 9{,}9480i)r]\,. \tag{12}$$

As it is required that in $u(r,t)$ being a function that depends on continuous functions in terms of $r\ y\ t$, z is interpolated for function of Bessel $J_0(z)$ by means of a polynomial function. In this way it is determined that:

$$J_0(z) = 0.0567z^3 - 0.3229z^2 + 0.0331z + 0.9971 \tag{13}$$

Solving and simplifying with respect to z it is obtained that:

$$J_0(r) = 0,9971 - (0.3293 - 0,3293i)r + (63,9101i)r^2 + (111,64 + 111,64i)r^3 \tag{14}$$

To D, it is obtained that $D = e^{(i\omega t)} = \cos(\omega t) + isen(\omega t)$, to A it is obtained that $A = -\frac{P_0}{\rho_f \omega} = -1,2631$.

To C: $J_o(i^{3/2}\alpha) = J_o(i^{3/2}14,0686) = J_o(-9,9480 + 9,9480i)$, such as $J_o(z) = \sum_{k=0}^{\infty} (-1)^k \frac{\left(\frac{1}{4}z^2\right)^k}{(k!)^2}$, it is obtained:

$$J_o(z) = \sum_{k=0}^{\infty} (-1)^k \frac{\left(\frac{1}{4}(-9,9480 + 9,9480i)^2\right)^k}{(k!)^2} = -2220,85 - 276,576i \tag{15}$$

In this way $u(r,t)$ it is written as:

$$u(r,t) = R_e\left\{-1,2631i\left(1 - \frac{0,9971 - (0,3293 - 0,3293i)r + (63,9101)r^2 + (111,64 + 111,64i)r^3}{-2220,85 - 276,576i}\right)\right\} \tag{16}$$

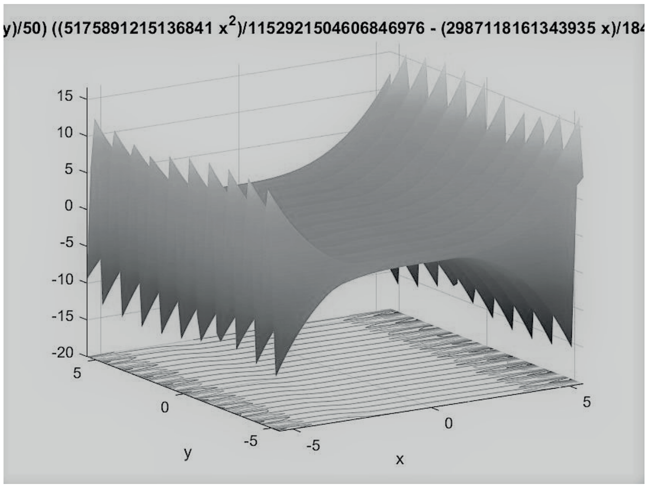
Taking the real part of the function the function is obtained to be minimized using the method of Newton.

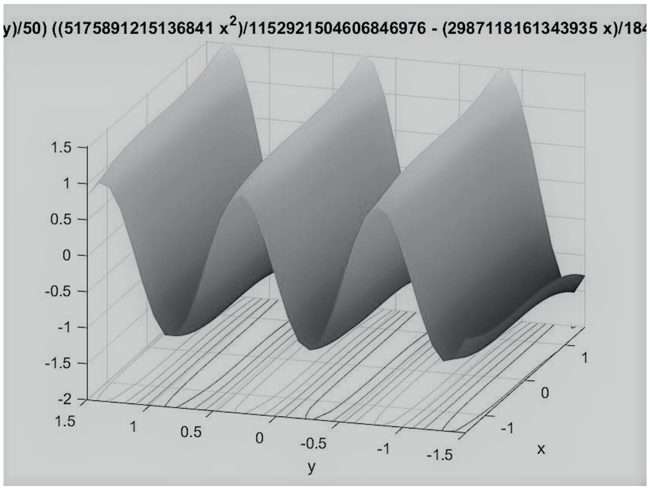
$$\begin{aligned} u(r,t) = &\left(0,0549r^3 + 0,0359r^2 + 0,0002r - 0,00007\right)\cos(5,74t) \\ &-(-0,07059r^3 - 0,00449r^2 + 0,000162r - 1,2637)sen(5,74t) \end{aligned} \tag{17}$$

The graphic situation of the objective function is shown below, in Figure 1, the trend of the minimum values that occur between (-5, 5) and between (-1.5, 1.5) can be observed respectively.

In Figure 2 a filter by zooming in the interval (0, 1) is obtained where the start value is chosen, x_k the iteration process of the function *u(r,t)*, where the existence of infinite minimum values for its estimation is better observed.

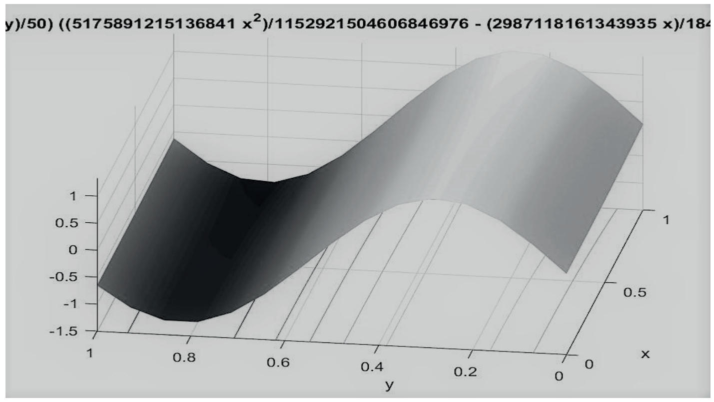
Figure 1. Solutions achieved by iterations.





Source: own.

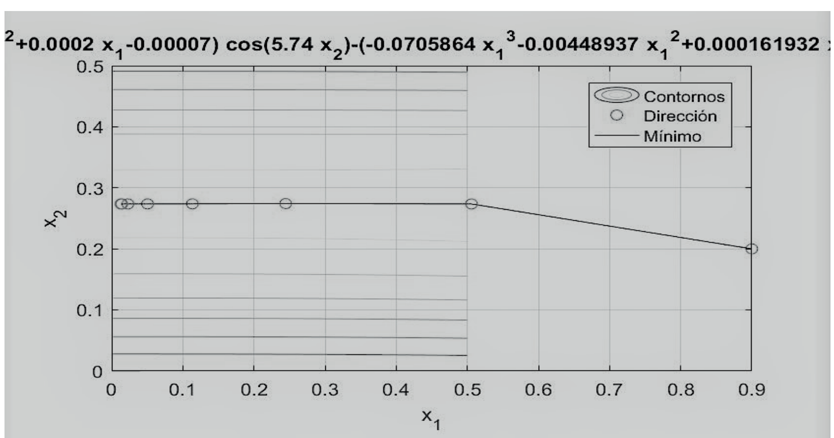
Figure 2. Solutions achieved by iterations between (0,1).



Source: own.

As it can be seen in Figure 2, of the function *u(r,t)* it has infinite minimum values. The method will be applied to the minimum value (0.013, 0.274), x_k are determined as (0.9, 0.2) respectively as start values, with, $\varepsilon = 1*10^{-10}$ and with a maximum of 9 iterations, the result is summarized with a value of the objective function *u(r,t) = 1,2636*. In the Figure 3, the trajectory followed in the process of estimating a minimum value in each of the iterations is shown.

Figure 3. Representation of the trajectory followed by the iteration process.



Source: own.

It is clear that the number of zeros allows to determine the conditions in which the flow is stationary. This can be expressed as the superposition of polynomials independent of time, each corresponding to each stationary. This behavior is observed, for example, in the solution of the wave equations, where a solution can be expanded in a superposition of stationary solutions independent of time.

4. Conclusions

The Womersley flow was optimized to determine the degree of convergence. This optimization process was carried out by using the Newton-Rapson method. Due to the fact that the complexity of the problem, it was required to apply a polynomial approximation of cubic order and this was the one used for the process of optimizing. In order for the method of Newton to converge quickly, and to obtain a better estimation of and a lower requirement in computational process.

The techniques through the modeling of continuous functions are being a promising alternative for the treatment of cancer with magnetic nanoparticles, in order to provide medication in a targeted manner and reduce the side effects of treatment by invasive procedures such as chemotherapy. To optimize the number of nanoparticles that effectively reach the cancerous tumor, it is necessary to understand the kinetics of the nanoparticles within the bloodstream.

The kinetics that follow the displacement of nanoparticles is determined by a set of parameters and variables, in this sense numerical models have been developed that solve the equations that govern such kinetics.

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