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Kinetic model of the dispersive interaction between a particle with an erythrocyte

Modelo cinético de la interacción dispersiva entre una partícula con un eritrocito

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ABSTRACT:

A kinetic model of interaction between nanomicroparticle (NMP) and an erythrocyte (RC) was developed considering an elastic type collision, taking into account that the main dispersion center in the delivery of drugs through the bloodstream are the RC. For the analysis of the model, three cases were considered where the position and speed of the MPN were varied. In case 1, the initial position of the MPN was varied with respect to the x axis; In case 2, there was a variation of the position with respect to the y axis, and finally, the speed with respect to the x axis was varied. This study allowed calculating the angle of dispersion (α) based on the impact parameter (s) with respect to the axis of symmetry of the RC. It was verified that in frontal collisions with s values close to the center of the axis of symmetry, the NMP presents the same incident trajectory, with a null angle of dispersion. In an oblique collision, the dispersion is greater and dependent on the initial position and the speed in its Cartesian components, thus a dependency with respect to the initial position is identified, as well as the direction of movement given by the speed components, which it is reflected in the variation of the angle of dispersion.

Palabras clave:
Nanoparticle delivery, Interacción partícula-Eritrocito, dispersión, Colisión elástica.

RESUMEN

Se desarrolló un modelo cinético de interacción entre nanomicropartícula (NMP) y un eritrocito (RC) considerando una colisión de tipo elástica, teniendo en cuenta que el principal centro de dispersión en la entrega de medicamentos por el torrente sanguíneo son los RC. Para el análisis del modelo se consideró tres casos donde se varió la posición y velocidad de la NMP. En el caso 1 se varió la posición inicial de la NMP con respecto al eje x; en el caso 2 hubo variación de la posición respecto al eje y, por último, se varió la velocidad con respecto al eje x. Este estudio permitió calcular el ángulo de dispersión (α) en función del parámetro de impacto (s) respecto al eje de simetría del RC. Se verificó que en colisiones frontales con valores de s cercanos al centro del eje de simetría, la NMP presenta la misma trayectoria incidente, con un ángulo de dispersión nulo. En una colisión oblicua la dispersión es mayor y dependiente de la posición inicial y la velocidad en sus componentes cartesianos, de esta forma se identifica una dependencia respecto a la posición inicial, así como el sentido del movimiento dado por las componentes de la velocidad, que se ve reflejado en la variación del ángulo de dispersión.

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1. Introduction

The distributing magnetic technique drugs in the bloodstream is a therapeutic method where the medication is distributed by means of particles of nanometric or micrometric size (MPN). The purpose is to direct the medication only to the target cells, reducing the effect on healthy tissue. These particles are constituted by a solid nucleus (magnetic material) with a surface generally covered with porous (Bio-polymers), where the medicine is inserted, its magnetic properties allow directing them through external fields and is known as Magnetic Drug Targeting, with its acronym in English MDT [1-6] . When the NMPs come into contact with the blood flow, a part of the particles has dispersion towards the bloodstream wall, this behavior reduces the effectiveness of the treatment, due to the reduction in the number of NMPs that effectively reach the target .[7-11]

Theoretical and experimental studies have shown that some important factors that affect the kinetics of NMPs are due to: the pulsatile movement of the blood flow, the interaction between NMP-erythrocyte and the deformations that erythrocytes (RC)[12-21] , it should be borne in mind that the most relevant dispersive centers in the kinetic of the trajectory of the NMP are the RC.

This paper shows the results of an analytical model development, in order to study the dispersion between NMP and RC considering, in the first approach, a null magnetic field and plasma as a Newtonian fluid. For this aim, the angle of dispersion of the NMP is related to an elastic collision with an RC.

2. Methodology

In this paper, blood plasma is approached as a laminar flow [22] , the RC as a non-deformable solid aggregate [23 26] , and the NMP in a spherical, rigid, porous and of a fixed diameter significantly smaller than the diameter of the RC[27][28],which determines a single point of impact between the NMP and the RC. Geometrically the RC presents a biconcave axial symmetry, the parametric function defined by the erythrocyte is taken from statistical studies carried out by Evans and Fung, which describes the RC model in non-deformable conditions[29], (1):

(1)

$$z = \pm 0{,}5\,(r_o)\left[1-\frac{x^2+y^2}{r_o^2}\right]^{1/2}\left[c_o + c_1\frac{x^2+y^2}{r_o^2} + c_2\left(\frac{x^2+y^2}{r_o^2}\right)^2\right]$$

Where, $r_o = 3{,}91\mu m$, $c_o = 0{,}207161$, $c_1 = 2{,}002558$, $c_2 = -1{,}122762$.

β

This equation gives information on the RC form, which is divided into two symmetrical parts along the plane *(x,y)* according to the erythrocyte reference system *(rs1)* The constants values were taken specifically from the work done by Rie Higuchi et al.[29], [30], where r_o corresponds to the direction on the axial axis (see Figure 1).

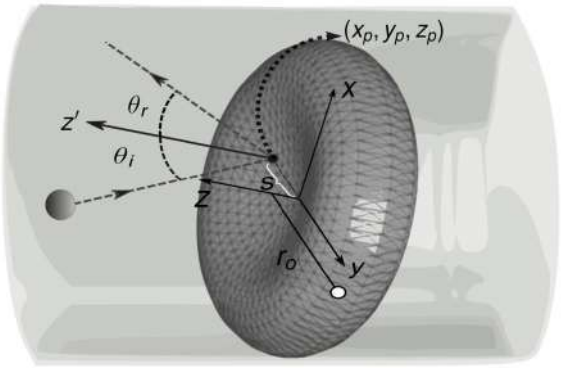

Figure 1. Reference frame *rs1* of the RC geometric model. Source: own.

A trajectory model of an NMP was developed when interacting with a RC in rest condition, which allows determining the profiles of the direction of exit of the trajectory, with a reference frame with respect to the NMP-RC interaction defined by, the plane tangent *(τ)* and the normal vector *(η)* to the surface, denoted *rs2* The angle of dispersion is related by an impact parameter, which corresponds to the distance between the contact point and the z-axis (see Figure 1 y 2).

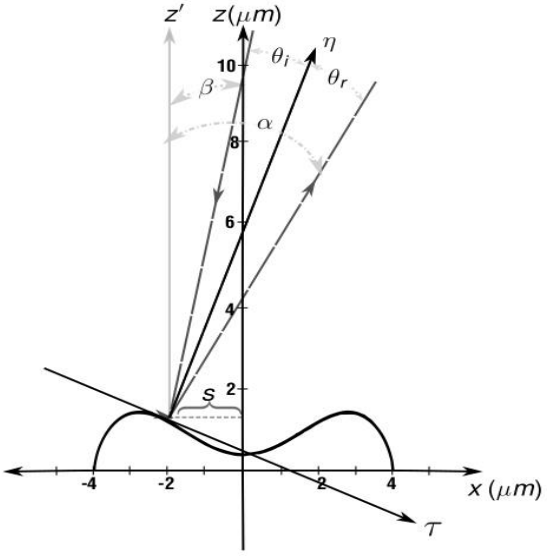

Figure. Representation, angles of incidence θ_i and dispersion θ_r corresponding to the normal vector with respect to the tangent line (η, τ) as well as the incident angle β and dispersion (α) with respect to the axis of symmetry of the erythrocyte. Source: own.

The linear trajectory with constant velocity that collides on the surface of the RC is described by (2).

$$\vec{r} = (v_{ox}t + x_o, v_{oy}t + y_o, v_{oz}t + z_o) \quad (2)$$

To find the point of impact (x_p, y_p, z_p) the vector components of the parametric equation (1) are matched with the trajectory of the particle (2), where a non-linear order 2 equation is obtained, which was solved by methods numerical in terms of parameter τ

$$v_{oz}t + z_o = 0{,}5\,(r_o)$$
$$\left[1 - \frac{(v_{ox}t+x_o)^2+(v_{oy}t+y_o)^2}{r_o^2}\right]^{\frac{1}{2}}\left[c_o + c_1\frac{(v_{ox}t+x_o)^2+(v_{oy}t+y_o)^2}{r_o^2} + \right. \quad (3)$$
$$\left. c_2\left(\frac{(v_{ox}t+x_o)^2+(v_{oy}t+y_o)^2}{r_o^2}\right)^2\right]$$

The *rs2* allows to obtain the normal vector to the tangent plane of parameters (η, τ) to calculate the angles θ_i and θ_r from *rs1* the incident angle β and the dispersion angle α are defined as shown in Figure 2.
For the analysis of the model, 3 particular cases were studied as shown in the following table

Variable	Case 1		Case 2	Case 3
	Evento 1	Evento 2		
$x_o\ (\mu m)$	$(-3{,}9\ ;\ 3{,}9)$	$(-3{,}9\ ;\ 3{,}9)$	0	$(-3{,}9\ ;\ 3{,}9)$
$y_o\ (\mu m)$	0	1	0	0
$z_o\ (\mu m)$	10	10	10	10
$v_{xo}\left(\frac{\mu m}{s}\right)$	0	0	$(-2{,}6\ ;\ 2{,}6)$	$-2{,}6$
$v_{yo}\left(\frac{\mu m}{s}\right)$ μm	0	0	0	0
$v_{zo}\left(\frac{}{s}\right)$	-10	-10	-10	$-2{,}6$

Table. Initial position and speed parameter. Source: own.

The first corresponds to the variation of the initial position (x_o, y_o, z_o) with respect to the x axis; the second presents the initial parameters of the first with variation of the position with respect to the *y* axis and the third the variation of the speed with respect to the *x* axis; of which the general description of the variation of the angle of dispersion according to the impact parameter, Figure 3 was obtained.

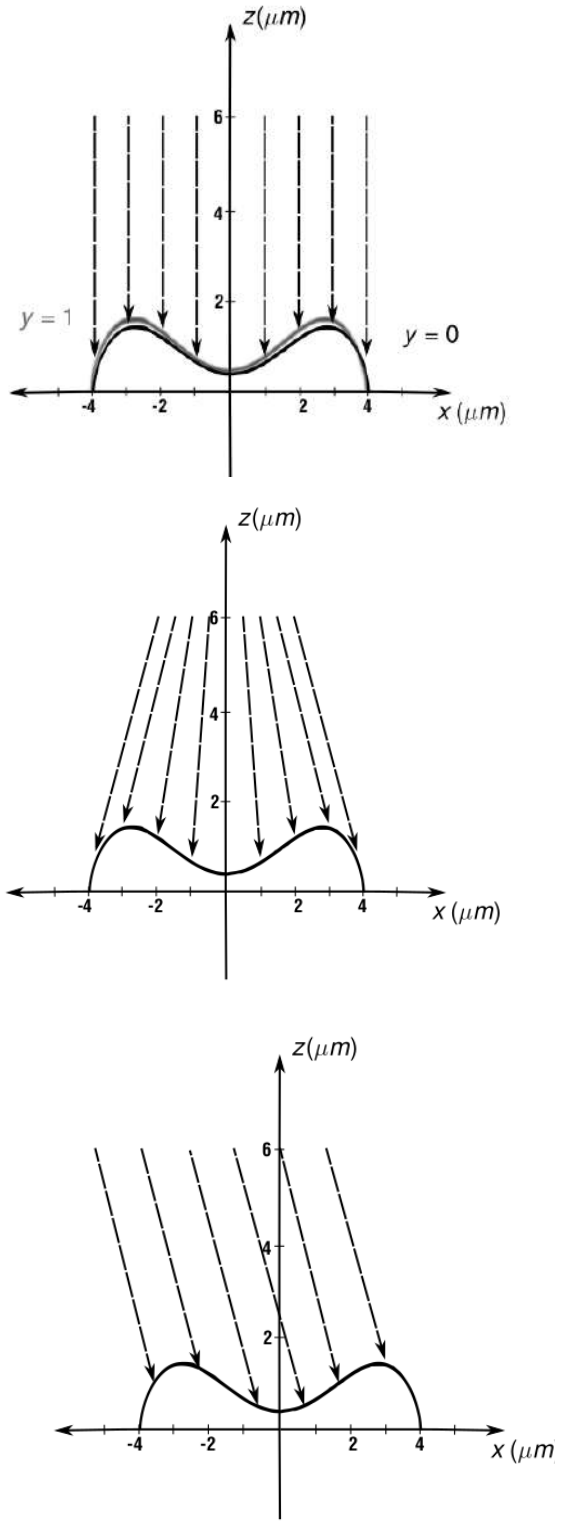

Figure 3 Incident trajectories of the particle for the three cases, with respect to the variation of the position on the x-axis. Source: own.

Case 1 consists of two events that relate the variation of the component on the x axis between $-r_o \leq x_o \leq r_o$ analyzing the cutting profiles in the plane *(x,z)* with respect to the variation of the axis and considering the first event when. $y_o = 0\mu m$ the second $y_o = 1\mu\, m$, which identifies the trajectory of the particular parallel to the central axis of symmetry of the erythrocyte, Figure (3A). Case 2 estimates the angle of dispersion by considering the initial position of the particle constant and varying the velocity of the component on the *x*-axis $x\,(v_{ox})$ between $[-2{,}6; 2{,}6]\mu\, m/s$ figure (3B). Case 3 relates the variation of the component in the x_o axis between $-r_o \leq x_o \leq r_o$ with constant velocity in its components v_{ox} and v_{0z} presenting a rectilinear trajectory with a constant angle to the axis of symmetry of the erythrocyte, figure (3C).

3. Results and Analysis

For case 1, figure (4A), represents 3 points of impact $\{a, b, c\}$ where the incident and reflected trajectory is observed; in the maximum values $\{-2{,}73\mu m \;\; and \;\; 2{,}73\,\mu m\}$ and minimum in $0{,}00\,\mu m$ of the surface of the RC, it is observed that the dispersion angle tends to zero. Figure (4B) shows the dispersion as a function of the impact parameter, a symmetry is observed in the variation of the angle of dispersion when the particle collides with the surface of the erythrocyte parallel to the axis of symmetry.

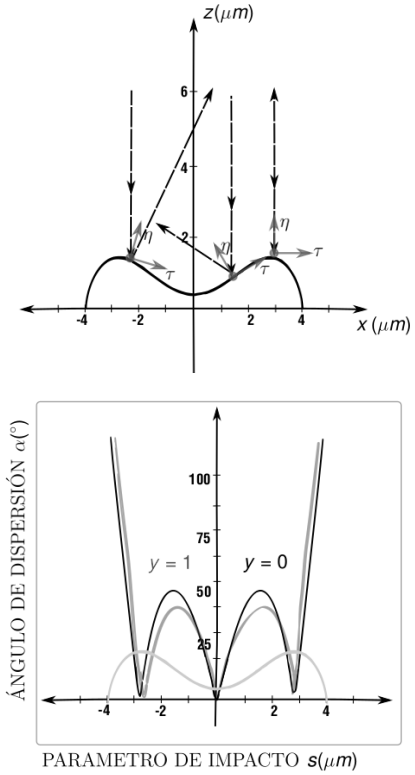

Figure 4A. Three points of impact between NMP-RC for case 1. B. Dispersion profile for the event *y=0yy=1* Source: own.

On the other hand, when analyzing the positive part in the x-axis of the figure (4B), it is eveident that the curve with parabolic tendency shows that its symmetry is with respect to the point where the surface changes its concavity $(Inflection\ point \pm 1{,}55\mu m)$ it is to say that the maximum value of the profile is presented there and to the extent that it approaches the maximum value of the surface, it again tends to zero and the regular behavior continues for each symmetrical part of the surface; at the border of the surface these values are not determined due to non-interaction. It can be concluded that the shape of the variation in the profile given by $y_o = 1\,\mu m$ retains the same symmetries mentioned for me $y_o = 0\,\mu m$ given the symmetrical shape of (1), varying the angle of dispersion at the inflection point.

In case 2, it can be observed that given the initial fixed position of coordinates $(0;10)\mu m$ the trajectory has a variable angle of exit with respect to the axis of symmetry, which generates values for the output profile between $-2{,}29 < s < 2{,}29$ where the collision actually occurs, in this way the ratio of the angle of dispersion to the central axis of the erythrocyte and the impact parameter, Figure 5, was obtained.

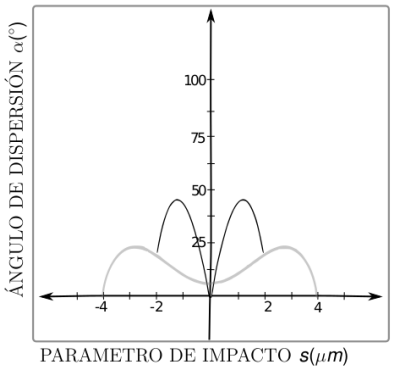

Figure 4. Red globule particle interaction, representation of the angle of dispersion as a function of the impact parameter for case2. Source: own.

The observed profile presents a symmetrical relationship in relation with the central axis of the RC surface. For *s>0* the dispersion angle has to be increased until it has its maximum value at the point where the surface changes its concavity $\pm 1{,}55\,\mu m$

In case 3, the incident trajectory has an exit angle defined by $v_{xo}\; and\; z_{o1}$ Table 1, which shows an exit profile of the trajectory with respect to the dispersion angle. In the figure 6 the greatest angle of dispersion is observed in $s \approx 2{,}96\mu m$, of $-2{,}57\mu m < s < -1{,}55\mu m$ an angle growth is observed until then decreases until $\approx 40^o$ it reaches in after $0{,}63\ \mu m$ to $1{,}53\ \mu m$ it again grows to 1,25 and finally decreases by $s = 2{,}21\,\mu m$ this being the last interaction. In general, it is observed that the angle of dispersion decreases with a tendency to zero, to the extent that the initial position is proportionally modified.

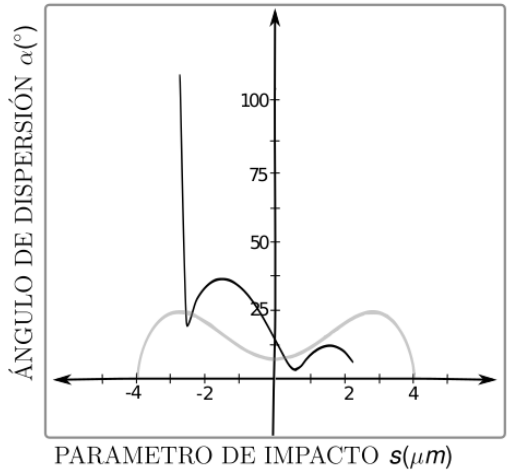

Figure 6 . Red globule particle interaction, representation of the angle of dispersion as a function of the impact parameter for case 3. Source: own.

Figure 7 shows the superposition of the respective profiles based on the exit direction of the trajectory, for the 3 cases studied. The maximum and minimum are evidenced, according to the position, trajectory and speed of the NMP. Case 2 presents a dispersion equal to case 1 event 2. In all 3 cases, the maximum angle of dispersion is observed according to the point of inflection and a minimum value of angle of dispersion in the greater curvature of the surface of the RC. In this way we can identify a smaller dispersion of the NMP when colliding with the RC.

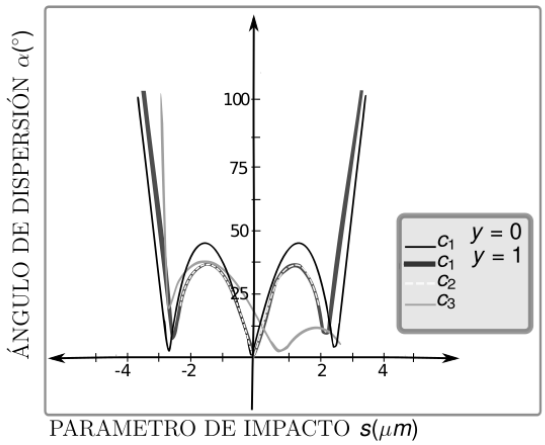

Figure 7 . Superposition of the dispersion profiles studied. Source: own.

Through the kinetic model developed for the study of the collision between a particle and an erythrocyte, a relationship between the angle of dispersion and the point of impact is obtained, which identifies a profile of the output path of the NMP, thus It allows to reduce the execution times of the program since it reduces the study to the analysis of the profiles.

4. Conclusions

The kinetic model of interaction between NMP-RC considering an elastic collision allowed to obtain the output path profiles that relate the angle of dispersion according to the impact parameter. Identifying a dependence on the initial position, as well as the direction of movement given by the velocity components, which is reflected in the variation of the angle of dispersion. Linear paths with constant velocity tend to retain symmetric profiles of alpha due to the surface of the RC described by the parametric in (1). In the three cases omitting the ends of the erythrocyte surface, maximum dispersion values corresponding to the point of inflection were observed. On the other hand, it should be noted that for case 1 and 2 an almost zero dispersion is observed with respect to the axis of symmetry and in case 3 there is a shift according to the angle of incidence presented by the initial trajectory of the NMP. In case 1 the extreme values of the angle are obtained just where the extreme values of the RC are obtained, figure (4B).

5. Future Jobs

It is recommended in future studies it is recommended to consider the variations of the parameters of table 1, which consider simultaneous variations for x_0 and y_0 in an $\mathbb{R}^3$ function and therefore variations in the simultaneous velocity components of v_{ox} and v_{oy}, it would also be interesting to study the interaction between NMP-RC where energy losses are considered at the time of the collision.

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