



## Mathematical Modelling of Drug Targeting Using Computational Methods

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### Article Information

DOI: 10.9734/BJMCS/2015/17633

#### Editor(s):

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Complete Peer review History: <http://www.sciencedomain.org/review-history.php?iid=1142&id=6&aid=9234>

Original Research Article

Received: 21 March 2015

Accepted: 21 April 2015

Published: 13 May 2015

### Abstract

Magnetic nanoparticles play a crucial role as drug carriers in the human body. In this investigation the particle movement is analysed knowing the local flow condition and using appropriate magnets. The particles are injected into the vascular system upstream from malignant tissue and captured at the tumor using an applied magnetic field.

The applied field was obtained by using a quadrupole magnet that couples to the magnetic nanoparticles inside the carrier particle and produces a force that attracts the particle to the tumor. The flux density components of the quadrupole magnet is calculated using Scilab.

This study also provides a mathematical model (I) needed for the development of drug targeting to the lungs in comparison with experimental results. The trajectories of magnetite particles of different sizes in the field of permanent quadrupole in the air and water were traced in different times with the help of numerical solver. It was found that the tendency of the particle to be captured by the magnet increases when air is chosen as the medium.

In the Investigation of model (II) the behavior of blood was considered as Hershel-bulkley fluid which is suitable for the micro vessel of radius 50 nm. Analytical expression was derived for predicting the volume fraction of embedded magnetic nanoparticles required to capture the carrier particle at the tumor.

A parametric analysis of magnetic targeting as a function of key variables including the size of the carrier particle and volume fraction is made. The assumptions to the model was made by comparing with the theoretical model done earlier [9] and implemented using mathematical software scilab 5.4.

**Keywords:** Magnetic drugtargeting; magnetic nanoparticles; volume fraction; microvasculature.

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## 1 Introduction

Mathematical modelling of targeted drug delivery system provides a quantitative description of the drug transportation in the biological system. Modelling of magnetic particle therapy involves interaction among electromagnetic fields, fluid mechanics and therapeutic phenomena.

The greatest challenge in treating Cancer and other localised diseases is getting medication to the affected tissue. Since every vessel in the circulatory system is linked, drugs taken orally or injected in to the blood stream spread throughout the body damaging the healthy tissues.

In an ideal drug targeting, drugs are chemically bound to magnetic nanoparticles injected into the body and steered to the site of the diseased tissue using external magnetic fields. Here it is important to note that magnetic particle steering and trapping will not always have 100% success rate and some particles will always be lost between the injection site and the target. The problem now is to increase the number of particles reaching the target and also to make them adhere for a longer time.

Nanoparticles are solid submicron colloidal polymeric carrier system ranging in size from 1 – 1000 nm are used as drug delivery agents. Magnetic nanoparticles are powerful and versatile diagnostic tool in the field of medicine. For biological applications they are coated with suitable molecules to facilitate biocompatibility in the body. Magnetic nanoparticles can be controlled by an external magnetic field and allows them to transport therapeutic agents to a targeted site in the body. The use of magnetic nanoparticles for this purpose is called magnetic drug targeting.

The differential equation governing the dynamics of fluid motion was considered here to be Lagrangian.

### 1.1 Prior Work

Furlani and Furlani [1,2,3] presented an analytical model for transport and capture of therapeutic magnetic nanoparticles in the human vasculature for targeted drug delivery applications. A wide range of approaches in design and implementation of magnetic particle based drug delivery system to date is given by M. D Kaminski et al. [4]. Theoretical analysis of applications of magnetic nanoparticles and micro particles into the lung epithelium was studied by P. Babinec et al. [5]. The motion of magnetic nano as well as microparticles in the field of cylindrical Halbach array was studied by Peter Babinec et al. [6]. This proved a potential source of magnetic field for magnetic drug targeting. A detailed discussion on the current and future prospective of the targeted drug delivery through the blood stream was presented by Yokoyama [7]. Lubbe et al. [8] gave an elaborate usage of MDT using magnetic nanoparticles as carrier particles through a review article. The behaviour of blood as Hershel bulkley fluid was considered more suitable for microvessel of radius 50  $\mu\text{m}$  by Sachin shaw et al. [9,10] Melania Babincova [11] found a growing number of published papers in the field of nano medicine showing unlimited potential of magnetic nanoparticles in the field of experimental and clinical Oncology. Analysis of particle trajectories for magnetic drug targeting with respect to physical boundary conditions was given by Alexander Heidseik et al. [12]. A comprehensive model of magnetic particle motion during magnetic drug targeting was developed by Erica M Cherry [13].

### 1.2 Motivation

Many of the existing models predicting magnetic targeting of nanoparticles *in vivo* utilize numerical methods to solve for particle transport. They do not provide explicit functional relations for the particle capture and only a few account for Rheology of blood in microvasculature. The analytical model presented is ideal for parametric analysis of magnetic targeting *in vivo* and should be useful for development of novel magnetic targeting methods and approach.

Advantage of using Scilab for numerical calculations is that it is better equipped to deal with the problem when the system is numerically unstable.

To design an appropriate magnetic field source, detailed knowledge about the particle trajectories and therefore the particle properties and influencing parameters is necessary.

The design space is too large to search experimentally. To reach deeper targets in addition to carrier optimization there is also a need to optimize the design and control of external magnets. Mathematical models are necessary to predict the transport of magnetic carrier particles through living tissue under the influence of magnetic fields.

## 2 Background

Magnetic transport of a carrier particle in the vascular system is governed by several factors.

They are magnetic force, viscous drag, Particle cell interaction, Inertia, buoyancy, gravity, Thermal kinetics, particle/fluid interaction.

We take into account the dominant magnetic and viscous force. Balancing the magnetic and fluidic forces

$$F_m \text{ and } F_f \text{ we have } F_m + F_f = 0 \quad (2.1.1)$$

A theoretical model is derived from the fundamental concepts Ref [1,2,3] which indicates the factor that influence a rheological parameter. In order to predict the model it was assumed that there are  $N_{mp}$  identical noninteracting magnetic nanoparticles embedded in the carrier particle. Each particle has a radius  $R_{mp}$  and volume  $V_{mp} = 4\pi/3R_{mp}^3$ .

The force on the magnetic particle is predicted using an effective dipole moment approach in which the particle is replaced by an equivalent point dipole which is located at its center.

The force depends on the magnetic force at the location of the dipole.

$$F_m = \mu(m_{p,eff} \cdot \nabla)H_a \text{ where } m_{p,eff} = V_p f(H_a) H_a \quad (2.1.2)$$

$H_a$  is the applied magnetic field intensity at the center of the carrier particle.

$\chi_{mp} = \frac{\mu_{mp}}{\mu_0} - 1$  and  $\mu_{mp}$  are the susceptibility and permeability of the particles.

Also  $\mu_0 = 4\pi \times 10^{-7}$  is the permeability of air.

The total magnetic force on the carrier particle is the sum of the forces on the embedded magnetic particle.

It was assumed that the blood is purely nonmagnetic with permeability  $\mu_0$ .

The fluidic force was predicted using stoke's approximation for the drag on a sphere in a laminar flow field.

$$F_f = -6\pi\eta R_{cp}(V_{cp} - V_f). \quad (2.1.3)$$

$R_{cp}$  is the radius of the carrier particle  $\eta$  the viscosity of blood and  $v_f$  is the velocity of blood flow. The vessel is assumed to be cylindrical and the blood flow is a laminar flow parallel to the axis.

The blood velocity is

$$v_f(x) = 2v_f[1 - (x/R_{bv})^2] \quad (2.1.4)$$

$v_f$  is average blood velocity  $R_{bv}$  is radius of the blood vessel.

The four equations given above were used in framing the models.

## 2.1 A Transport Model for Drug Targeting with Nano Particles

Analytical model was developed for the purpose of magnetic drug targeting into the lung using a Quadrupole magnet. A planar model of permanent quadrupole represents the distribution of flux density in transversal plane of infinite long permanent magnets arranged to quadrupole with zero value of perpendicular component of flux density Ref [14]. The quadrupole consists of eight sphenoid blocks, in the section, of uniformly magnetized neodymium earth magnets with magnetic energy product 37 MG.Oe (megagauss-oersted; NdFeB N37) magnetization orientation revolved in 135° between adjacent blocks. The geometry of the quadrupole is determined by the radii of inscribed and circumscribed circle, i.e. 1.4 cm and 4.5 cm in this case respectively. The saturation magnetisation  $M_{sp} = 4.78 \times 10^5$  A.m-1.

Magnetostatic problems are those in which the fields are time-independent. In this case, the field intensity (H) and flux density (B) must obey equations  $\nabla \times H = J$ ,  $\nabla \cdot B = 0$ , with a constitutive relationship between B and H for each material  $B = \mu H$ .

If a material is nonlinear  $\mu = B/H(B)$ .

## 2.2 Calculating Magnetic Flux Density of a Permanent Quadrupole Using Scilab

The flux density of the Quadrupole magnet was computed using Ref [14] by determining the B-field outside an infinitely long cylindrical magnet that has an alternating radial polarization and a linear second quadrant demagnetization curve of the form

$$B = \mu H + \mu_0 M_s(\varphi) \quad (2.3.1)$$

Let  $R_1$  and  $R_2$  denote the inner and outer radii of the cylinder, respectively. As the magnet is infinitely long, the problem reduces to a 2D boundary value problem (BVP). We use the solution method presented in Ref [2] with the magnetization inside the cylinder given by

$$M_s(\varphi) = M(\varphi); \quad M(\varphi) = \sum_{i=1}^{\infty} M_i \cos(i\varphi) \quad (2.3.2)$$

$$M_i = \frac{M_s}{i\pi} \sum_{k=1}^{N_{pole}} (-1)^k \left[ \sin \frac{(2k-1)i\pi}{N_{pole}} - \sin \frac{(2k+1)i\pi}{N_{pole}} \right] \quad (2.3.3)$$

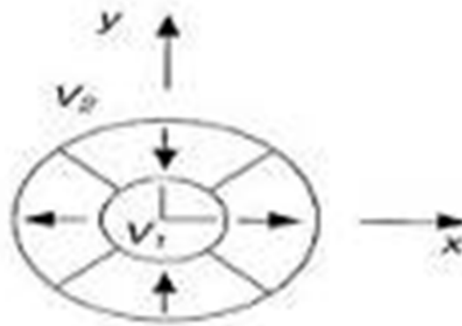
$N_{pole}$  is the number of poles. A solution is sought for the region  $V_2$  outside the cylinder. The coefficients of interest are  $V_i^{(2)}$  and  $U_i^{(2)}$ . From the Orthogonality of  $\sin(i\varphi)$  and  $\cos(i\varphi)$  we find that  $V_i^{(2)} = 0$  for all  $i$  Fig. 1.

The coefficients  $U_i^{(2)}$  are given by  $U_i^{(2)}(M_i, R_1, R_2, \mu)$  which is calculated by solving the differential equation

$$\frac{d^2 U_i^{in}}{dr^2} + \frac{1}{r} \frac{dU_i^{in}}{dr} - \frac{i^2}{r^2} U_i^{in} = -D_i(r), \quad = -\frac{M_i}{r} \quad (2.3.4)$$

Scilab 5.4 is used to solve the above stiff differential equation. The value for  $M_i$  was first calculated and found to be  $2.535868 \times 10^6$ . The differential equation was solved by simulating the value of  $i$  and the values of  $U$  obtained. The field components

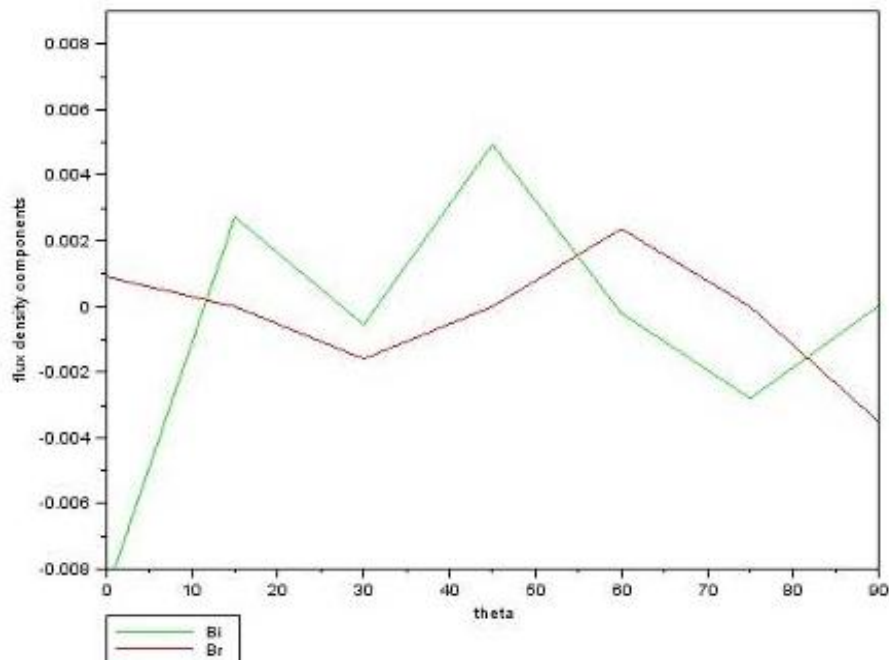
$$\begin{aligned} B_r^{(2)}(r, \varphi) &= \mu_0 \sum_{i=1}^{\infty} i r^{-(i+1)} U_i^{(2)} \cos(i\varphi) \\ B_\varphi^{(2)}(r, \varphi) &= \mu_0 \sum_{i=1}^{\infty} i r^{-(i+1)} U_i^{(2)} \sin(i\varphi) \end{aligned} \quad (2.3.5)$$



**Fig. 1. Geometry of a quadrupole**

are calculated using Scilab and the corresponding values are plotted against the theta values. The field analysis is done using an eight pole cylindrical magnet with  $R_1 = 1.4$  cm,  $R_2 = 4.5$ cm,  $M_{sp} = 4.78 \times 10^{-5}$  A/m<sup>-1</sup> and  $\mu = \mu_0$ .

The field components  $B_r$  and  $B_\phi$  were calculated at  $r = 1.4$  cm and  $\phi$  varying between  $0^\circ$  and  $90^\circ$ . The figure shows that  $B_r$  peaks between  $\theta = 60^\circ$  and  $70^\circ$ . In the same way  $B_\phi = B_1$  peaks at  $\phi = 30^\circ$  Fig. 2.



**Fig. 2. Flux density components of the quadrupole magnet**

The gradient of the flux density components are calculated using the formula

$$B_0 = \frac{1}{r} \sqrt{B_r^2 + B_\phi^2}$$

$$\begin{aligned}
 B_r &= -0.0087409 \quad 0.0027252 \quad -0.0005523 \quad 0.0049388 \quad -0.0001975 \quad -0.0027936 \quad 0.0000213 \\
 B_\phi &= 0.0009101 \quad 0. \quad -0.0015925 \quad 0. \quad 0.0023726 \quad 0 \quad -0.0035183 \\
 B_r^2 &= 1.163704895 \times 10^{-4}; \quad B_\phi^2 = 2.137200391 \times 10^{-5}; \quad B_0 = 1.17363748 \times 10^{-2};
 \end{aligned}
 \tag{2.3.6}$$

This mathematical model is used for magnetic drug targeting in the lungs.

### 3 A Mathematical Model for Nano Magnetic Drug Delivery Into The Lungs in Comparison with Experimental Results

Theoretical analysis and possible application of engineered magnetic nanoparticles and micro particles in the lung therapy has already been studied. Several equipment for more effective delivery of drugs into the lung epithelium has been proposed earlier. This study provides an analytical method needed for development of drug targeting to lung in comparison with experimental results given by Ref [5].

Aerosolization therapy for lung diseases has been applied for a long time. The lung is a perfect point of entry not only for local therapy but also for systematic delivery of therapeutic substances. Recent technical improvements, with regard to both the production and delivery of aerosols indicate that appropriate inhalation techniques may be the therapeutic way forward for a variety of diseases. Since the nano carrier system may be administered to the airways easily, a number of respiratory diseases may be approached using nanoparticles.

The applied field is obtained by using a Quadrupole magnet described above.

Movement of magnetic particles in the plane in magnetic field with flux density  $B$  in fluid ambient with viscosity  $\eta$ , which is not moving, is described by system of ordinary differential equations (ODE).

$$\begin{aligned}
 \frac{dx}{dt} &= v_{p,x} \\
 \frac{dy}{dt} &= v_{p,y} \\
 \frac{dv_{p,x}}{dt} &= \frac{1}{mp} \left\{ \frac{Vp}{\mu} f(B(x,y)) \left[ B_x(x,y) \frac{\partial B_x}{\partial x} + B_y(x,y) \frac{\partial B_x}{\partial y} \right] - 6\pi\eta R_p v_{p,x} \right\} \\
 \frac{dv_{p,y}}{dt} &= \frac{1}{mp} \left\{ \frac{Vp}{\mu} f(B(x,y)) \left[ B_x(x,y) \frac{\partial B_y}{\partial x} + B_y(x,y) \frac{\partial B_y}{\partial y} \right] - 6\pi\eta R_p v_{p,y} \right\}
 \end{aligned}
 \tag{3.1.1}$$

where  $m_p = V_p \rho_p$  and  $V_p = 4/3\pi r^3$  are the mass and volume of the particles respectively.

This system of equations is obtained by combining the expressions from (2.1.1) to (2.1.4)

Gradient of flux density components is taken from (2.3.6).

The trajectory of magnetite ( $Fe_3O_4$ ) particles, with density  $\rho = 5000 \text{ kg.m}^{-3}$  and a saturation magnetization  $M_{sp} = 4.78 \times 10^5 \text{ A.m}^{-1}$ , in the magnetic field created by quadrupole consisting of permanent NdFeB N37 magnets is calculated numerically by solving equations(3.1.1) in non moving and nonmagnetic fluid, with viscosity equal to that of water or air.

i.e.  $\eta = 1.003 \times 10^{-3} \text{ N.s.m}^{-2}$  or  $\eta = 1.82 \times 10^{-5} \text{ N.s.m}^{-2}$  respectively.

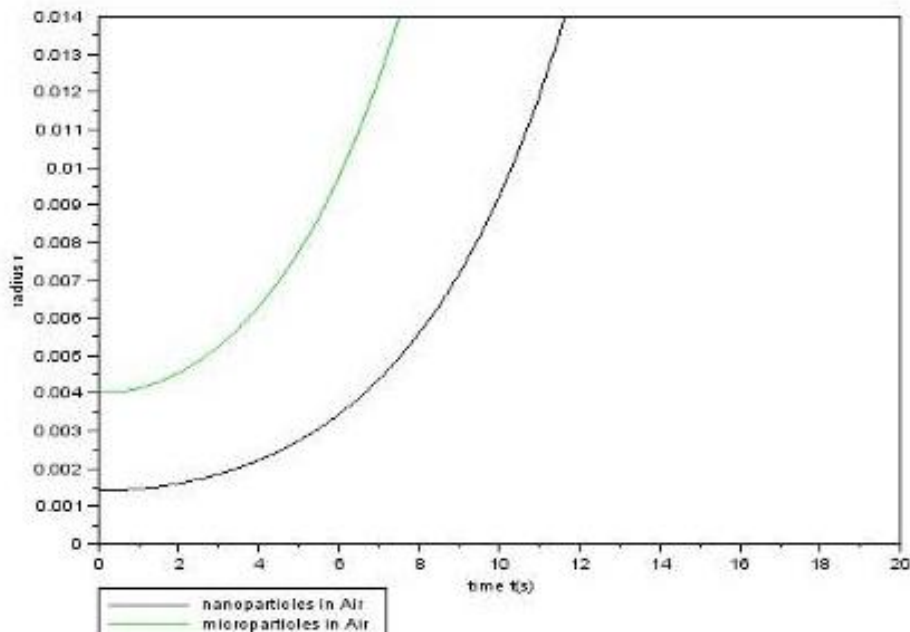
### 3.1 Computations Using Scilab

Scilab 5.4 numerical solver was used for solving the set of equations (3.1.1). Computations were done for nanoparticles with radius 50 nm, which are often used in magnetic drug targeting, as well as microparticles with radius 10  $\mu\text{m}$ , which can be used for magnetic separation. The trajectories of magnetite particles of each size in the air as fluid ambient was solved numerically and the trajectory traced. The snapshots in Ref [11] was taken as a theoretical model. Initial conditions for calculations were: Randomly position the nanoparticles in the circle with radius 0.4 cm from the center of quadrupole and zero initial velocity. The particles were bound to move under the action of the magnetic force. Computation of trajectory for each particle was stopped after it reached internal boundary of quadrupole, approximately at a distance 1.4 cm from the center. The time of capture was calculated and graph was traced. It was seen that microparticles were captured faster than nanoparticles. Also small nanoparticles were attracted in a longer, but still reasonable time approximately after 16s. Trajectories of magnetite particles with different sizes, microparticles with radius 10  $\mu\text{m}$  and nanoparticles with radius 50 nm, in the field of permanent quadrupole in the air and in water in different times were traced.

### 3.2 Results and Discussions for Model (I)

The trajectories of magnetite particles of different sizes in the field of permanent quadrupole in the air and water were traced in different times with the help of numerical solver (Figs. 3 and 4). The tendency of the particle to be captured by the magnet increases when air is chosen as the medium.

The time taken for the microparticle to reach the boundary is smaller in the medium of air when compared to the medium of water. Similarly the time taken for the nanoparticle to reach the boundary in the medium of air is less than that in the medium of water. The trajectories prove the finding in Ref [6]. Long movement time can be diminished by using smaller magnetic particles or by increasing the magnetic field of the Quadrupole.



**Fig. 3. Trajectory of particles in air**

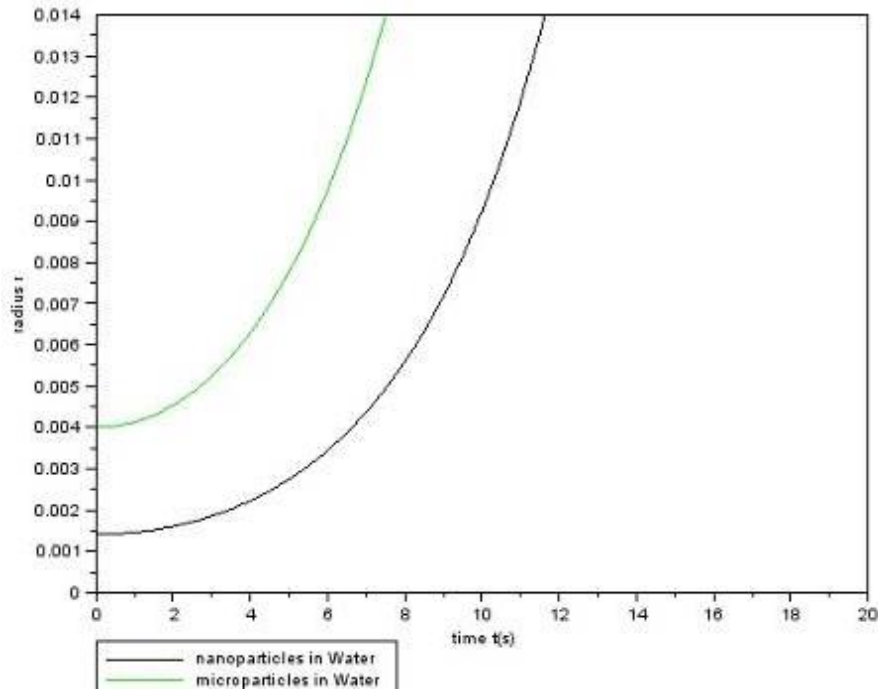


Fig. 4. Trajectory of particles in water

#### 4 Quadrupole Magnet Targeting in the Analysis of Hershel Bulkley Fluid in an Impermeable Microvessel Model (II)

In this investigation behaviour of blood was considered as a Hershel bulkley fluid. The applied magnetic field is obtained by using a Quadrupole magnet mentioned in the earlier section. Several factors that influence the magnetic targeting of the carrier particle are considered in the present problem. The computations are done using scilab 5.4 and the results are graphically displayed.

The mean velocity  $v_f$  is obtained by [10]

$$v_f = \frac{1}{\eta} \frac{dp^{1/n}}{dz} \frac{n}{n+1} R_v^{1+\frac{1}{n}} A(\zeta_c) \quad (4.1.1)$$

The Reynolds number  $R_i^*$  and Bingham number  $B_i^*$  are written as

$$R_e^* = \frac{v_{cp}^2 - n d_{cp}^n}{m}$$

$$B_i^* = \frac{\tau_y}{m \left( \frac{v_{cp} n}{d_{cp}} \right)}$$

where  $d_{cp}$ ,  $\rho$ ,  $\tau_y$ ,  $m$  and  $n$  are the diameter of particle, density, Yieldstress, Hershelbulkley model parameter and flow behaviour index in the fluid.  $\zeta_c$  is the Rheological parameter which goes to zero when  $n = 1$  and  $A(\zeta_c)$  tends to unity.  $C_D$  is the drag force.

$C_D = 24X(\eta)/Q^*$ , where the dynamic parameter is defined as  $Q^*$ .



The fluidic force on the spherical carrier particle in a laminar flow of Hershel Bulkley fluid is written as:

$$F_f = -1/2(\pi\rho R_{cp}^2 V_{cp}^2 C_D) \quad (4.1.2)$$

The component form is given by

$$F_{fx} = -12\pi X(\eta)R_{cp}^2[\tau_y + \eta(v_{cp,x}/2R_{cp})^n] \quad (4.1.3)$$

$$F_{fy} = -12\pi X(\eta)R_{cp}^2[\tau_y + \eta((v_{cp,z}-v_f)/2R_{cp})^n] \quad (4.1.4)$$

Where  $v_f$  is the average velocity of the fluid as given in eq. (4.1.1) for the microvessel.

In this study it is assumed that the effective viscosity  $\eta = 1.8 \times 10^4$  pa.s, at the temperature 300k;  $dp/dz = 2 \times 10^4$  N/m<sup>2</sup>;  $\tau_y = 4 \times 10^{-3}$  N/ m<sup>2</sup> as in Ref [9-10].

The magnetic force components are given by:

$$F_{mx} = (3\mu_0 N_{mp} V_{mp} B_0^2 x)/\mu^2 \quad (4.1.5)$$

$$F_{mz} = (3\mu_0 N_{mp} V_{mp} B_0^2 z)/\mu^2 \quad (4.1.6)$$

#### 4.1 Equations of Motion

The equations of motion for a carrier particle travelling through a micro vessel can be written in component form by substituting Eqs. (4.1.3) to (4.1.6), into Eq. (1.1.1).

We solve for the velocity components in the x-z plane and obtain,

$$V_{cp,x} = 2R_{cp} \left( \frac{\mu_0 N_{mp} V_{mp} B_0^2}{4\pi\eta X(\eta) R_{cp}^2 \mu^2} x - \frac{\tau_y}{\eta} \right)^{1/n} \quad (4.2.1)$$

$$V_{cp,z} = 2R_{cp} \left( \frac{\mu_0 N_{mp} V_{mp} B_0^2}{4\pi\eta X(\eta) R_{cp}^2 \mu^2} z - \frac{\tau_y}{\eta} \right)^{1/n} + v_f \quad (4.2.2)$$

Velocity  $v_f$  is given in eq. (4.1.1). The axial and radial motion of the carrier particle travelling through the micro vessel is obtained by integrating these equations. The above two equations are coupled together to predict the particle trajectory (x(t),y(t)).

#### 4.2 Solution Procedures

The axial position of the particle is given by

$$z = z_0 + V_{cp,z}t \quad (4.3.1)$$

where  $V_{cp,z}$  is the average axial velocity of the carrier particle. The total volume occupied by the nano particles is  $N_{mp}V_{mp}$ , this can be represented in terms of volume fraction  $\beta_{vf}V_{cp}$  of the carrier particle itself.

$$\text{i.e } N_{mp}V_{mp} = \beta_{vf}V_{cp} \quad (4.3.2)$$

Using eqn. (4.3.1) in eqn. (4.2.1)

$$dx/dt = 2R_{cp} \left( \frac{\mu_0 \beta_{vf} V_{cp} B_0^2}{4\pi\eta X(\eta) R_{cp}^2 \mu^2} x - \frac{\tau_y}{\eta} \right)^{1/n} \quad (4.3.3)$$

integrating this equation both sides we get

$$\int_{x_0}^{x(t)} dx = 2R_{cp} \int_{t_0}^t \left( \frac{\mu_0 \beta_{vf} V_{cp} B_0^2}{4\pi\eta X(\eta) R_{cp}^2 \mu^2} x - \frac{\tau_y}{\eta} \right)^{1/n} dt \quad (4.3.4)$$

$$x(t) = x(t_0) + 2R_{cp} \int_{t_0}^t \left( \frac{\mu_0 \beta_{vf} V_{cp} B_0^2}{4\pi\eta X(\eta) R_{cp}^2 \mu^2} x - \frac{\tau_y}{\eta} \right)^{1/n} dt \quad (4.3.5)$$

### 4.3 Special case Solution Procedures

To obtain an analytical solution, for non-invasive targeting systems we have  $\left( \frac{\mu_0 N_{mp} V_{mp} B_0^2}{4\pi\eta X(\eta) R_{cp}^2 \mu^2} \right) \ll 1$ , hence the fluidic force is dominant in eqn. (3.1.6). By [3], we simplify the analysis by assuming that the average axial velocity of the carrier particle:

$$V_{cp,z} = v_f \quad (4.4.1)$$

With this result we modify the above eqn as

$$z = z_0 + v_f t \quad (4.4.2)$$

To predict the volume fraction of magnetic particles required to ensure capture of carrier particle we assume that the motion starts from the top of the microvessel. The particle is assumed to be captured if its trajectory reaches inner wall of the blood vessel where  $R_{bv}$  the radius of the microvessel.

$$x(t_0) = R_{bv}, \quad z = 0, \quad x(t) = -R_{bv}$$

Using the values in the equation of trajectory (4.3.5) we get the volume fraction for the Newtonian fluid.

( $n=1$ ) which can be obtained as

$$\beta_{vf} = 3 R_{bv} \frac{\zeta \eta \mu_0}{R_{cp}^2 B_0^2} \frac{v_f}{z_0} \quad \text{where } x(\eta) = (\zeta) \quad (4.4.3)$$

## 5 Results and Discussions

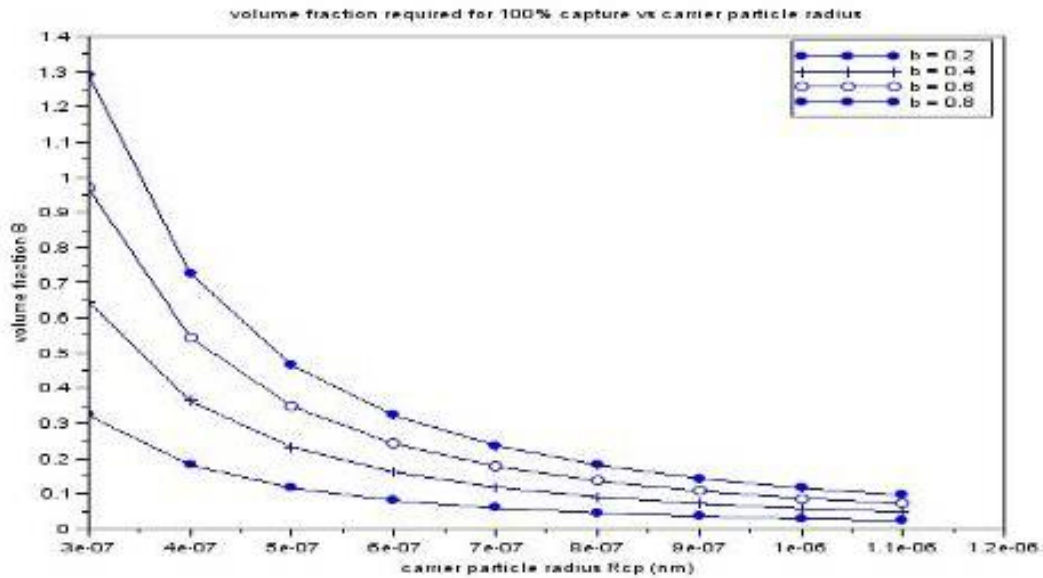
The nanoparticles that are used in the carrier particles are  $Fe_3O_4$  particles and biocompatible with a density  $5000 \text{Kg/m}^3$ . In the present investigation, our aim is to study the effect of the external magnetic field to capture the drug carrier particle at the tumour position in the Hershel Bulkley blood flow in the micro vessel. The applied force is given by a Quadupole magnet which is positioned at a distance 2.5 cm from the axis of the microvessel whose radius is 50nm. We assume  $\zeta = b$ .

The present result with  $n = 1$  and  $b = 0.2, 0.4, 0.6, 0.8$  the volume fraction is plotted against  $R_{cp}$  in Fig. 5 which reveals that for fixed values of the parameter  $b$ , the volume fraction of the magnetic particle decreases with increase in the radius of the carrier particle. Also, it can be noticed from the figure that the volume fraction decreases with the value of the non-dimensional parameter  $b$ . For smaller values of  $R_{cp}$ , there is larger difference in volume fraction with varying  $b$ . This means that the carrier particle needs less volume fraction to be captured by the magnet when  $b$  is increased.

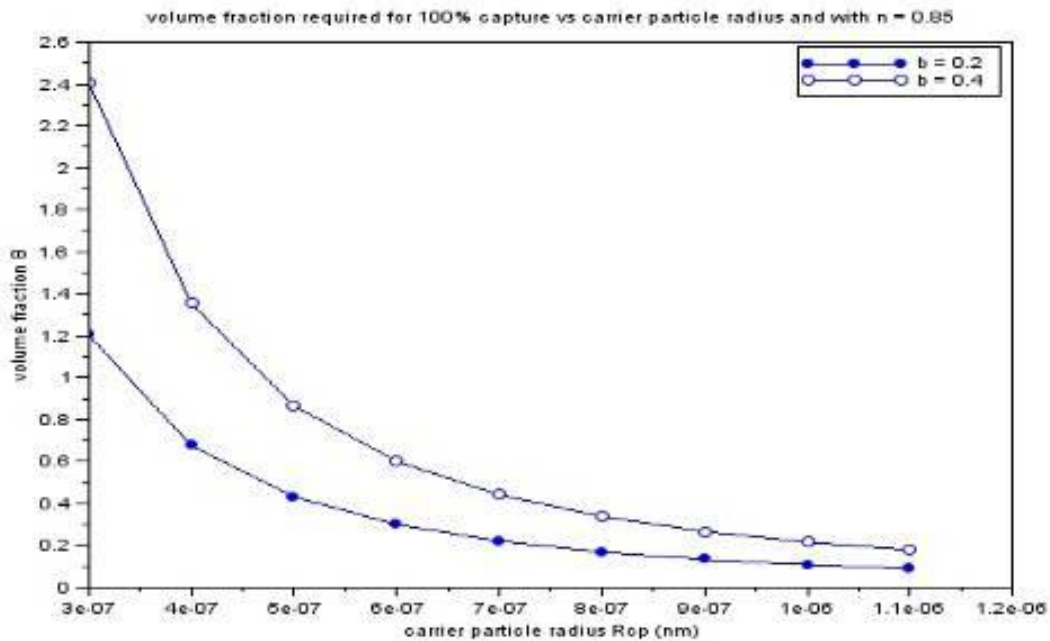
Also three different values of the flow behaviour index  $n = 0.85, 1, 1.15$  were considered in the present investigation, to represent Newtonian ( $n=1$ ), shear thinning ( $n<1$ ) and shear thickening ( $n>1$ ) characteristics of the blood.

From Fig. 6, it was noticed that for shear thickening fluids ( $n > 1$ ), lesser volume fraction was noticed with lower values of  $R_{cp}$ .

From Fig. 7 for shear thinning fluids ( $n < 1$ ), more volume fraction was seen with lesser values of  $R_{cp}$ .



**Fig. 5. Volume fraction required for 100% capture vs particle radius**



**Fig. 6. Volume fraction required for 100% capture vs particle radius  $n = 0.85$**

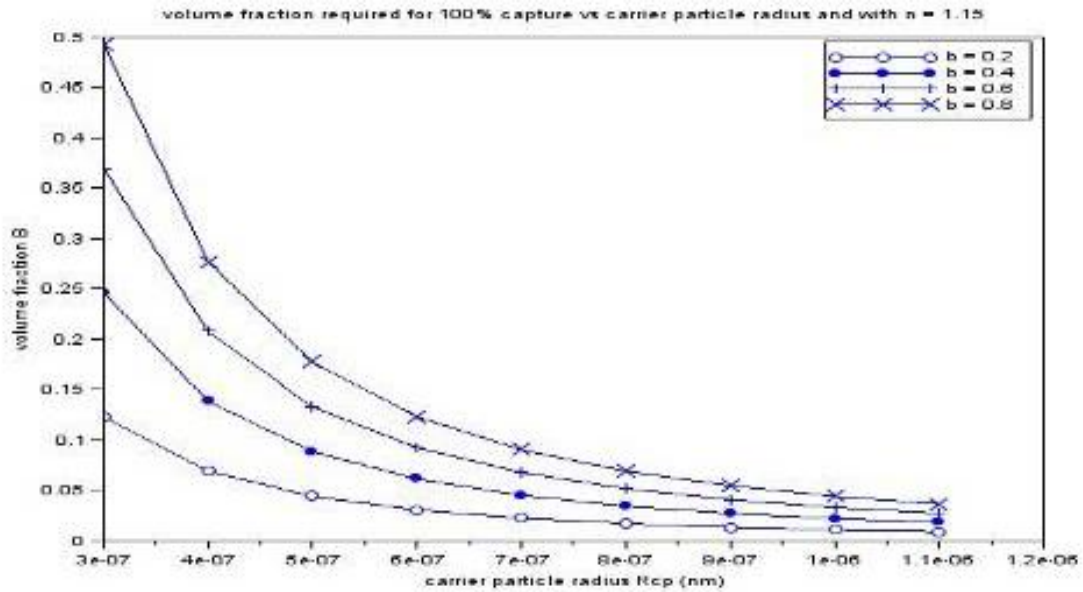


Fig. 7. Volume fraction required for 100% capture vs particleradius n =1.15

The trajectory of the particle corresponding to different values of the flow behaviour index  $n$  of hershel bulkley fluid has been plotted in Fig. 8. It was seen that for different values of the flow behaviour index viz  $n = 0.85$ ,  $n = 1.15$  the tendency of the carrier particle to be captured by the magnet increased with the rheology of the blood changing from shear thinning to shear thickening.

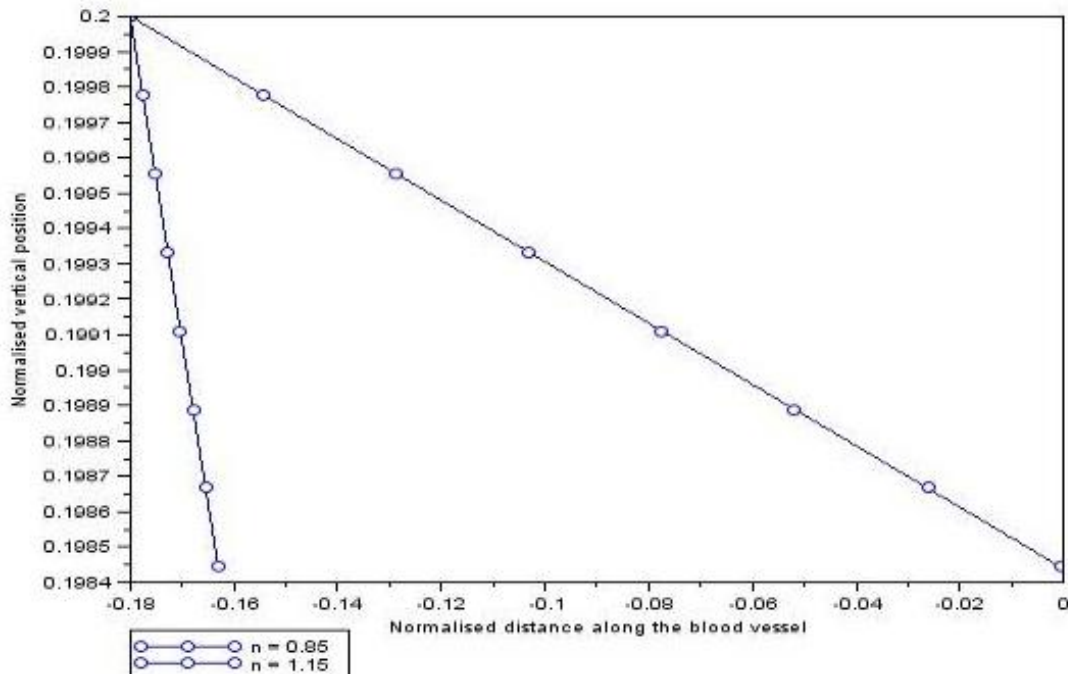


Fig. 8. Comparison of the trajectories of carrier particles for different values of n

## **6 Conclusions**

The aim of the investigation is to achieve a high concentration of drug in the target position by considering the more realistic nature of blood flow in the micro vessel i.e. by assuming blood as hershel bulkley fluid. The size of the carrier particles, volume fraction, and the rheology of the blood play a vital role on the trajectory of the carrier particle. Also the tendency to be captured by the magnet increases when the rheology of the parameter changes from shear thinning to shear thickening. The volume fraction is inversely proportional to the gradient  $b$  of the quadrupole magnet. Hence by a suitable construction of a quadrupole magnet the drug can be released at the tumour site irrespective of the distance of the magnetic nanoparticle from the axis of the magnet.

## **Competing Interests**

Authors have declared that no competing interests exist.

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