Numerical modeling of the effect of field configurations on the magnetic nanoparticle delivery system

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ABSTRACT

This paper presents the details of our studies on the numerical modeling of magnetic nanoparticle drug delivery using Ferrohydrodynamics based numerical models. The magnetic field and fluid flow were governed by Maxwell and the Navier-Stokes equations. A magnetic volume force couples the magnetic field to a fluid-flow problem in the blood-vessel domain described by the Navier-Stokes equations. The magnetic field generates magnetic volume forces that affect the flow field in the blood vessel. The fluid has the properties of blood (e.g. viscosity, flow rate and others) and magnetic characteristics of nanoparticles and hence becomes a ferrofluid. This helped in understanding the effect of variation of magnetic field distribution on the fluid velocity profiles. Two different field configurations, with symmetric and asymmetric pole fields, were considered and the fluid velocities in different gradient fields were compared. The results clearly showed that the fluid velocity decreased as the magnetic field increased.

Keywords: Nano drug delivery, magnetic nanoparticle, Comsol, Navier-Stokes equation, Maxwell equations

1 INTRODUCTION

Targeted drug delivery can be classified into at least six different groups based on the mechanism, application used and the carrier employed [1]. It can be used for the treatment of human malignancies such as brain cancers [2, 3] and in other diseases to reduce systemic toxicity. Further, the efficacy of drugs may be increased by active targeting wherein the drug embedded nanoparticles to site of action either by conjugates of specific antibodies or by homing peptides specific for a marker on the surface of target [3]. Currently, active drug delivery is mainly achieved using systemic injection of nanoparticle vehicles through the complex biological system and specific retention at the site of action [2, 3]. Such methods are assisted by external forces generated through magnetic fields particularly in magnetic drug delivery systems. Typically the blood cells are of few microns size (white ~ *10 -14 μm*, red ~ *8 μm*), through which nanoparticles can easily be maneuvered through diffusion. Interestingly, proteins and genes *5* to *50 nms*, (genes are much smaller in size than proteins) having similar sizes to that of the intended size of the nanoparticles are not expected to interfere in their motion.

Magnetic drug delivery, being one of the important active drug targeting systems, is commonly used to increase the concentration of the drug at a defined target site and away from the reticular endothelial system, with the aid of a magnetic field [1]. These systems currently utilize magnetic nanoparticles as the primary carriers for taking the drug towards targeted cells. Normally, nanoparticles are injected through an artery in the presence of an external magnetic field of sufficient strength and gradient to retain the carrier at the targeted site [4]. A magnetic field gradient can also be used to drive the particles towards an identified target. This magnetic field provides the steering mechanism that can potentially control the speed and direction of the particle [5]. It was clinically shown that the nanoparticle can be driven few centimeters, even against the diffusion and blood stream velocities, in the presence of sufficiently strong enough fields [6].

However, the design, optimization and investigations to ascertain the delivery to a targeted site through experimental analysis are quite complex, time consuming, and expensive. Hence, modeling is often used as an efficient way of understanding the mechanisms in detail. This involves not only modeling the nanoparticle movement, but also the physiological system through which the particles are transported.

Modeling of the blood circulation in arteries, veins, and in other parts of the body has been attempted earlier [7]

using the conventional convection-diffusion equation. This is one of the simplistic models of the blood circulation based on physiological forces. However, there are many other factors that affect nanoparticle transport in drug delivery such as the particle size relative to the blood vessel, pressure drop due to the collisions of these particles to the walls, variation in buoyancy forces based on the density, frictional, adhesive and different contact and non-contact forces. Further, inside the human body, within the constraints provided by the presence of complex fluids, the use of oscillatory magnetic fields may be necessary to overcome the particle mechanical arrest/containment. This can ensure the alignment of the particle magnetic moments with the rotating field vector, which provides the alternate pathways to maneuver away from any obstacles, especially in the presence of a complex assembly of fluids and semisolids, as is seen in the human body. Though, It was shown by Dinh and co-workers that this could be achieved with a reasonable success [8], the effect of magnetic field configuration and different field gradients on the transport of the nanoparticles is still not well understood. Hence, this paper aimed to study the effect of magnetic field on the velocity of the nanoparticles including the pressure drop within the blood vessel and across the diameter through using numerical modelling methods. This paper investigates the effect of magnetic field configuration on the flow profiles of the fluid with nanoparticles.

2 NUMERICAL MODELLING

These simulation studies were performed using COMSOL multiphysics software. Numerical analysis mainly utilized two sets of equations namely Maxwell equations and Navier Stokes equations for magnetic field and fluid flow. The details of the equations, the coupling procedure adopted and the boundary conditions were described in the following sections.

2.1 Magnetic field equations

The magnetic field problem is defined using Maxwell's equations for the static case. Maxwell's laws relating the magnetic field h (a/m) and the current density j (a/ m^2) are:

$$\nabla \times H = J \tag{1}$$

$$\nabla \times B = 0 \tag{2}$$

A magnetic field equation is derived followign fundamental magnetic principles as follows.

$$\nabla \times \left(\frac{1}{\mu} \nabla \times A - M \right) = J \tag{3}$$

2.2 Fluid Flow equations

The velocity and pressure fields in the blood stream are modeled based on navier stokes equations, describing the time-dependent mass and momentum balances for an incompressible flow.

$$\rho \frac{\partial u}{\partial t} - \nabla \cdot \eta \left(\nabla u + (\nabla u)^T \right) + \rho u \cdot \nabla u + \nabla \rho = F \tag{4}$$

$$\nabla \cdot u = 0 \tag{5}$$

Where η is the dynamic viscosity ($kg/m.s$), u is the velocity (m/s), ρ is the blood density (kg/m^3), p *is* the pressure (n/m^2), and f is the volume force (n/m^3)

2.3 Coupling

The hydrodynamic problem is coupled to the magnetostatics through the magnetic volume force due to the fluid magnetization under the influence of the magnetic field. This volume force can be represented by the following

$$F = |M|\nabla|MH| \tag{6}$$

2.4 Boundary conditions

For the magnetic field problem, a magnetic insulation boundary condition was applied. For the fluid flow problem, on the vessel walls, no-slip conditions, $u = v = 0$ were applied. At the outlet, an outlet pressure condition, $p = 0$ was applied. At the inlet boundary, parabolic flow profile on the normal inflow velocity according to $4U_m\, s(1-s)$ was applied, where s is a boundary segment length parameter that goes from *0* to *1* along the inlet boundary segment and U_m is the maximal flow velocity.

Some of the important parameter used in this simulation are: Relative magnetic permeability – 1, fluid density and dynamic viscosity – 1060 kg/m^3 and 0.005 Pa*sec, heart beat rate 1/sec.

3 RESUTLTS AND DISCUSSION

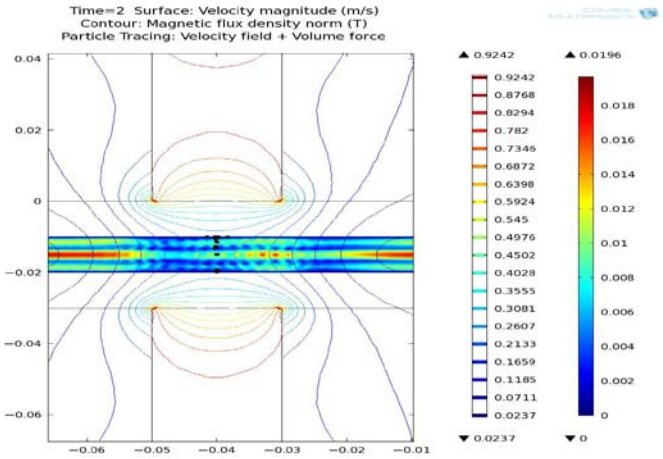

Figure. 1: A 2-D simulation of the fluid (along with nanoparticles) velocity profile

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Figure. 1 shows the particle tracing paths simulated in COMSOL. Basically, this function allows applying different forces on the particles. Two main forces were applied on the particle, magnetic volume force and drag force. Then, the simulation was run again with the particle within the flow to observe the particles under the specified forces. The graph above shows the particles were colliding and accumulating under the magnetic tip where the magnetic field is high. This occurred during which time the (heart) inflow velocity vanishes. It was concluded that the magnetic field will be more dominate in the region where the velocity of the blood will vanish.

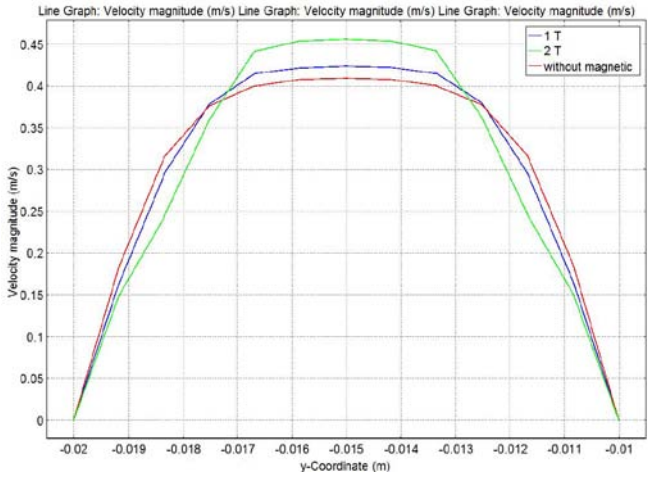

Figure 2. Variation of velocity along the diameter of the simulated blood vessel

Figure 2 showes the velocity profile for the three cases plotted across the blood vessel right under the magnet. This picture concludes that the velcoity will be high in the middle of blood vessel whereas the blood velocity near the walls will be very low because it is affected by the magnetic field and as a result the velocity will decrease.

For the 3-dimensional model, two types of electromagnets were simulated to see the difference in the magnetic field strength produced by electromagnet with symmetric and asymmetric pole faces as shown in Figure 3. (a, b).

Also the blood vessel was modeled with two branches to study the possibility of controlling the magnetic nanoparticles within the flow by placing the electromagnet on one of the two branches and see if that will affect the flow of the nanoparticles. The figures below show the study of the magnetic field effect in the magnetic nanoparticles. The pictures in Figures 3. (a, b) show that the fluid velocity in the flat tips configuration of the electromagnet is less than the sharp tip configuration shown before. This shows the gradient field is better suitable than the symmetric field configuration, to generate better particle velocities.

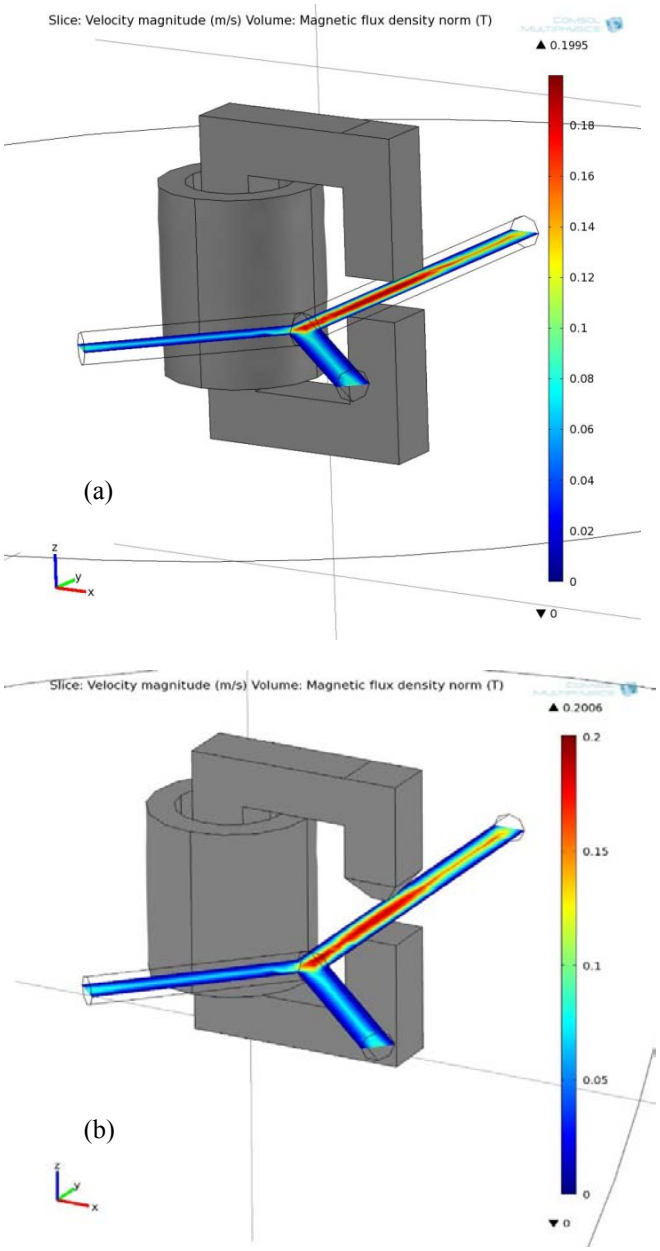

Figure 3: Variation of fluid/particle velocity with (a) Flat pole and (b) asymmetric configuration of the electromagnet

4. SUMMARY

This study clearly demonstrated the importance of numerical modeling, especially in the context of understanding the flow characteristics of magnetic nanoparticles in the presence of magnetic field, especially in the in-vivo drug delivery applications. This modeling showed that the flow velocity is a minimum at the center of the magnetic field. The magnetic field configuration seems

to play a crucial role in improving the field gradient and there by affecting the flow velocities.

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