Computational study of the optimum gradient magnetic field for the navigation of spherical particles into targeted areas

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Abstract. Spherical magnetic nanoparticles coated with drugs are navigated to targeted areas, for the treatment of cancer. The particles are navigated by magnetic field gradients that can be produced by an MRI device. In the present work, a computational study for the estimation of the time evolution of the gradient magnetic field is presented in order to ensure the optimum driving of the particles into the targeted area. For this purpose, the present method takes under consideration all the forces acting on the particles that make them move. The method is based on an iteration algorithm that intents to minimize the deviation of the particles from a desired trajectory. In this way, the gradient magnetic field is temporarily adjusted in a suitable way so that the particles’ distances from the trajectory are decreased. Using the above mentioned method, it is clear that with the increase of the optimization parameters, i.e the modification of the gradient magnetic field, the particles are moved closer to the desired trajectory. Moreover, it is found that the present numerical model can navigate particles into the desired trajectory with efficiency above 90%.

1. Introduction

Drug delivery by magnetic nanoparticles in cancer tumors through blood vessels is considered. The benefits of using this method are numerous. Firstly, the quantity of the drug required to reach therapeutic levels is being reduced. Moreover, the drug concentration at targeted sites is increased. For the magnetic navigation of the drug, the use of magnetic nanoparticles is necessary. The anti-tumor agents are loaded on the surface of the magnetic nanoparticles. The magnetic field that is required in order to navigate the particles inside the human arteries is produced by a Magnetic Resonance Imaging (MRI) system.

The major factors, which influence the efficiency of the usage of magnetic nanoparticles for biomedical applications in the magnetic driving, are the size and the magnetization of the biocompatible nanoparticles. Many of these particles are being trapped in the liver and spleen and are excreted via the kidneys. Particles with small size imply a small magnetic response, thus the use of huge magnets are imperative \cite{1}. Using paramagnetic nanoparticles, their magnetic response is maximized, as they are formed into chains under the influence of a steady magnetic field. The size of aggregates is very important and it depends on different parameters \cite{2}. After the navigation into the infected area by gradient magnetic fields, the nanoparticles lose their magnetization in the absence of the magnetic field. The nanoparticles, which do not reach the tumor, continue to circulate into the human blood and are being opsonized and cleared by the macrophages.

Experimental data indicate the maximum value of the gradient magnetic field for steering the nanoparticles in the desired direction \cite{3}. Due to the complex geometry of the arteries, the gradient magnetic field should be changed continuously.
2. Numerical Model

For the propulsion model of the particles seven major forces are considered; i.e. the magnetic force from MRIs Main Magnet static field, as well as the Magnetic field gradient force from the special Propulsion Gradient Coils. The static field caters for the aggregation of nanoparticles, while the magnetic gradient navigates the agglomerations. Moreover, two kind of forces, contact and drag forces are also considered. The contact forces are firstly developed between the aggregated nanoparticles and secondly between nanoparticles and walls. The Stokes’ drag force for each particle is considered, while only spherical particles are considered in this study. In addition, forces due to gravity and buoyancy, are included. The numerical model for all the above mentioned forces is given in [4]. Finally, attractive forces, such as the Van der Walls forces, are included in the present model [5].

3. Numerical Method

The OpenFoam platform [6] was used for the calculation of the flow field and the uncoupled equations of particles motion. The simulation process goes as follows; initially, the fluid flow is determined using the incompressible Navier-Stokes equations and the PISO method. Upon finding the flow field (pressure and velocity), the motion of particles is evaluated by the Lagrangian method. The equations are solved in time by the Euler time marching method. The stability of the algorithm is guaranteed through a time step of the order of $10^{-6}$ s. The method is based on an iteration algorithm that intent to minimize the deviation of the particles from a desired trajectory, which starts from the middle of the inlet and passes through the middle of the desired tube. The trajectory is predefined in the computational platform by a 10degree polynomial. In a two-dimensional simulation, the gradient magnetic field is temporarily adjusted perpendicular to the desired trajectory. This happens in a suitable way such that the particles’ distance from the trajectory to be decreased. To verify the optimal gradient magnetic field a Covariance Matrix Adaptation Evolution Strategy (CMAES) was used in order to drive the particles into the desired area [7].

![Figure 1. Y-shaped geometry.](image)

4. Results

For the evaluation of the potentials of this numerical model, a series of simulations with different numbers of optimization parameters for the magnetic field were performed. For this reason, the combined flow of particles and water solution in a Y-shaped geometry (2D) was simulated, as shown...
in Figure 1. The inlet of the fluid is in the left of the geometry and there are two outlet branches in the right side. Between the two outlet branches is selected an angle of 60° degrees. Both diameters of the main and outlet branches are kept constant at 2.5 mm. The overall length of the simulated geometry was 0.036 m. The velocity of the fluid was 12.2 mm/s in the main branch of the geometry and 6.1 mm/s in the outlet branches [3]. One million particles were simulated. Each of the simulated particles has hydrodynamic diameter equal to 1 um and simulates aggregations of nanoparticles. The simulation was under a uniform transverse magnetic field of magnitude $B_0 = 1$ T.

Initially, the CMAES optimization strategy algorithm provides the OpenFOAM program with random values of gradient magnetic field. In the end of each simulation, the computational platform checks the distance between the particles and the desired trajectory. If all particles are in the desired trajectory, the simulation ends. If not, the optimization platform provides new values of gradient magnetic field in order to eliminate the distance of particles from the desired trajectory. In this way, the appropriate values of the gradient magnetic field are found for the particles' navigation into the targeted areas. Lower or higher values of the gradient magnetic field are rejected from the computational method, because in the first case the nanoparticles are not navigated into the desired area and in the second case, they are attached to the vessels’ walls.

| Time Step (s) | Color | mT/m |
|--------------|-------|------|
| Initial      | Red   | 0    |
| 0.2          | Blue  | -499.9 |
| 0.4          | Pink  | 500  |
| 0.6          | Cyan  | 152.9 |
| 0.8          | Yellow| 482.9 |
| 1            | Orange| 423.9 |
| 1.2          | Grey  | 315  |
| 1.4          | Black | 9.8  |

From our calculations, it is clear that the present model can simulate the motion of the particles in a realistic manner and estimate the gradient magnetic field, in order to navigate the simulated particles into the desired trajectory, as it is depicted in Table 1. This model can drive the particles in prescribed areas, with efficiency more than 90% in the number of particles. On the other hand, a small amount of particles is stuck to the walls and remains there for the rest of the simulation, as it is shown in Figure 2.

Figure 2. Desired trajectory (green line) and positions of each particle in each time step.

The same simulation as before was re-performed with more changes of the gradient magnetic field. Each one of these changes is considered as one optimization parameter. In the present study, the optimization parameters were increased from 8 to 18, i.e the corresponding changes of the gradient magnetic field. The particles’ distance from the desired trajectory was measured just before the particles pass the outlet of the geometry.
a) Figure 3. Distribution of particles for: a) a simulation with 8 optimization parameters, b) a simulation with 18 optimization parameters. The black lines indicate the boundaries and the green line the desired trajectory.

The particles are getting closer to the desired trajectory, while the optimization parameters are increasing, as is showed in figure 3a,b. This comparison shows that the numerical method can drive successfully the particles into prespecified areas.

5. Discussion

In this work, a computational study of the optimum gradient magnetic field for the navigation of spherical particles into targeted areas is presented. The computational method can simulate an MRI system working under experimental conditions and drive particles into the desired trajectory with efficiency more than 90% in the number of particles. The results indicate that the more optimization parameters used, the smaller the distance from the desired trajectory is. Due to the fact that the particles' distance is minimized, we conclude that the present numerical model can drive the particles into specified areas. In order to eliminate particles' distances, more optimization parameters are needed. Also, it is known that the existed MRIs' can produce small changes in the gradient magnetic field at each instant. The computational method can simulate the gradient magnetic field of an MRI, when many optimization parameters are used. Thus, this requires more computational time.

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