



# Analysis of High Gradient Ferromagnetic Seeding for Targeted Drug Delivery

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## INTRODUCTION

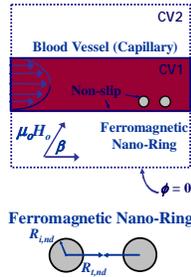
- The reduction of side effects at non-target organs, e.g., hair loss in cancer treatment, is one of the goals of targeted drug delivery research.
- One important consequence of side effects and drug deactivation is that they usually limit the dose of a drug that could otherwise be administered in large quantities to treat a diseased tissue or organ. In many cases, this prolongs the treatment regimen or simply diminishes the effectiveness of the treatment.
- One way to achieve drug targeting to a site in the body is to incorporate magnetic particles into drug carriers and then to retain them at a site using an externally applied magnetic field.
- However, it has been reported that the use of only external magnets in magnetic drug targeting (MDT) is restricted to regions in the body that are not too deep below the skin and that do not experience high blood velocities.

## OBJECTIVES

- The feasibility of using internally positioned, ferromagnetic "nano-dockers" to enhance the force on and hence retention of magnetic drug carrier particles (MDCPs) at a specific site is determined.
- The hypothesis is to determine whether high gradient magnetic separation (HGMS) principles can be applied to MDT, wherein it is surmised that the nano-dockers will locally increase the magnetic force on a MDCP and hence increase its retention at a specified site above that which would occur without the nano-docker present.
- The conditions for which the ferromagnetic nano-dockers effectively retain spherical MDCPs in a capillary of typical size are investigated.
- The variables studied include the average blood velocity ( $u_b = 0.1 - 0.5$  cm/s), strength of the homogeneous and externally applied magnetic field ( $\mu_0 H_0 = 0.0 - 1.0$  T), size ( $R_{nd} = 0.4 - 0.8$   $\mu$ m radius) of the nano-dockers (409 SS,  $M_{nd,s} = 1357$  kA m<sup>-1</sup>), and size ( $R_p = 0.1 - 1.0$   $\mu$ m radius) and magnetite ( $M_{m,p} = 455$  kA m<sup>-1</sup>) content ( $x_{m,p} = 2 - 80$  wt%) of the MDCPs.

## SCHEMATIC

Figure 1 (above) shows a 2-D schematic of the control volume used to model the MDT system. A ferromagnetic nano-ring or torus (i.e., nano-docker) of radius  $R_p$  and internal radius  $R_i$  is represented in the 2-D configuration as two parallel wires of radii  $R_i$  set at a distance  $2R_p$  apart from each other. This nano-ring is placed at a strategic position inside a capillary to study its ability to retain drug particles under the influence of an externally applied magnetic field of strength  $\mu_0 H_0$  positioned at angle  $\beta$  to the flow of blood. Two different control volumes (CV) are used for determining the magnetic capture of the drug carrier particles by the ferromagnetic filaments. CV1 (inner continuous blue box) is used to determine the x-y components of the blood velocity by solving the Navier-Stokes and mass continuity equations. CV2 (outer discontinuous blue box) is used to solve Maxwell's continuity equation for the magnetic flux B. To reduce computational costs, only the bottom half of the system depicted in (A) is evaluated in both CVs.



## DESCRIPTION/ASSUMPTIONS

- The idea is to first inject the strongly ferromagnetic nano-dockers into blood stream and collect them magnetically at the desired site. Then to inject the less ferromagnetic MDCPs into blood stream and collect them at the site by capturing them with the nano-dockers.
- The control volume (CV) consists of a 2-D dimensionless box representing a capillary;  $R_{i,nd}$  the internal radius of the ferromagnetic torus (represented as two parallel wires), is assumed to be the characteristic length with its magnitude set at half the torus radius  $R_{i,nd}$ .
- The model accounts for both magnetic and drag forces acting on the magnetic particles only. For simplicity, wall, lift and interparticle magnetic forces are not considered while both the gravitational and inertial forces are assumed to be negligible at the flow conditions investigated in this study.
- Additional assumptions include the blood to be a homogeneous, incompressible Newtonian fluid flowing at a constant, non-pulsating velocity.
- Non-slip boundary conditions are applied at every interface in contact with the blood stream.
- The velocity at the inlet of the CV is defined by a parabolic profile with average velocity  $u_0$ .

## PARTICLE TRAJECTORY EQUATIONS

The trajectory lines (or streamlines) of the magnetic drug carrier particles, defined by their velocity components,  $v_{p,x}$  and  $v_{p,y}$ , are determined by the dynamic equilibrium between two main forces, i.e., the drag and magnetic forces. Both the gravitational and inertial forces (i.e., those involving particle acceleration) are neglected, as they are relatively small compared to the other two forces in an aqueous system at the length scales investigated here. The magnetic-drag force balance leads to the following expressions for the two components of the magnetic drug carrier velocity<sup>1</sup>:

$$v_{p,x} = v_x + \frac{V_{m,p}}{u_0 M_{nd} H} \left[ \left( \frac{1}{R_{i,nd}} \frac{\partial \phi}{\partial \xi_x} - H_0 \cos \beta \right) \frac{1}{R_{i,nd}} \frac{\partial^2 \phi}{\partial \xi_x^2} + \left( \frac{1}{R_{i,nd}} \frac{\partial \phi}{\partial \xi_y} - H_0 \sin \beta \right) \frac{1}{R_{i,nd}} \frac{\partial^2 \phi}{\partial \xi_x \partial \xi_y} \right]$$

$$v_{p,y} = v_y + \frac{V_{m,p}}{u_0 M_{nd} H} \left[ \left( \frac{1}{R_{i,nd}} \frac{\partial \phi}{\partial \xi_x} - H_0 \cos \beta \right) \frac{1}{R_{i,nd}} \frac{\partial^2 \phi}{\partial \xi_x \partial \xi_y} + \left( \frac{1}{R_{i,nd}} \frac{\partial \phi}{\partial \xi_y} - H_0 \sin \beta \right) \frac{1}{R_{i,nd}} \frac{\partial^2 \phi}{\partial \xi_y^2} \right]$$

$$V_{m,p} = \frac{2}{9} R_p^2 \omega_{fm,p} \frac{\mu_0}{R_{i,nd} n_B} M_{nd} M_{fm,p} \quad M_{nd} = 2\alpha_{nd} H_0 \quad M_{fm,p} = 3\alpha_{fm,p} H$$

$$H = |\mathbf{H}_0 - \nabla \phi| \quad \alpha_{nd} = \min \left( 1, \frac{M_{nd,s}}{2H_0} \right) \quad \alpha_{fm,p} = \min \left( 1, \frac{M_{fm,p,s}}{3H} \right)$$

The components of the blood velocity,  $v_x$  and  $v_y$ , were obtained previously by solving the Navier Stokes and Continuity equations in CV1 and assuming non-slip BC at every solid-liquid interface. The scalar magnetic potential  $\phi$  was obtained by solving Maxwell's equation  $\nabla^2 \phi = 0$  in CV2 and assuming  $\phi = 0$  at every boundary.

## TYPICAL SIMULATION RESULTS

- The performance of the MDT system was evaluated by analyzing the streamlines, which represent the MDCP trajectories in the blood stream, to determine the fraction of them that are attracted to and hence retained by a nano-docker positioned in a capillary. The collection efficiency (CE) is defined as this fraction, but in terms of percent. The streamlines are defined by  $(v_{p,x}, v_{p,y})$  and determined from the simultaneous solution of the equations presented above.

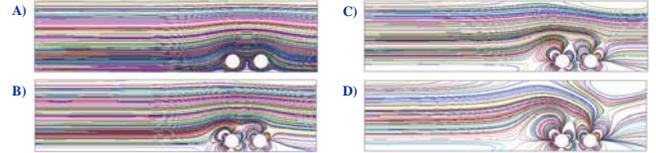


Figure 2 (above) shows typical simulation results for the streamlines of the MDCPs in a capillary of diameter  $d_c = 8$   $\mu$ m.  $R_{i,nd} = 0.8$   $\mu$ m,  $R_p = 0.4$   $\mu$ m,  $u_0 = 0.1$  cm/s, and  $\mu_0 H_0 = 0.1$  T: A) just blood flow with no MDCPs present; B) MDCPs with  $x_{m,p} = 0.02$ ; C) MDCPs with  $x_{m,p} = 0.2$ ; and D) MDCPs with  $x_{m,p} = 0.5$ . The fraction of the streamlines captured by the probe represents its collection efficiency (CE). The CEs for the results in Figures 2B, 2C, and 2D are 27.4, 63.3 and 100%, respectively.

## COLLECTION EFFICIENCY RESULTS

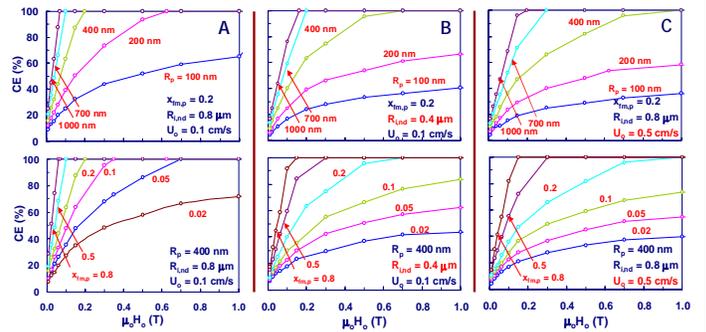


Figure 3 (above) provides the results from a parametric study on the CE of the nano-docker in a capillary. The top graphs show the CE of the MDCPs by a nano-docker (409 SS) in an 8  $\mu$ m capillary as function of the magnetic field strength  $\mu_0 H_0$  and the radius ( $R_p$ ), and the bottom graphs show the same but for the weight fraction of magnetite ( $x_{m,p}$ ), and both sets of graphs for A)  $R_{i,nd} = 0.8$   $\mu$ m and  $u_0 = 0.1$  cm/s. Conditions in B) are identical to those in A) except for the nano-docker radius ( $R_{i,nd} = 0.4$   $\mu$ m). Conditions in C) are identical to those in A) except for the blood velocity ( $u_0 = 0.5$  cm/s). The results show the robustness of the nano-docker concept, with very high CEs being realized for a wide range of conditions, even with MDCPs of small size and low magnetite content. The results also indicate that smaller ferromagnetic seeds (B) or larger blood velocities (C) do not significantly alter the viability of the nano-docker concept in capturing MDCPs. What is most intriguing is that CEs of 100% are indeed achievable at surprisingly low magnetic field strengths and for a low amount of ferromagnetic material in the MDCPs.

## CONCLUSIONS

- This exploratory study showed that the proposed MDT system, utilizing the non-invasive nano-docker concept to increase the magnetic force on the MDCPs, has considerable promise as an effective drug-targeting tool.
- It was determined that the collection efficiency increases with increases in the strength of the magnetic field, size of the magnetic drug particle, and its susceptibility, and with decreases in the average blood velocity, with all the results being intuitively expected.
- It was also shown that 100% collection efficiencies of the MDCPs by the nano-dockers were ideally achievable at relatively moderate conditions, but this remarkable ability varied widely depending on the system parameters.
- Overall, this study represents a first attempt at applying HGMS principles to MDT. In the future, more detailed models will be developed in an attempt to more realistically predict the system efficiencies.

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## REFERENCE

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