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CONSTRUCTAL OPTIMIZATION OF MAGNETIC FIELD SOURCE IN MAGNETIC DRUG TARGETING THERAPY

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Abstract. Magnetic drug targeting (MDT) is a promising, developing, non-intrusive therapy used to treat malfunctions in organism such as tumoral entities, stenoses, and thrombosis. Body forces are produced by external magnetic fields of high gradient to precisely guide the medication towards regions of interest, aiming to destroy the affected tissues and avoid the healthy cells. The MDT medication, deposited super-paramagnetic nanoparticles (SPN), is entrained by the hemodynamics of the arterial tree to the region of interest (ROI). Key to the success of MDT is the high gradient magnetic field, hence its source, here a permanent magnet. This study presents a constructal optimized array of permanent magnets for high gradient magnetic field.

Key words: Constructal law, Optimization, Magnetic drug targeting, Permanent magnet, Numerical simulation.

1. INTRODUCTION

Magnetic drug targeting is a noninvasive modern technique to reduce the side effects related to the excessive distribution of powerful medication and improve its efficiency. In this therapy, the medication carried by superparamagnetic nanoparticles and injected in the blood stream interacts with an external magnetic field aimed at targeting the drug and fixing it mostly in the region of interest (ROI) for optimal delivery [1–6].

For example, tumor formations excision may be improved by destroying more of the affected tissue rather than healthy tissue through magnetic drug targeted therapies. Worth noting, magnetic targeting has also industrial applications (*e.g.*, micro stirring devices) [7].

The constructal optimization is related to the magnetic drug targeting therapy, one of the many applications that require high gradients and intense magnetic fields, in order to retain and guide the SPION medication [8] into the region of interest, such as tumors, with the aim to maximizing the efficiency of the therapy.

In this paper we focus on the analysis and optimization of a static magnetic field source (*e.g.*, a permanent magnet), able to generate a high gradient magnetic field, to obtain a localized and an as high as possible fluid flow – magnetic field interaction that may prolong the time of residence of the medication in the region of interest (ROI). To this aim, we investigated the interaction of the aggregate fluid (blood and magnetic drug) with the magnetic field.

The magnetic field source is permanent magnet as magnet field source that is divided into an array of slot magnets. The numerical simulations were performed in the finite element method (FEM) technique. The main purpose is to generate a high gradient and powerful magnetic field, using an array of permanent magnets, following a simple criterion – each setup has the same amount of magnetic energy, and the same footprint on the skin.

2. THE MATHEMATICAL MODEL

In this study we neglect the flow-vessel walls structural interactions. Previous studies [6] revealed that, although a problem of concern in many circumstances, it is less so in magnetic drug targeting. The magnetic drug transport and fixation problem is analyzed by coupling the magnetic field model to the fluid flow. The

aggregate fluid – blood and medication – has the magnetic properties of the drug carrier (a superparamagnetic material). First, the static magnetic field problem of the permanent magnet is solved for to find the (magnetization) body forces. Next, the fluid-flow interaction is studied. In this two-step approach we neglect the reaction of the flow upon the external magnetic field. The reason is the relatively low velocity field in hemodynamic.

The magnetic field model is governed by:

Ampère's law

$$\nabla \times \mathbf{H} = 0 \; ; \tag{1}$$

Magnetic flux law

$$\nabla \cdot \mathbf{B} = 0 \; ; \tag{2}$$

Constitutive law

$$\textit{permanent magnet} \;\; \mathbf{B} = \mu_0 \mu_{r,mag} \mathbf{H} + \mathbf{B}_{rem},$$

$$\textit{aggregate fluid (blood and medication)} \;\; \mathbf{B} = \mu_0 \left[\mathbf{H} + \mathbf{M}_{ff}(\mathbf{H}) \right], \tag{3}$$

$$\textit{elsewhere} \;\; \mathbf{B} = \mu_0 \mathbf{H},$$

where μ_0 [H/m] is the magnetic permeability of free space, $\mu_{r,mag}$ the relative magnetic permeability of the permanent magnet, **H** [A/m] the magnetic field strength, **B** [T] the magnetic flux density, $\mathbf{B}_{rem}$ [T] the remanent magnetic flux density, and $\mathbf{M}_{ff}$ [A/m] the magnetization of the aggregate fluid, a function of **H.**

Using the magnetic vector potential **A** [Wb/m] (and the divergence free gauge condition)

$$\mathbf{B} = \nabla \times \mathbf{A} \; , \; \nabla \cdot \mathbf{A} = 0 \; , \tag{4}$$

the mathematical model for the magnetic field problem is

$$\nabla \times \left(\mu_0^{-1} \mu_r^{-1} \nabla \times \mathbf{A} \right) = 0 \, . \tag{5}$$

Magnetic insulation ($\mathbf{n} \times \mathbf{A} = 0$) boundary conditions close the magnetic field problem. The mathematical model (1)–(5) is solved using FEM [9]. The magnetic body forces (MBF), $\mathbf{f}_{mg}$ [N/m^3], that occur in a magnetisable medium, such as the blood and magnetic medication aggregate, may be obtained using the energy, *i.e.*, the theorem of the generalized forces

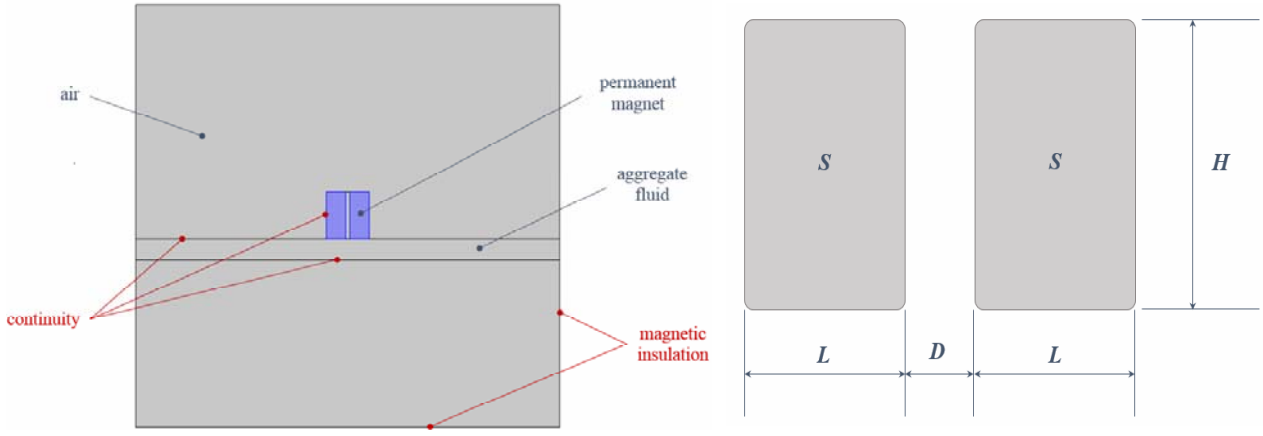
$$\mathbf{f}_{mg} = (\mathbf{M} \cdot \nabla) \, \mathbf{H}. \tag{6}$$

It is assumed that the fixation process is "non-thermal", which means that the system is in thermal equilibrium both internally and with its surrounding environment (at 37ºC).

Concerning the hemodynamic problem of the medication transportation, it is assumed that the flow of the aggregate, magnetisable medium (blood and medication) does not modify the magnetic field produced by the permanent magnet, *i.e.*, the magnet may influence the flow whereas the flow does not modify the magnetic field. Furthermore, all media except for the permanent magnet and the aggregate magnetizable medium (blood and medication) have no magnetic properties therefore their structure, positions, and shapes are not accounted for.

3. THE CONSTRUCTAL OPTIMZATION

The particular positioning of the magnet – along the blood vessel trajectory – suggest its shape: a parallelepiped with a longer side parallel to the blood vessel, and two smaller, equal sides, defining a face orthogonal to the vessel. Figure 1a displays a qualitative sketch of the computational domain.



a) the 2D computational domain and boundary conditions for $n_s = 2$ magnetic slots

b) optimization parameters: AR = H/L, and GS = D. The permanent magnet has the per unit length volume $\mathrm{Vol} = H \cdot \left[n_S \cdot L + (n_S - 1) \cdot L \right] = \text{const.}$ Here the number of slots $n_s = 2$.

Fig. 1 – The boundary conditions and the geometric optimization parameters.

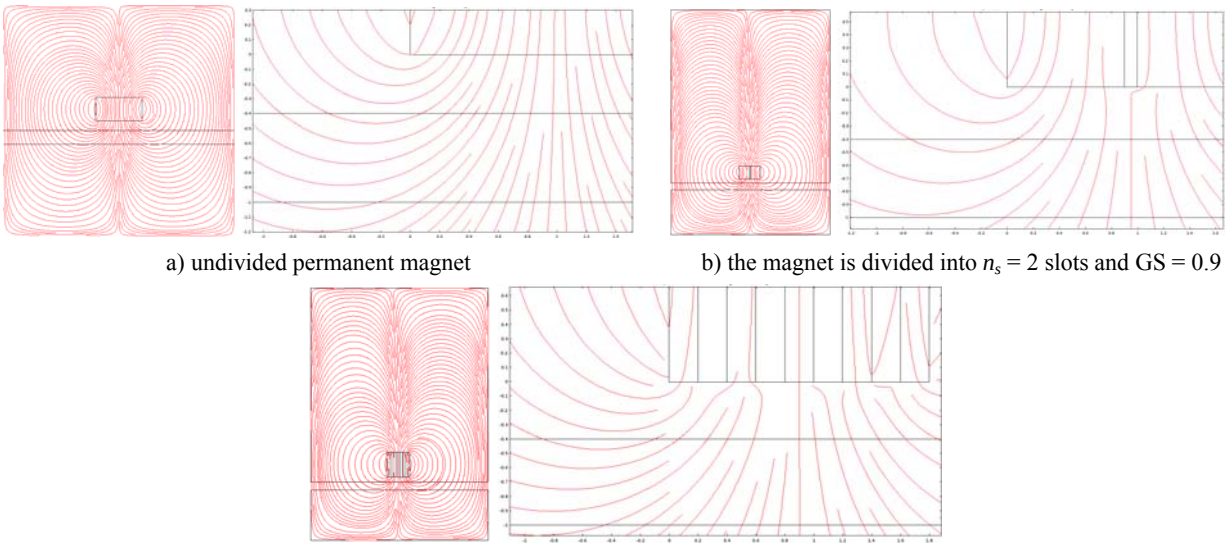
In this study, we present the optimization principle using a 2D computational domain, along a crosscut plane through the magnet and the vessel. The full 3D analysis and the effect of the pulsatile flow make the object of a future work.

The constructal optimization refers to a permanent magnet of fixed volume, Vol [m^3], with the total magnetic energy, $W_{p,mag} = \int_{\mathrm{Vol}} (\mathbf{B} \cdot \mathbf{H})/2 \, \mathrm{d}v \cong \mathrm{Vol} \cdot (B_{rem} H_c)/2$, where H_c [A/m] is its coercive field. As suggested by eq. (6), the more non-uniform the magnetic field is the larger the body forces are. In particular, if the magnetic field is uniform then the magnetization forces are null.

In view this assertion, the optimization strategy in this study relies on dividing the magnet, successively, in several identical parts – called "slots" –, while keeping the total volume of the initial, undivided magnet. We introduce the *slot aspect ratio*, AR (height/length). Assuming that the slots are equally spaced, we define a second parameter, the *gap size*, GS, where "gap" is the spacing between the slots (Fig. 1b). The optimum design is decided in terms of the horizontal and vertical components of the MBFs, evaluated at a distance that corresponds, roughly, to the distance from the magnet basis to the wall of the blood vessel that conveys the medication.

4. NUMERICAL SIMULATION RESULTS

Figure 2 shows the magnetic field for several cases: the undivided permanent magnet, the magnet divided into $n_s = 2$ slots with a GS = 0.9, and the permanent magnet divided into $n_s = 5$ slots, with GS = 0.5. The magnetic field is highly non-uniform at the margins of the magnet, where the highest gradients occur. The division of the permanent magnet into slots introduces local gaps that increase, locally, the magnetic field gradient. However, qualitatively, the gap size should be as large as the distances from the magnet basis to the vessel. On the other hand, increasing GS produces slots with too large ARs, which would result in too weak magnetic energy in the region of the blood vessel. It turns that GS upper margin is related to the upper limit of the slot AR. Another factor that impacts on the spatial variation of the magnetic field produced by the permanent magnet is the distance to the source – the magnetic flux density decreases with the inverse of the distance, and the magnetic energy with the square of it. These two factors, GS and the distance to the source are interplaying and an optimal design of the magnet should account for both.



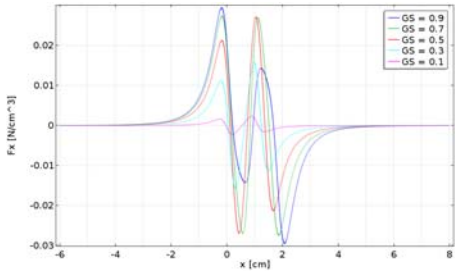
a) undivided permanent magnet

b) the magnet is divided into n_s = 2 slots and GS = 0.9

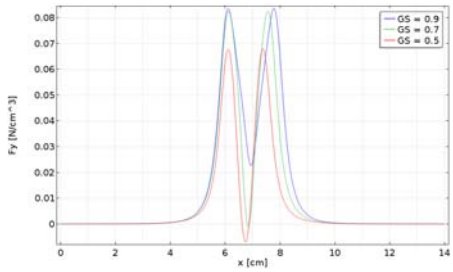
c) the magnet is divided into n_s = 5 and GS = 0.5

Fig. 2 – The magnetic flux density for different divisions of the permanent magnet. Geometric dimensions are in centimeters.

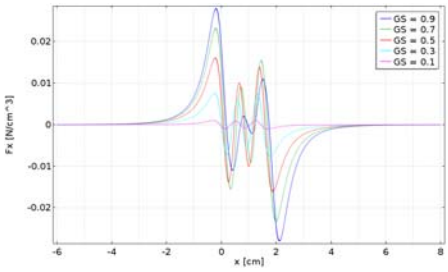
Two parametric optimisation paths that imply the solution to the magnetic field are conducted as follows. First, for each number of magnetic slots in the interval {1, 2, 3, 4,} and for the slot AR = 0.5,…,0.9, the MBFs along the vessel wall are computed and compared. Figure 3 shows the O*x* components of the MBFs.



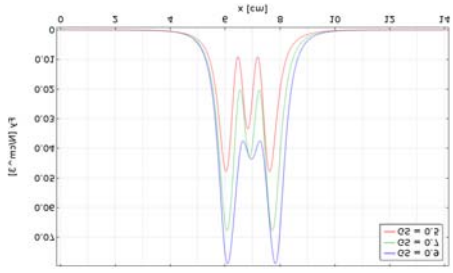
a) two slots, $f_{mg,\underline{x}}$



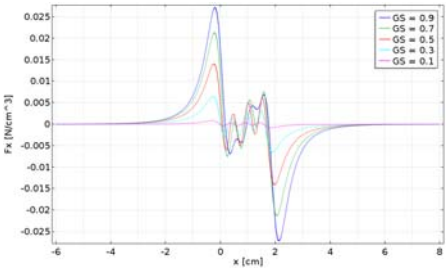
b) two slots, $f_{mg,\underline{y}}$



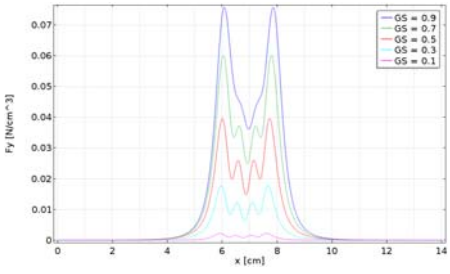
c) three slots, $f_{mg,\underline{x}}$



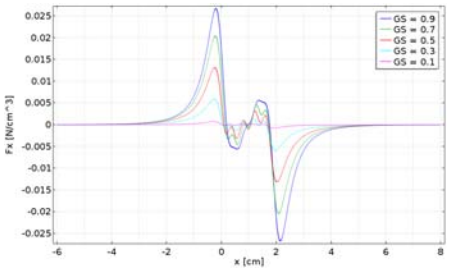
d) three slots, $f_{mg,\underline{y}}$



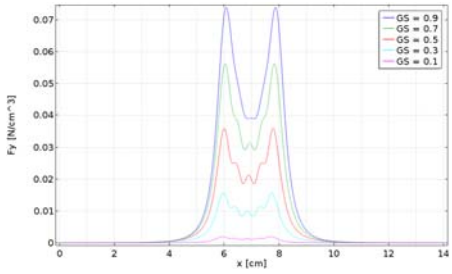
e) four slots, $f_{mg,\underline{x}}$



f) four slots, $f_{mg,\underline{y}}$



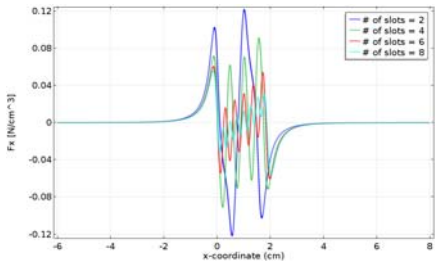
g) five slots, $f_{mg,\underline{x}}$



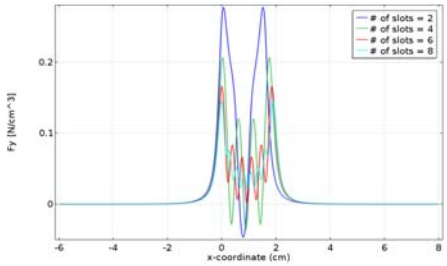
h) five slots, $f_{mg,\underline{y}}$

Fig. 3 – The magnetic body forces for different slot aspect ratios, at different slots number.

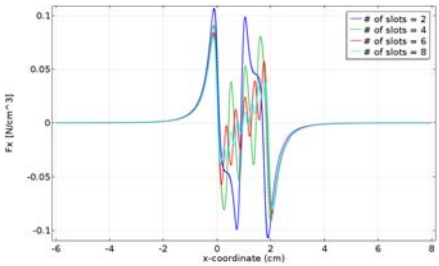
The O*x* component, $f_{mg,x}$, may perturb the aggregate flow, but this would happen during the low flow rate interval of the pulsatile flow. Its effect may be important and worth discussing for pulsatile flow. Therefore we turn our attention on the O*y* component, which acts into attracting the medication towards the magnet. It is worth noting the ROI for medication targeting has to be situated between the magnet and the blood vessel or the effect of the magnetic field is detrimental.



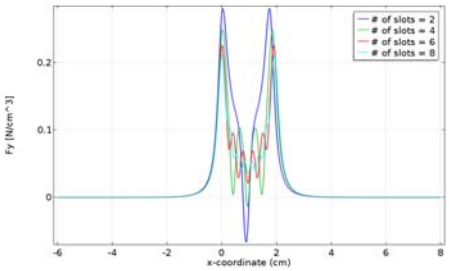
a) GS = 0.6, $f_{mg,\underline{x}}$



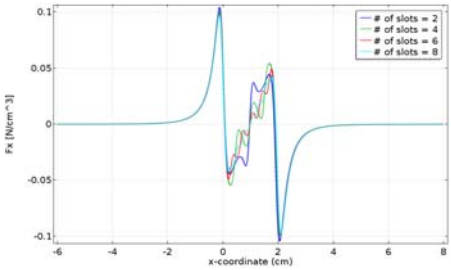
b) GS = 0.6, $f_{mg,\underline{y}}$



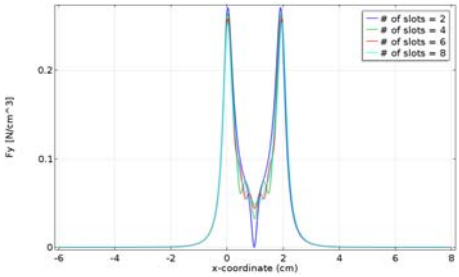
c) GS = 0.8, $f_{mg,\underline{x}}$



d) GS = 0.8, $f_{mg,\underline{y}}$



e) GS = 0.95, $f_{mg,\underline{x}}$



f) GS = 0.95, $f_{mg,\underline{y}}$

Fig. 4 – The magnetic body forces for different slot aspect ratios, at different gap sizes.

The amplitude of $f_{mg,y}$ decreases slightly with the number of slots, and more significantly with the GS size. On the other hand, larger GSs lead to smaller oscillations in amplitude (for $n_s = 2$ and Gs = 0.9, $f_{mg,y}$ shows off also negative values, *i.e.*, the magnetic field acts repulsively). We may conjecture that the design with

GS = 0.7 and n_s = 5 (Fig. 3h) seems to optimal. Next, the parameter of interest is for GS. For GS = 0.6,…,0.95, the magnet is divided into n_s = 1,..,8 slots, and the MBFs along the vessel wall are computed and compared. Figure 4 shows the MBF along the top part of the vessel wall. The same observation on $f_{mg,x}$ stands here too. In what concerns $f_{mg,y}$, for smaller GSs, the larger n_s is the more uniform but smaller is the amplitude. For larger GSs, the same is true but the maximum peaks are invariant. Also, for small GSs and reduced *ns* the O*y* component may register negative value, which is undesirable. Finally, the decision on the best design is to be taken according to the size, shape, and relative position with respect to the magnet of the ROI.

5. CONCLUSIONS

The constructal optimization presented in this study is related to the magnetic drug targeting therapy, one of the many applications that require high gradients and intense magnetic fields. The constructal optimization refers to a permanent magnet of fixed volume hence total magnetic energy, as the magnetic field source. The particular positioning of the magnet – along the blood vessel trajectory – suggest its shape: a parallelepiped with a longer side parallel to the blood vessel, and two smaller, equal sides, defining a face orthogonal to the vessel. It was assumed that the flow of the aggregate, magnetic medium (blood and medication) does not modify the magnetic field produced by the permanent magnet, *i.e.*, the magnet may influence the flow whereas the flow does not modify the magnetic field.

The optimization strategy relies on dividing the magnet, successively, in several identical parts – "slots" – while keeping the total volume of the initial, undivided magnet. The *slot aspect ratio*, AR (height/length) and the *gap size*, GS, where "gap" is the spacing between the slots, are the two design parameters. The optimum design is decided in terms of the horizontal and vertical components of the MBFs, evaluated at a distance that corresponds, roughly, to the distance from the magnet basis to the wall of the blood vessel that conveys the medication.

The Ox component, $f_{mg,x}$, may perturb the aggregate flow, but this would happen during the low flow rate interval of the pulsatile flow. Its effect may be important and worth discussing for pulsatile flow. Therefore, the attention here is devoted to the O*y* component, which acts into attracting the medication towards the magnet. It is worth noting the ROI for medication targeting has to be situated between the magnet and the blood vessel or the effect of the magnetic field is detrimental. The decision on the best design is to be taken according to the size, shape, and relative position with respect to the magnet of the ROI.

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