NEW MODIFIED VISCOELASTIC SOLUTION ASSOCIATED WITH MAGNETIC FIELD EFFECT FOR THE ADVANCED TREATMENT OF KNEE OSTEOARTHRITIS

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Osteoarthritis (OA) is the most common form of arthritis in the knee joint which leads to the need to develop or improve treatments with the main purpose of reducing the pain and functional destruction of the joint and maintaining the mobility of the joint. For this purpose, the use of magnetic nanoparticles (MNPs) in drug delivery systems is proposed. The technique involves the use of external permanent magnets to control the viscoelastic solution into the targeted area. This paper presents the influence of the geometry and dimensions of the external magnets on the generated magnetic field.

Keywords: COMSOL Multiphysics, magnetic field, knee osteoarthritis treatment

1. Introduction

OA is manifested by severe pain in the joint, caused by cartilage destruction, which prevents optimal functioning of the knee and in chronic cases causing the patient's immobility [1, 2]. The treatment of osteoarthritis is vast, ranging from non-pharmacological methods such as physical therapy or weight loss, to pharmacological treatments that involve the use of drugs, such as orally administered anti-inflammatory or vitamins, intra-articularly steroid injections and in the final stage total knee arthroplasty (TKA) is used for a total replacement of the joint, which is not recommended especially to young patients because it is an invasive painful surgery which limits the future activities of patients [3, 4]. Controlled drug delivery is a modern non-invasive technique used to reduce the side effects associated with the over-distribution of powerful drugs, by increasing their effectiveness. The therapy aims to optimize the delivery of these drugs fixed in the matrix of superparamagnetic nanoparticles, by injecting them into the knee joint, where they interact with an external magnetic field, meant to deliver the drugs and fix them in the region of interest [5, 6]. MNPs such as iron oxide (Fe_2O_3) have the superparamagnetism property which allows the ferrofluid (the viscoelastic solution formed by magnetic nanoparticles embedded in a matrix with clinical properties for treatment) to be controlled from the outside using magnets

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[7]. This technique has the advantage of prolonging the action time of the treatment by constant maintenance in the affected area, ensuring a faster healing. This is directly dependent on the physical (geometry, dimensions) and magnetic properties of the magnets used, but also on their position in the external environment [8]. Since it is proven that the introduction of MNPs in viscoelastic solutions for the treatment of osteoarthritis does not have undesirable harmful effects on the human body, this work aims to choose the optimum geometry and positions of the magnets, by simulating mathematical models in the COMSOL Multiphysics program, which highlights the magnetic field generated.

2. Materials and method

Mathematical modeling is an important part of the development of scientific and engineering fields, which requires a connection between idea and prototype, in order to be able to perform mathematical simulation.

In a scientific and engineering study the modeling process in COMSOL Multiphysics is carried out in several steps:

a) CAD import interface. COMSOL Multiphysics contains a whole series of tools for drawing the studied mechanism. It also allows the import of the drawing made with the help of other programs (AUTOCAD, CATIA). COMSOL Multiphysics allows you to choose a predefined model, closest to the physical laws that govern the model studied. Initially, the magnetic field issue of the magnet is solved to discover the magnetization. It is correlated with the properties of the ferrofluid present in the joint.

b) Realization of the mathematical model. The mathematical model for the magnetic field is useful for identifying the constants and scalar expressions needed to solve the magnetostatic issue. The source of the magnetic field is a system of permanent magnets. This model is governed by two laws:

- Ampere Law: $\nabla \times H = 0$; (1)
- Law of magnetic flux: $\nabla B = 0$; (2)

A ferrofluid is a fluid consisting of ferromagnetic colloidal particles suspended in a carrier fluid. The ferrofluid used in this application is composed of an iron oxide, known as magnetite, which is in the form of superparamagnetic nanoparticles. The ferrofluid, a drug carrier, behaves as a magnetizable fluid that possesses the magnetic properties of the material from which the magnetic nanoparticles are made, namely, the properties of magnetite.

The experiment is based on the following hypothesis: if the most efficient matrix of magnets is selected and applied, the best results of the treatment will be obtained. The purpose is to investigate the way how the recovery treatment ensures the optimization of the results and the shortening of the recovery time of the knee disorders. In this paper, the realization plan focuses on the analysis and optimization of a static magnetic field source, represented by permanent magnets, capable of generating a high magnetic field gradient, in order to locate and concentrate as many nanoparticles as possible, which interact with the magnetic field to extend the drug's action time in the area of interest. In pursuit of this objective, a simple two-dimensional model for studying the interaction between ferrofluid and magnetic field is investigated followed by researching 2D observations in a practical application based on the results obtained for the optimal configuration. During the experiment, several magnet configurations were observed in which the volume and the distances between them vary. After the modeling on cases different magnetic fields are obtained. The most important movements of the knee are flexion and extension, to which the associated movements in plane, rotation and translation are coupled. For this reason, the two extreme positions of the knee, namely the 0° position and the 90° position, will be considered in this study. In order to be able to analyze the different situations of positioning the magnets, the forces that appear behind the patella are measured. These forces are measured in [N/m^3] and the volumetric force is evaluated, as described by the Navier-Stokes equations implemented in COMSOL, in the Fluid Dynamics module. This can be expressed as a pressure relative to the unit of length [N/m^2=Pa]/[m]=[N/m^3]. The following figure (Figure 1) shows the geometries used in the two modeling studies.

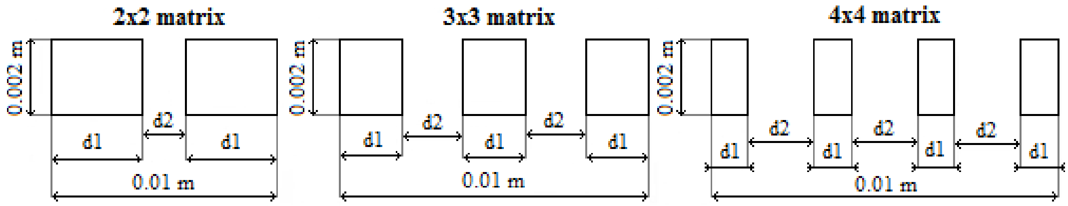

Fig. 1: Magnet matrix for 2D models: a) 2 magnets; b) 3 magnets; c) 4 magnets.

Two approaches to solving this problem were considered. The first method was based on a simple division of a magnet with the dimensions of 0.01x0.002 m in matrices of 2, 3 and 4 magnets respectively. Using this approach, the properties of the magnets are handled by reducing the surface area as well as the total energy of the magnets. The conditions for dividing the magnets are illustrated, observing a division of the permanent magnets according to the gradient of the ratio d1/d2, where d1 represents the length of a magnet, and d2 the distance between the magnets. Thus, the geometries can be divided for each type of matrix separately in three other cases correlated with the values of the ratio d1/d2, namely:

1) Case I: d1/d2<1;
2) Case II: d1/d2=1;
3) Case III: d1/d2>1.

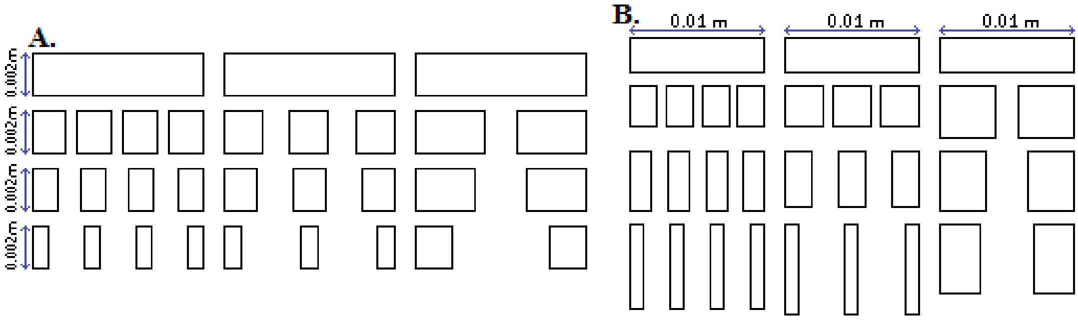

Fig 2: COMSOL geometries for the modeling studies: A - study 1 and B - study 2

In the figure above (Figure 2,A) we have the different geometries divided by cases, considering both the number of magnets and the distances between them, used in modeling. These conditions bring to our attention a number of 9 cases. The situation of the existence of a single magnet will be analyzed in order to be able to make comparisons case-by-case. The second part of the modeling (Figure 2,B) follows the same idea of dividing a magnet into matrices of 2, 3 or 4 magnets, but considers an area of action 10 times larger than the previous one, based on the justification, that a surface that covers the entire area of interest would have a greater efficiency. Similarly, the previous optimization will keep the positioning of the magnets correlated with the gradient of the ratio d1/d2. In this second modeling study, the size of the magnets is reflected in the volumetric forces it generates. Thus, we obtained a total of 18 cases for extreme positions. The geometries consider changing the two dimensions of the magnets but keeping the same energy throughout the system. The volume of the components will represent the common denominator in all.

3. Results and discussion

The practical results consist in the mathematical simulation of the ferrofluid, highlighting the magnetic flux density and the field lines generated for each case studied. The magnet with the side of 0.002m and the height of 0.01m will represent our reference magnet. In the following figure (Figure 3) is presented the cases of the existence of a matrix of 2 magnets positioned at an increasing distance, for the first optimization process. It is found that as the distance between the magnets increases, the forces on the Ox and Oy axes decrease, as the ferrofluid tends to move under normal conditions without encountering opposing forces. The magnitude of the magnetic field generated by a matrix of two magnets decreases from case a) to case c).

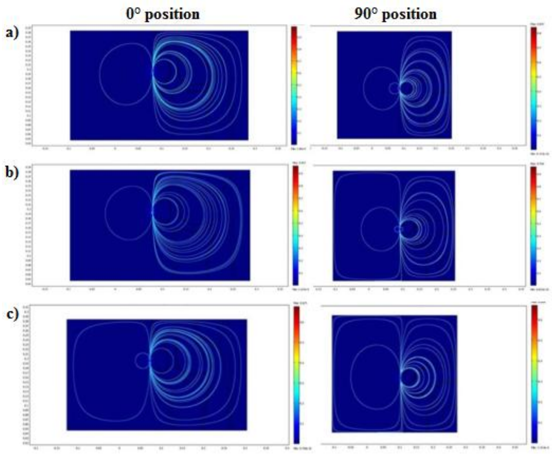

Fig.3: COMSOL modeling illustrating induction and magnetic field when using 2 magnets with the dimensions: a) 0.004x0.002m (d1/d2<1), b) 0.0034x0.002m (d1/d2=1),c) 0.002x0.002m (d1/d2>1)

The value of the remaining induction (Brem) reaches the value of 1.218517 [T] (1.22 T) in the area related to the location of the ferrofluid and affects it through two components: one in the direction of the axis Ox - Fx, and one in the direction of the axis Oy - Fy. When using a single magnet (the reference), the forces for position 0° (extension) are Fx=-4.20776 [N / m ^ 3] and Fy=0.371098 [N/m^3] and for position 90° (flexion), Fx=-4.211314 [N/m^3] and Fy=1.13 [N/m^3]. Based on these values we can conclude that the movement of the knee from one position to another brings changes in the magnetic field predominantly in the Oy direction, in order to attract the ferrofluid towards the back of the patella. This is favorable, as the Fy force opposes the delocalization of the ferrofluid from behind the patelo-femoral area. The magnet exerts a magnetic induction on the patella of 1.226259 [T], while in the target area it feels a smaller value, 1.218517 [T]. Following the same simulation procedures, the cases with 3x3 and 4x4 matrices illustrated in Figures 4 and Figure 5 will show the same tendency of the ferrofluid displacement, drawn horizontally by the force Fx to the magnets and raised to the patella by the force Fy.

The data in the following tables (Tables 1 and 2) help to interpret the graphs in Figure 6, which show the influence of parameter d2 on the intensity of the magnetic field. According to the representations, the irregular behavior of the magnets positioned in 4x4 matrices can be observed. This inflection of the curve determines us to consider the 4x4 matrix the best choice for joint applications. A similarity can be observed between the matrices of 2 magnets and 4 magnets, but only for the first case of the ratio d1/d2. The curve corresponding to the 2x2 matrix shows a linear evolution that is unfavorable for drug delivery.

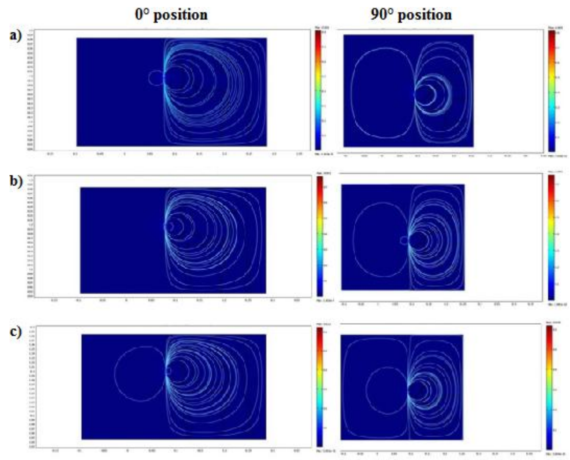

Fig. 4:COMSOL modeling illustrating induction and magnetic field when using 3 magnets with the dimensions: a) 0.00225x0.002m (d1/d2<1), b) 0.002x0.002m (d1/d2=1), c) 0.001x0.002m (d1/d2>1)

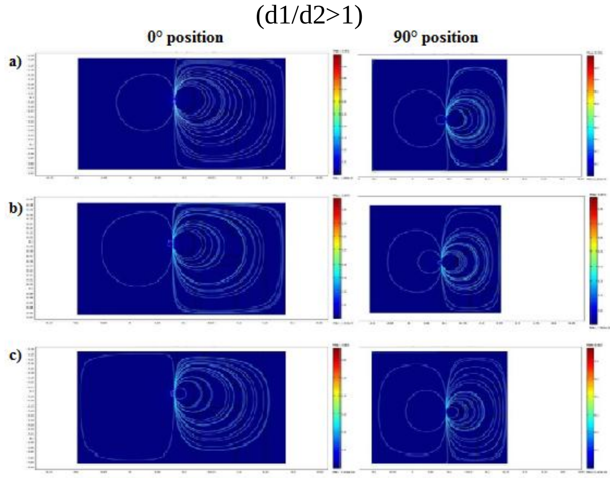

Fig. 5 COMSOL modeling illustrating induction and magnetic field when using 4 magnets with the dimensions: a) 0.002x0.002m (d1/d<1), b) 0.001429x0.002m (d1/d2=1), c) 0.001x0.002m (d1/d2>1)

The volumetric forces (Fx) acting on the Ox axis tend to attract the ferrofluid to the magnets, while the Fy forces on the Oy axis tend to withstand the slip of the ferrofluid under the forces of existing pressure in the joint.

The results of the mathematical modeling for the second optimization process are presented below. For the first case of the 2-magnet matrix, shown in Figure 6, Fx=-5787.15 N/m3, a value 5000 times higher than in the first optimization process. It is considered that in the first simulations the division of the magnets had as a consequence also the decrease of the total energy in the system.

Similar to the previous cases, with the increase of the distance between the magnets the volumetric force on the Ox axis, which has the role of attracting the particles, decreases. This is also substantiated by the fact that these magnets are closer as they have a more unitary behavior tending to form a single magnet.

Table 1

The values of the volumetric forces generated after modeling in COMSOL the 9 cases of magnet configuration for the knee joint at 0 °

Forces	Conditions	2 magnets	3 magnets	4 magnets	1 magnet 0.01x0.04	1 magnet 0.002x0.01
F_ffx [N/m^3]	Case I: $d_1/d_2<1$	-2.677207	-1.544629	-2.686054	-675.868462	-4.20776
	Case II: $d_1/d_2=1$	-1.500033	-1.218848	-1.107127		
	Case III: $d_1/d_2>1$	-0.605071	-0.298958	-0.667311		
F_ffy [N/m^3]	Case I: $d_1/d_2<1$	0.23623	0.132684	0.237069	79.579543	0.371098
	Case II: $d_1/d_2=1$	0.128839	0.105626	0.095158		
	Case III: $d_1/d_2>1$	0.053892	0.025224	0.058891		

Table 2

The values of the volumetric forces generated after modeling in COMSOL the 9 cases of magnet configuration for the knee joint at 90 °

Forces	Conditions	2 magnets	3 magnets	4 magnets	1 magnet 0.01x0.04	1 magnet 0.002x0.01
F_ffx [N/m^3]	Case I: $d_1/d_2<1$	-4.040907	-2.830486	-4.058452	-318.605131	-4.211314
	Case II: $d_1/d_2=1$	-2.74248	-2.266462	-2.03011		
	Case III: $d_1/d_2>1$	-0.984864	-0.551917	-0.990473		
F_ffy [N/m^3]	Case I: $d_1/d_2<1$	1.089556	0.751898	1.09923	67.541691	1.130408
	Case II: $d_1/d_2=1$	0.721633	0.609243	0.539532		
	Case III: $d_1/d_2>1$	0.2575	0.144148	0.261463		

According to Figure 7, it is possible to observe the identifying colors of the magnetic flux density, according to which the yellow color for case a) suggests the presence of a magnetic field with the induction near 1.2 T. In cases b) and c) the interactions between the magnets cause a decrease of the power of attraction. An undesirable effect that appears in the cases presented is the behavior of the volumetric force in the direction of Oy, which only records high negative values and for this reason tend to move the ferrofluid in the direction of the gravity force, opposite to our objectives.

According to the following table (Table 3), the values of the volumetric force Fy are predominantly negative, the case of positioning four magnets on the same line being the only variant that presents an optimal behavior between all the 3 choices of magnets for this second modeling study.

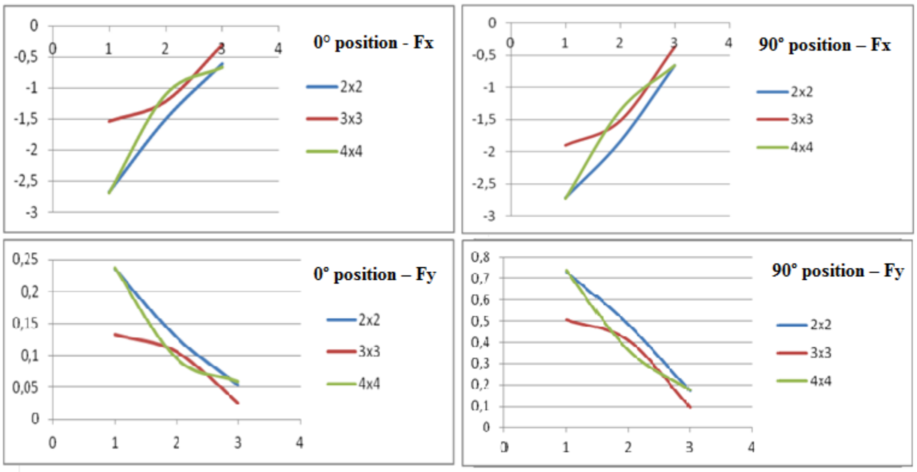

Fig. 6: Representation of the 3 curves given by the volumetric forces Fx and Fy on the corresponding directions Ox and Oy applied on the model of the joint in position of extension (left) and of flexion (right) for the first optimization process

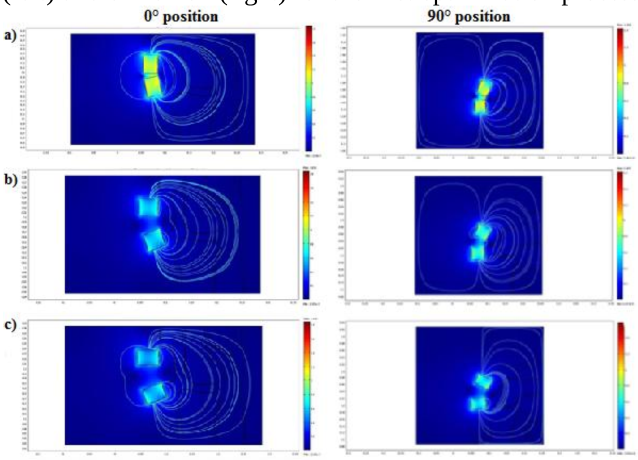

Fig. 7: COMSOL modeling illustrating induction and magnetic field when using 2 magnets with the dimensions: a) 0.04x0.03m (d1/d2<1), 0.035x0.035m (d1/d2=1), c) 0.03x0.04m (d1/d2>1)

Table 3

The values of the volumetric forces generated following the modeling in COMSOL of the 9 cases of magnet configuration of the second process for the knee joint at 0°

Forces	Conditions	2 magnets	3 magnets	4 magnets
F_ffx[N/m^3]	Case I: $d_1/d_2<1$	-5787.148562	-52.804538	-769.02699
	Case II: $d_1/d_2=1$	-2812.83292	27.980095	-238.696417
	Case III: $d_1/d_2>1$	-2553.342974	-26.418441	-51.826946
F_ffy[N/m^3]	Case I: $d_1/d_2<1$	-816.07387	-249.575446	-234.165625
	Case II: $d_1/d_2=1$	-1764.591395	-159.027015	218.835868
	Case III: $d_1/d_2>1$	-1707.281901	39.54396	58.474645

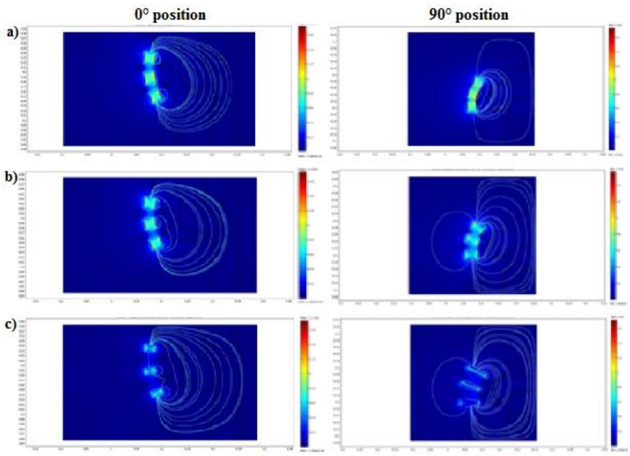

Fig. 8: COMSOL modeling illustrating induction and magnetic field when using 3 magnets with dimensions: a) 0.03x0.025m (d1/d2<1), 0.02x0.035m (d1/d2=1), c) 0.01x0.055m (d1/d2>1)

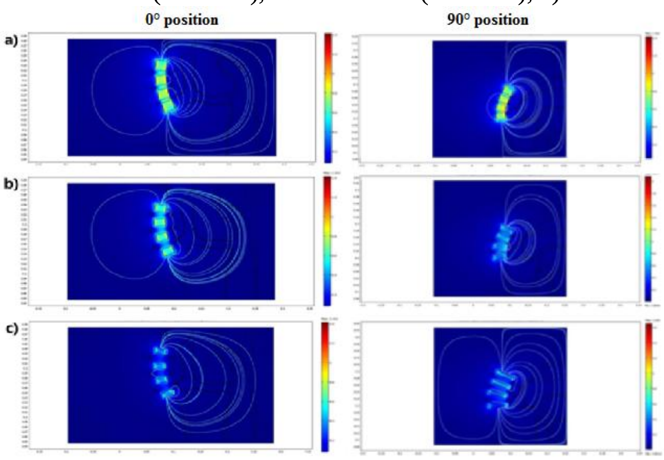

Fig. 9: COMSOL modeling illustrating induction and magnetic field when using 4 magnets with dimensions: a) 0.02x0.025m (d1/d2<1), b) 0.015x0.035m (d1/d2=1), c) 0.01x0.05m (d1/d2>1)

Table 4

The values of the volumetric forces generated following the modeling in COMSOL of the 9 cases of magnet configuration of the second process for the knee joint at 90°

Forces	Conditions	2 magnets	3 magnets	4 magnets
F_ffx[N/m^3]	Case I: $d_1/d_2<1$	-1837.395508	-1547.774242	-1387.155461
	Case II: $d_1/d_2=1$	-1223.25802	-821.797657	-1113.182765
	Case III: $d_1/d_2>1$	-796.643546	-172.381984	-680.469698
F_ffy[N/m^3]	Case I: $d_1/d_2<1$	1422.907126	951.632468	583.505956
	Case II: $d_1/d_2=1$	1710.927069	880.339808	789.183377
	Case III: $d_1/d_2>1$	1647.965021	223.488876	471.026188

The choice of the four-magnet matrix is also attested by the values obtained for mathematical modeling in the flexion position at a 90° angle of the knee joint. Although the choice of a two-magnet matrix generates the strongest magnetic field, the graph of the volumetric forces curves on the Ox direction, applied to the 0° angle joint model (Figure 10) is supported by the 90 ° simulation results of the knee joint. This denotes the stability of the magnets both in flexion and extension position and not just in the extension position of the joint.

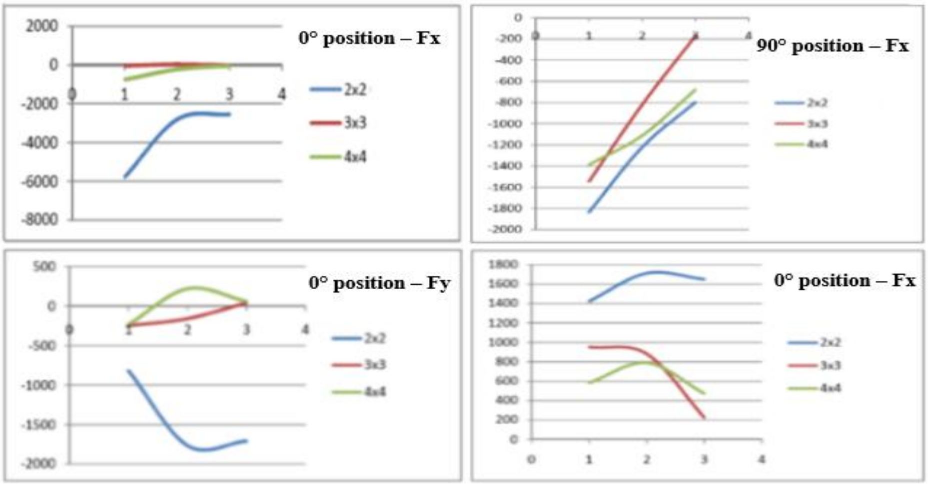

Fig. 10: Representation of the 3 curves given by the volumetric forces Fx and Fy on the corresponding directions Ox and Oy applied on the model of the joint in position of extension (left) and of flexion (right) for the second optimization process

After comparing the volumetric forces it generates, the dimensions of the chosen magnets are too large and not recommended in terms of functionality. Following the second modeling study an optimization of two cases considered appropriate for controlled drug delivery in the case of knee joint disorders was attempted. The two positioning variants chosen for optimization were: two magnets - Case I (Figure 11a)) and four magnets - Case I (Figure 11b)).

Following the optimization process of the dimensions, according to the following tables from which the values of the volumetric forces corresponding to each case result, it can be observed that for the extreme position at 0°, the volumetric force Fy in the case of the choice of two magnets, considerably reduced its values, while the component on Ox retains its power at Fx = -473.203232.

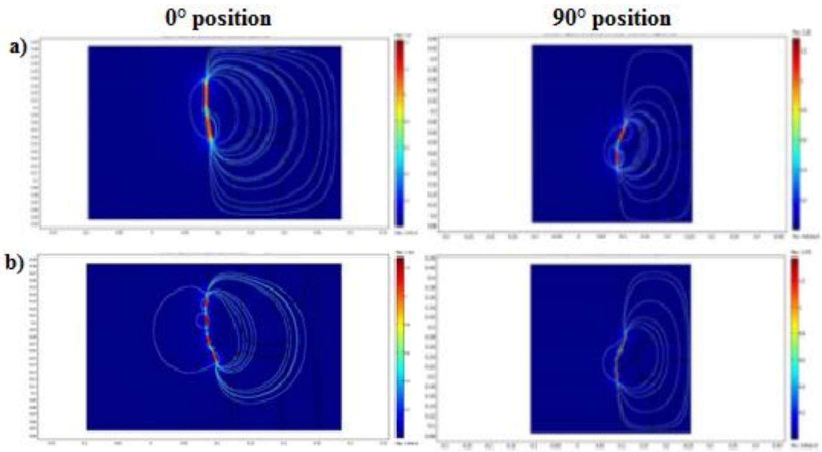

Fig. 11: COMSOL modeling illustrating the induction and magnetic field for cases: a) 2x2 matrix after the optimization process and b) 4x4 matrix after the optimization process

Table 5

The values of the volumetric forces generated after the modeling in COMSOL of the 2 cases of optimization of the magnet configuration for the knee joint at 0°

Conditions	2x2 magnet optimizations caz I	4x4 magnet optimization caz I
Case I: d1/d2<1	Fx = -473.203232 "B = 1.42" ⬇ Fx = -641.068931	Fx = -19.214933 "B = 1.42" ⬇ Fx = -26.031303
Case II: d1/d2=1		
Case III: d1/d2>1		
Case I: d1/d2<1	Fy = -111.376672 "B = 1.42" ⬇ Fy = -150.886805	Fx = -11.09014 "B = 1.42" ⬇ Fy = -15.024293
Case II: d1/d2=1		
Case III: d1/d2>1		

Table 6

The values of the volumetric forces generated after the modeling in COMSOL of the 2 cases of optimization of the magnet configuration for the knee joint at 90°

Conditions	2x2 magnet optimizations caz I	4x4 magnet optimization caz I
Case I: d1/d2<1	Fx = -473.203232 "B = 1.42" ⬇ Fx = -641.068931	Fx = -19.214933 "B = 1.42" ⬇ Fx = -26.031303
Case II: d1/d2=1		
Case III: d1/d2>1		
Case I: d1/d2<1	Fy = -111.376672 "B = 1.42" ⬇ Fy = -150.886805	Fx = -11.09014 "B = 1.42" ⬇ Fy = -15.024293

4. Conclusions

In order to have the best results in the delivery of drugs in the patelo-femoral target area, according to the results obtained after the mathematical modeling of the magnets, we can conclude that we need a matrix consisting of 4 lines of 4 magnets that can be fixed near the patella at distances related to the ratio: d1/d2<1, in order to have a maximum concentration of functionalized magnetic nanoparticles near the knee patella. In the case of the second modeling study, in order to have the best results in the delivery of drugs in the patella-femoral target area, according to the results obtained after the mathematical modeling of the magnets, we can conclude that we need a matrix consisting of 2 lines of 2 magnets that can be fixed near the patella, at distances related to the ratio: d1/d2<1, in order to have a maximum concentration of functionalized magnetic nanoparticles. In order to compensate for the negative values of the volumetric force on the Oy axis we will choose magnets with a larger Fx component, which can be achieved by increasing the remnant induction of the magnet from 1.22 T to 1.42 T.

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