Design magnetic matrices for cell technology supporting devices

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Design magnetic matrices for cell technology supporting devices

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Abstract. Biomedical applications of magnetic materials are a hot topic of present day research. Special attention is paid for design and development of appropriate instrumentation. In this work magnetic system consisting of an equidistant set of commercial permanent magnets (6 × 4 assay) was proposed, designed and tested for further employment in the experiments in cell cultivation experiments. Magnetic field distribution was experimentally measured in 3 axes: OX, OY, OZ by gaussmeter. The results were statistically analyzed. Constant magnetic field near the center of XY plane was relatively homogeneous but at edges significant value of magnetic field gradient was observed. With increasing of Z distance, the decreasing of magnetic field strength was observed. Obtained parameters of a designed system are satisfactory and therefore it can be recommended for cell cultivation experiments when application of external magnetic field is desired.

1. Introduction

A biomedical and pharmaceutical application of magnetic nanomaterials is a rapidly growing area stimulating development of new magnetic materials and special instrumentation [1-3]. The control and manipulation of living cells by an external stimulus is important direction for better understanding of separation, identification, allocation of cells growth in magnetic biosensors and tissue engineering applications [4-5].

The fundamental principles of the interaction of living cells of different type or particular tissues with applied magnetic field of controlled strength are not yet fully understood. At the same time, they certainly should be taken into account and analyzed as complex processes involving such parameters as magnetic flux density, magnetic field gradient and superposition of magnetic susceptibility of cell and nearby environment. As the generation of a constant magnetic field up to 1 Tesla does not depend on complex or expensive instrumentation, it can be created with an externally located magnetic system such as properly arranged assembly of the permanent magnets.

The present-day request is to study the role of the static magnetic field of certain and well controlled strength and configuration in the course of *"in vitro"* development of the cell cultures. In this kind of experiments both control (without external magnetic field application) and experimental (under application of a controlled magnetic field) studies must be done in the same conditions except the magnetic field presence.

Recently, we have proposed a new approach for cultivation of selected cell cultures which might be useful for regenerative medicine and biosensor applications. Human dermal fibroblast cultures were grown onto the surface of polyacrylamide gels and ferrogels [6] and their adhesive and proliferative activities were studied. Polyacrylamide gels with different cross-linking density of the polymer network and polyacrylamide-based ferrogel (FG) with embedded magnetic nanoparticles of the iron oxide obtained by the laser target evaporation technique (LTE) [7] were synthesized and studied. Electrophysical LTE technique has very special advantage providing very large size of the batch [8] greatly requested for nanomedicine and diagnostics [9]. The obtained results showed clear influence of the presence of LTE MNPs on the cell culture features and cell culture development and therefore this research direction seems to be specially promising for cellular technologies and tissue engineering applications.

In this work, we have proposed, designed and tested a magnetic system consisting of an equidistant set of the similar commercial permanent magnets (6×4 assay) in order to get insight on the potential of its experimental usage in the next-step biological studies with cells culturing in a magnetic field. The main focus was made on the evaluation of magnetic field distribution in space taking into account both magnetic field strength and degree of homogeneity for the dimensions requested by cell cultivation conditions.

2. Experiment

Standard cell culturing tablet is supposed to be placed behind or above the magnetic system consisting of a set of similar permanent magnets embedded in 24-well polystyrene plate (figure 1). For these experiments it is important to know magnetic field distribution in space around the magnetic system and define such characteristics as magnetic field strength and degree of homogeneity. The last to characteristics were carefully studied in the present work.
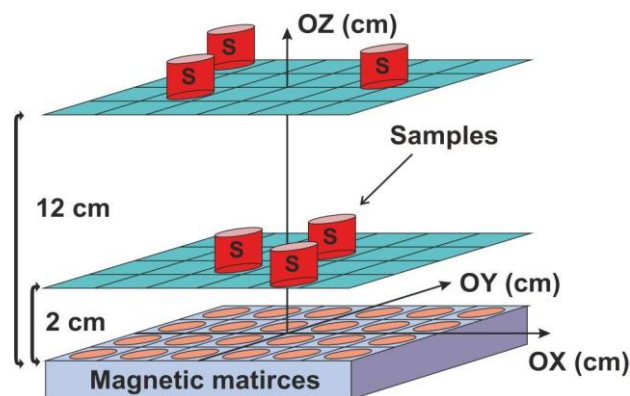

Figure 1. General scheme of cells culturing experiments using specially designed magnetic system for the creation of external magnetic field of desired strength.

The magnetic matrix was designed based on 24-well polystyrene plate (Techno Plastic Products, Trasadingen, Switzerland) widely introduced for cells culturing. All wells were filed with commercially available cylindrical permanent magnet (NdFeB) samples of 15 mm in length and 14 mm in diameter. Prior to magnetic characterization the whole system was heated up to 130 $^{\circ}$C and kept at this temperature for 2 hours in order to imitated sterilization conditions requested for cell cultivation in a future.

Magnetic field distribution was measured experimentally by gaussmeter (State register number of approved type measuring instruments 28134 - 04). Magnetic measurements were carried out in 3 axes: OX from - 6 to +6 cm with 1 cm step; OY from - 4 to +4 cm with 1 cm step and OZ from 0 to 15 cm with 1 cm step. The matrix was divided into 24 areas of 4 cm^2 each of which included one permanent magnet (figure 2).

Systematic error was considered in accordance with gaussmeter metrology characteristic using formula (1) (γ - limits of the main relative error of measurement of magnetic induction with permanent magnetic field measurements (%), B_L - limit of gaussmeter (Oe), B_M - gaussmeter readings (Oe))

$$\gamma = \pm\left[2,0 + 0,1\cdot\left(\frac{B_L}{B_M} - 1\right)\right].\tag{1}$$

Random error was considered by three measurements in certain points with various coordinates (X = -6, -4, 0 cm; Y = -4, -2, 0 cm; Z = 1, 2, 4, 7, 10, 13 cm). Magnetic field approximation in XY plane was performed by the least squares method using parabolic function (2) (H - magnetic field (Oe), x - OX coordinate (cm), y - OY coordinate (cm))

$$H = Ax^2 + By^2 + Cx + Dy + E.\tag{2}$$

The degree of field heterogeneity was estimated using the coefficient of variation δ defined in accordance with equation (3). An increase in the coefficient of variation indicates an increase in the degree of heterogeneity (σ - root-mean-square deviation, $\overline{H}$ - the arithmetic average value of the magnetic field):

$$\delta = \frac{\sigma}{\overline{H}}\cdot 100\%.\tag{3}$$

Consider an example of a detailed calculation of magnetic field variation coefficient. Zone formed by the permanent magnets with certain numbers (for example 1 - 7 or 8-10, 14-17) in the XY plane is selected for certain Z. In the selected zone, created magnetic field is averaged over all points located in centers of magnets and at a distance of ±1 cm along OX and OY from the centers of corresponding magnets. Using the data for these points for magnetic field, root-mean-square deviation is calculated and then coefficient of variation is calculated by equation (3).
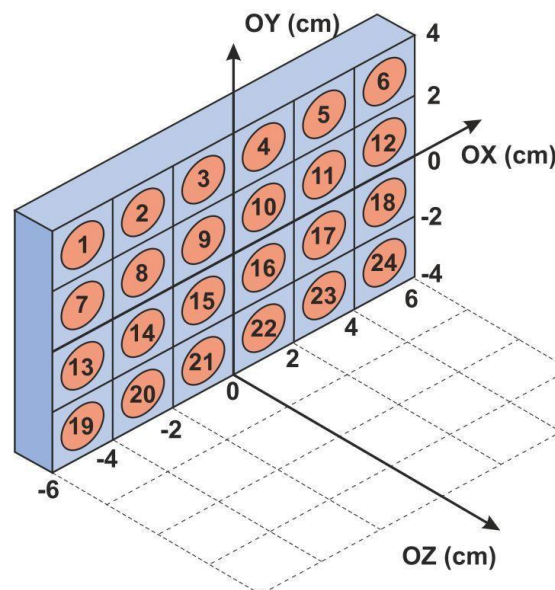

Figure 2. Magnetic matrices - geometry of particular zones for magnetic measurements and description of the coordinate system.

3. Results and discussion

At a distance of Z = 0 cm from the surface of the magnets, the magnetic field distribution is non-uniform. Maximum values of magnetic field strength were observed in the centers of permanent magnets and related values exceed the value of about 1400 Oe. The exceptions are magnets 11 and 20 where the field does not exceed 900 Oe. (figure 3(a)). They can be different reasons for local properties deviation. First of all used commercial magnets on purpose aiming to design relatively cheap and simple system. Apart from certain deviation of their initial properties heat treatment can make additional contribution.
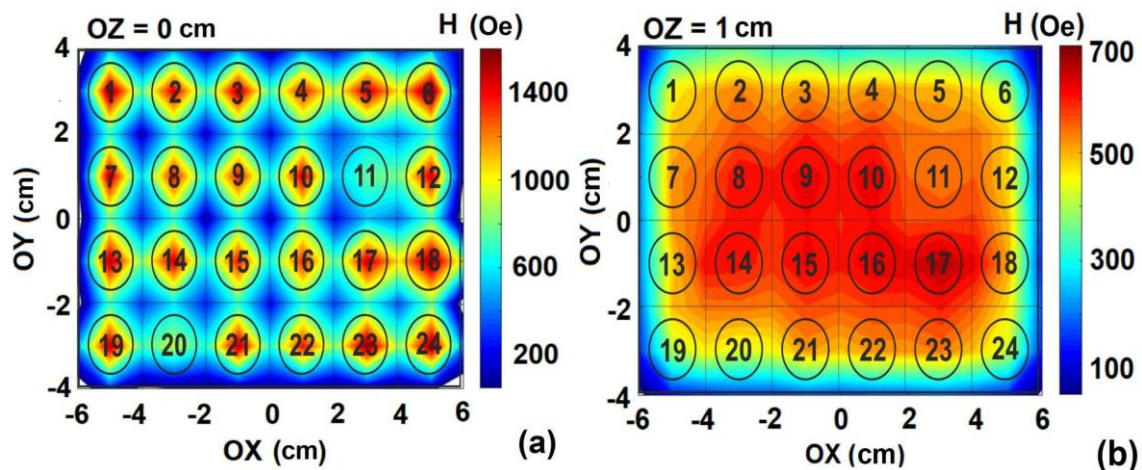

Figure 3. Magnetic field distribution created by the magnetic system in XY plane: (a) - Z = 0 cm; (b) - Z = 1 cm. Numbers match individual magnets embedded in matrix positions.

At Z = 0 cm from the surface of the magnets distance the high field heterogeneity was observed and therefore it is not recommended to carry out an experiment according to the scheme (see figure 1). Starting from a distance of Z = 1 cm, the local magnetic field of zone formed by magnets with number (8-10, 14-17) (figure 3(b)) is distributed relatively uniformly. The average value of magnetic field strength in this zone is about 605 Oe, coefficient of magnetic field variation is 1 %. For area formed by all magnets (1 - 24), there is lower average magnetic field strength (460 Oe) and higher magnetic field variation coefficient (4%) than in zone (8-10, 14-17). It means that in area formed by extreme magnets, there is lower magnetic field strength with a relatively high magnetic field gradient directed from the edges of the matrix to the center in XY plane, so in this direction, the magnetic samples will be affected by the force from magnetic field.

At the distance Z = 2 cm from the plane of the magnetic system the zone of relative homogeneity narrows to zone corresponding to the position of the magnets (9, 10, 15, 16), the average magnetic field strength of which is close to 440 Oe value and the coefficient of magnetic field variation become as high as 1 % (figure 4 (a)). Starting from this distance, the distribution of the magnetic field in the XY plane can be satisfactorily approximated by a parabolic function (figure 4 (b)). The zone formed by (1 - 24) magnets is characterized by the average magnetic field strength of about 310 Oe and the coefficient of magnetic field variation of 4 % is the same as the coefficient of magnetic field variation calculated for Z = 1 cm. It means that degree of magnetic field heterogeneity does not change at increasing distance from 1 cm to 2 cm and we are dealing with quite wide interval of homogeneity. The last observation has special practical importance showing that small displacements in the interval of Z from 1 to 2 cm are not critical for the experimental arrangements of the magnetic system and 24-well polystyrene plate itself.
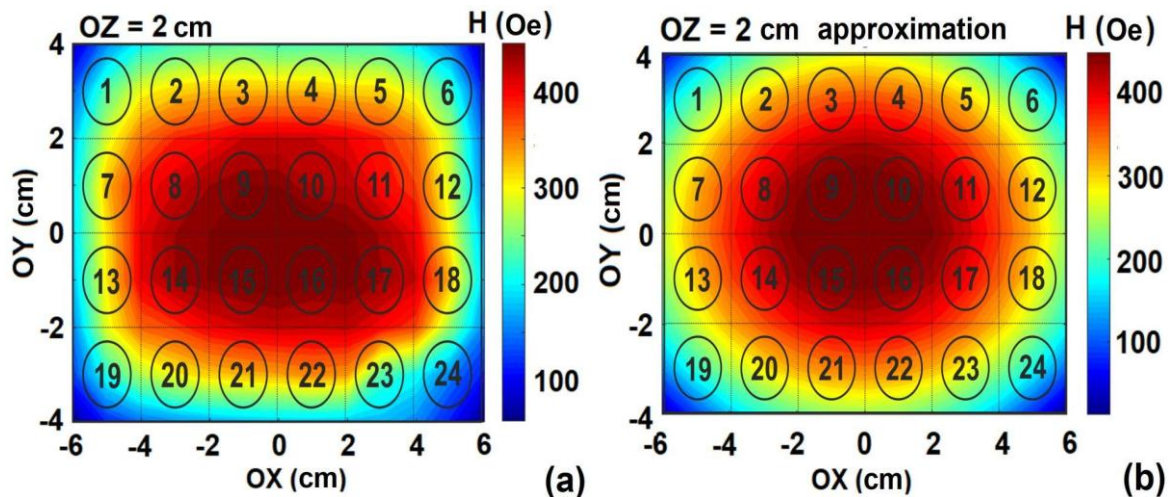
Figure 4. Magnetic field distribution created by the magnetic system in XY plane: (a) - Z = 2 cm; (b) - Z = 2 cm approximation by parabolic function. Numbers match individual magnets embedded in matrix positions.

The visualization on the figure 4(a) shows that the magnetic field strength of the magnet 11 has a lower value than the others in the zone of relative homogeneity (8 - 10, 14 - 17) that was also evident in figure 1(a, b).

At a distance of Z = 12 cm (figure 5), a zone of relative homogeneity is formed by magnets (3, 4, 8 - 11, 14 - 17, 21, 22). In this area, the average magnetic field strengthis about 35 Oe (which is an order of magnitude less than at Z = 1 cm) and coefficient of magnetic field variation is as high as 1 %. However, the coefficient variation of magnetic field of the zone formed by (1-24) magnets is 1.5 %, that means it become much less than at the other distances. The results show that as the distance along the OZ axis increases, the strength of the magnetic field created by the magnetic system decreases, and the field uniformity increases.

Thus, by varying the distance along the axis OZ and axis XY, it is possible to achieve the required magnetic field parameters for the designed magnetic system. In all measurements described above, the relative error did not exceed 8%.
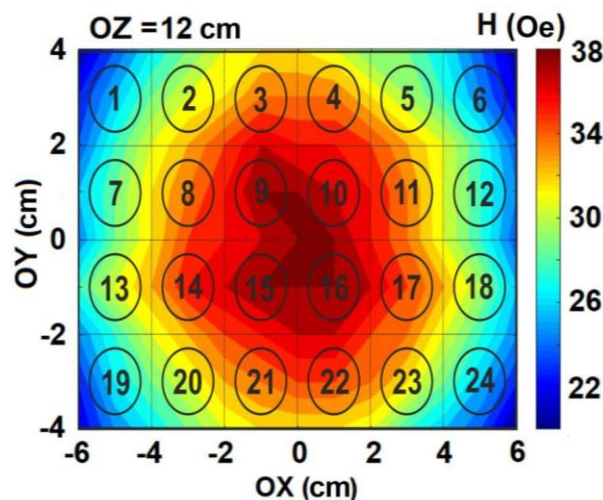

Figure 5. Experimentally measured magnetic field distribution for the field created by the magnetic system in XY plane at a distance Z = 12 cm. Numbers match individual magnets embedded in the matrix positions.

Created by the system of permanent magnets magnetic field has maximum strength value in central area at all Z positions. It can be explained even in frame of rather simple model of magnetic matrix as a magnetic dipole which is located in center of matrix (for symmetry reasons). In this case, magnetic induction can be described by the equation (4) for the magnetic field of dipole ($\vec{\mu}$ - vector of dipole magnetic moment, $\vec{r}$ - radius vector to observation point, $\vec{B}$ - induction magnetic field):

$$\vec{B} = \frac{\mu_0}{4\pi}\left(\frac{3(\vec{\mu}\cdot\vec{r})\vec{r}}{r^5} - \frac{\vec{\mu}}{r^3} \right) \tag{4}$$

Direction of the magnetic dipole vector in the present model is parallel to the OZ axis (figure 1). The smaller the angle between $\vec{\mu}$ and $\vec{r}$ the bigger the value of induction of magnetic field. It means that maximum of induction of magnetic field will be observed near the center of XY.

4. Conclusions

As a result of the work, a magnetic matrix was created to study the effect of the magnetic field on living cells, the experiment scheme of which is shown in figure 2. The uniform field distribution starts with Z = 1 cm. The zone of homogeneity is near the center of XY plane the coefficient variation of magnetic field don't above 1 %. With increasing distance on axis OZ magnetic field strength decrease (OZ = 1 cm, H_{max} = 680 Oe; OZ = 12 cm H_{max} = 38 Oe), and the field uniformity of the extreme magnets increases (coefficient variation of magnetic field decrease from 4 % at Z = 1 cm to 1.5 % at Z = 12 cm for all magnets). The strength of the acting magnetic field can also be changed by varying the distance between the samples and the center of the magnetic matrix in the XY plane. At the center of the XY plane, the field is more uniform; closer to the edge of the XY plane, there is a high magnetic field gradient and, therefore, inhomogeneity of the field.

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