

MAGNETOPHORETIC ANALYSIS OF CELLS AND MAGNETIC CARRIERS

J. Plavins

Institute of Physics, Latvian Academy of Sciences, Miera iela 32, Salaspils, LV-2169, Latvia

INTRODUCTION: Many areas in biotechnology and medicine related to cellular biology often require physical isolation of functionally-specific types of cells from biologically heterogeneous suspensions. Efficient use of magnetic methods is based, first of all, on sufficient differences in magnetic susceptibilities of biological cells and secondly, on the availability of reliable magnetic susceptibility values for all relevant cells present in a suspension. If natural magnetic properties of all blood cells except phagocytes are considered, magnetic separation methods, and in particular HGMS methods, have been successfully applied mostly to red blood cells by virtue of the presence of paramagnetic Fe atoms in intracellular hemoglobin. However, present development trends in separation technologies have highlighted massive interest in studying the differences which lie on the surface of cells by means of conjugating a wide variety of specific immunomagnetic labels to antibodies that target specific molecules on the surface of a cell, thus adding to the otherwise insufficient overall magnetic susceptibility of targeted population for subsequent magnetic enrichment or isolation using appropriate HGM or OGM separation devices [1]. To optimize the separation process it is necessary to determine magnetic susceptibility distributions of suspended populations of cells. Though more complicated than open gradient devices, the HGM systems are in a position to offer increased sensitivity and resolution for magnetic susceptibility measurements and fractionation due to the possibility of generating considerably higher magnetic field gradients.

METHODS: The magnetophoretic force F_m acting on a weakly magnetic cell or carrier in a gradient magnetic field is

$$F_m = 1/2 \mu_0 V Dc \tilde{N} H^2 \quad (1)$$

where μ_0 is the magnetic permeability of vacuum, V is the volume of the suspended cell in question, Dc is the difference in magnetic susceptibility between the cell and the suspending medium and $\tilde{N} H^2$ is the product of the intensity of a magnetic field H and its gradient $gradH$ across the cell. The values of $H gradH$ can be calculated for the ferromagnetic cylinder in a transversal magnetic field [2], and in the widely utilized directions along the magnetic field intensity H and

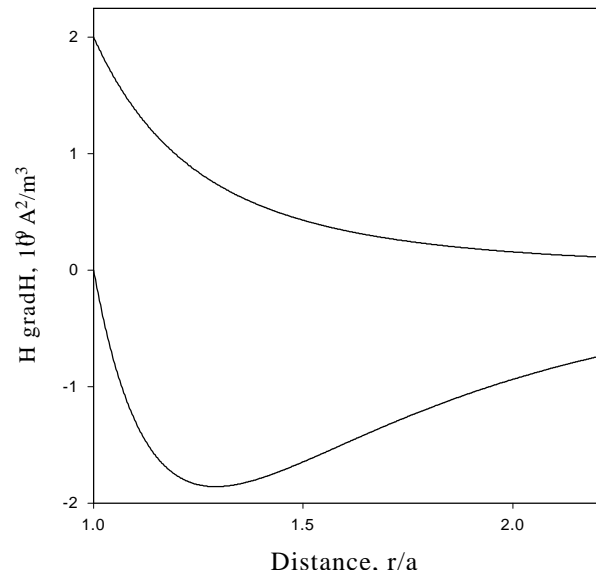


Fig. 1: $H gradH$ as a function of the distance r/a from the surface of a magnetized stainless steel cylinder (diameter 50 mm, $M_s = 1.51 \times 10^5$ A/m) in the direction of the field intensity H (top curve; values are multiplied by the factor 1/10 for comparison) and perpendicular to H (bottom curve).

perpendicular to H , it is equal to

$$2KH^2 a^2 / r^3 (Ka^2 / r^2 \pm 1). \quad (2)$$

$K = 1$ for $H \ll M_s/2$, whereas for $H > M_s/2$, $\mathbf{m} \approx 1$ and $K \approx M_s/2H$; \mathbf{m} and M_s refer to the magnetic permeability and magnetization of saturated material; a is the radius of the cylinder; and r defines the distance from the center of the cylinder. Fig.1 demonstrates that in the direction along the field F_m peaks on the surface of the cylinder; whereas, in the direction perpendicular to the magnetic field the absolute value of F_m on the surface is negligibly small and reaches the maximum value at $r/a = 1.292$, where it is still more than an order of magnitude smaller than the value on the surface in the direction of the field. Further away from the surface this difference levels out and drops to about 10% at $r/a = 4.36$.

RESULTS: The aforementioned negative gradient in the vicinity of a ferromagnetic cylinder in the direction perpendicular to a magnetic field is often used to exert a repulsive magnetophoretic force in order to perform magnetic fractionation in a continuous mode with respect to cells or carriers, which contain ferromagnetic colloidal particles or are labeled with immunomagnetic microspheres or colloidal particles. Thus, it is of practical interest to study the force profile in this direction in more detail. The trends shown in Fig.2 are calculated on the basis of expression (2).

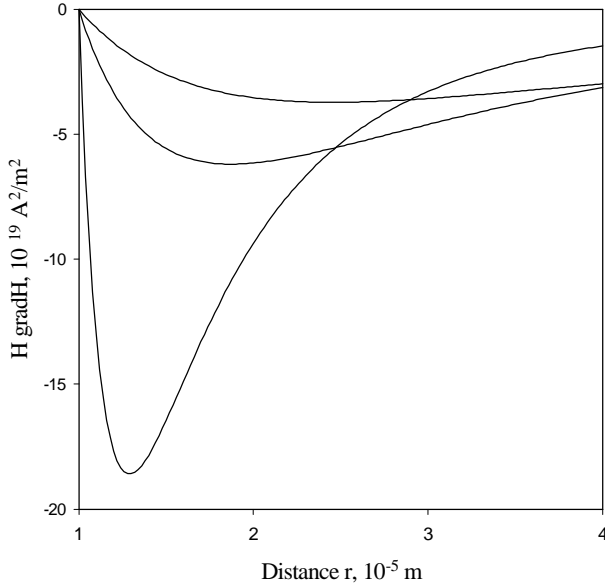


Fig. 2: Repulsive branch of $H \text{ grad}H$ as a function of the distance r from the surface of a ferromagnetic cylinder for different diameters of the cylinder (from bottom curve up: 20, 50 and 100 μm).

Presented curves, first of all, are indicative of marked differences in $H \text{ grad}H$ values in the close proximity of the peak value for different cylinder sizes. It is quite clear that the size and/or magnetic properties of cells or carriers are to be considered very carefully in order to attain an optimum balance between the intensity and the reach of the gradient of a magnetic field in the given direction.

The sensitivity of the magnetophoretic technique for measuring magnetic susceptibilities of suspended cells or carriers is considered under the assumption that the force of gravity may be neglected, and that the magnetophoretic force causing the displacement s_m of an individual cell or carrier during the act of measurement Dt is opposed solely by the viscous drag and thermal agitation.

The translational Brownian displacements d , each of which is assumed to be random despite the presence of the gradient of a

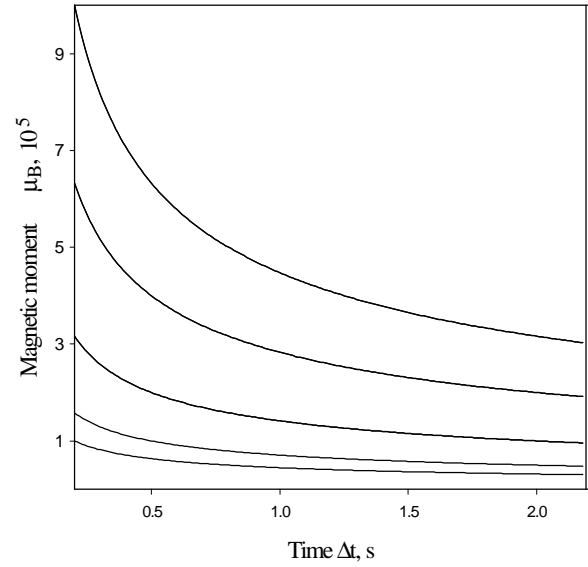


Fig. 3: The smallest difference in the magnetic moment inherent to an individual carrier/cell in Bohr magnetons μ_B , the magnetophoretic technique will detect as a function of the characteristic duration of measurement Dt for different characteristic sizes of carriers/cells in the presence of $H\tilde{N}H = 8 \times 10^{17} \text{ A}^2/\text{m}^3$ (from the bottom curve up: 20, 8, 2, 0.5, 0.2 μm).

magnetic field, is given by $d = D^{1/2}Dt^{1/2}$. D is the coefficient of translational diffusion expressed as $kT/6\eta R$, where Boltzmann constant $k = 1.38 \times 10^{-23} \text{ J/K}$, T is the absolute temperature, η is the dynamic viscosity of the medium, and R is the radius of a carrier or cell. D ranges from 10^{-14} to $10^{-12} \text{ m}^2/\text{s}$ for diameters of larger blood cells down to microcarriers still detectable by light microscopy. Assuming that for characteristic Reynolds numbers the opposing drag force equals $6\eta Rv$, where v is the velocity of a suspended cell/carrier, the magnetophoretic displacement, in accordance with (1), yields

$$s_m = 2\mathbf{m}/9\eta R^2 Dc \tilde{N}H^2 Dt. \quad (3)$$

From the above considerations it follows that the smallest difference in the relative magnetic susceptibility Dc , which in spite of thermal agitation in the suspending media is still detectable using a magnetophoretic technique, is proportional to parameter $Dt^{1/2} R^{-5/2}$.

DISCUSSION & CONCLUSIONS: It is obvious that magnetophoretic analysis of cells and magnetic carriers using a HGM systems is a useful and

sensitive tool for measuring magnetic susceptibilities of different populations of natural or labeled biological cells. Moreover, HGM systems offer various configurations and profiles of attractive and repulsive forces, which can be efficiently applied for the batch - as well as for the continuous - mode of magnetic fractionation. By virtue of the fact that the values of each component of the product $H \text{ grad}H$ along the magnetophoretic trajectory keep increasing or decreasing depending upon the specific profile of the magnetophoretic force utilized in a device, this analytical tool has the potential of measuring magnetization values for different magnetic field intensities and building magnetization curves for individual cells and carriers which subsequently can be used for more in-depth analysis of magnetic properties [3]. Sizing of individual carriers combined with analyzing their respective magnetophoretic velocities makes it possible to plot the volumes of individual microspheres containing colloidal magnetic particles versus volume magnetic susceptibilities, and further application of correlation analysis to scatter plots allow the study of localization patterns of colloidal magnetic particles within an ensemble of carriers [4].

REFERENCES: ¹K.E.McCloskey, K.Comella, J.J.Chalmers, et al (2001) *Biotechn.Bioeng.* **75**:642-55. ²S.J.Gill, C.P.Malone, M.Downing (1960) *Rev.Sci.Instr.* **31**: 1299-1303. ³R.Ali-zade, J.Lukin, M.Maiorov, et al (1987) *Study of magnetic properties of magnetic colloid-filled polymer carriers* in 12th Riga Meeting on Magnetohydrodynamics (Russ), Zinatne Press, 91-94. ⁴J.Plavins, M.Lauva, S.Krisko, et al (1985) *Magnitn.Gidrodin.* (Russ) **2**: 130-132.