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Modeling Force Density Distributions on Biomolecular Nanoparticles Undergoing Magnetic Separation

Magnetic nanoparticles discussed in recent articles in *MB&T* [1] to [3] are rapidly becoming popular for separation of biomolecules. This article uses free magnetic finite element software to visualize force distributions acting on biomedical nanoparticles undergoing magnetic separation in microarrays.

Magnetic properties of typical magnetic nanoparticles are shown in Figure 1. The curves are for 1-micron diameter MyOne dynabeads made of highly cross-linked polystyrene with an even dispersion of magnetic material (gamma Fe_2O_3 and Fe_3O_4). To encase the magnetic material and provide a defined smooth surface the beads are further coated with a thin polymer shell. As dynabeads consist of a combination of various ferromagnetic iron oxides, their properties vary with flux density *B*. Further, due to the small size of the iron domains, the particles are superparamagnetic and in theory the coercivity and remanence should equal to zero. The core sizes are less than 15 nm. The magnetic susceptibility of MyOne dynabeads is 1.4 and their specific gravity is 1.8 [4]. These dynabeads are used in microarrays for profiling of gene expressions, genomes and microRNA. They are also used for carriers in immunoassays and immunodiagnostics. Their features include a large surface area, high capacity, good magnetic force and a slow sedimentation rate during incubation. MyOne dynabeads are tailor-made for use in automated protocols where high throughput is crucial.

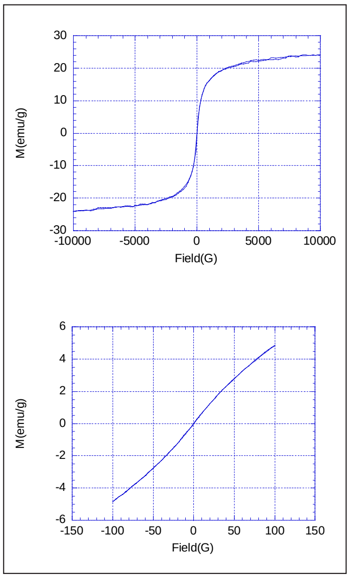

Figure 1. Superparamagnetic hysteresis curve (full and near origin) of MyOne dynabeads [1].

A typical application of dynabeads is to place them in a solution in a multi-well microplate. The standard 96-well microplate [5] shown in Figure 2 often has a permanent magnet or permanent magnet array placed above the wells and moved downward toward the solution to attract its dynabeads.

To model the magnetic force acting on particles such as dynabeads, magnetic force density expressions have been derived [6], [7] and have been shown to be accurate [7]. The best graphical means of displaying regions where the vertical magnetic force f_{mz} exceeds that of gravity is a color plot of the ratio:

$$\frac{f_{mz}}{f_g} = \frac{1}{f_g 2\mu_o}(1 - \frac{1}{\mu_r})[\frac{\partial}{\partial z}(B^2)] \qquad (1)$$

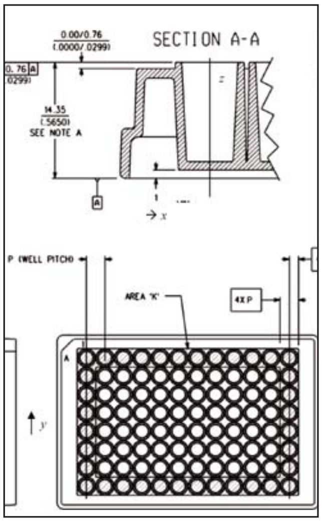

Fig. 2. Drawings of 96-well standard microplate [5] for biomolecular screening. The lower view is in the horizontal xy plane, while the upper view is a section of one well in the xz plane. Dimension are in mm (inches in parenthesis), with standard well pitch of 9 mm. All microplate materials have the same permeability as air.

where f_g is the gravitational force per unit volume and μr is the relative permeability of the nanoparticle. Note that other forces such as buoyancy and surface tension are neglected. The force density of gravity equals the mass density ρ times the gravitational acceleration *g*, and thus:

$$f_g = \rho g \qquad (2)$$

Substituting (2) into (1) obtains:

$$\frac{f_{mz}}{f_g} = \frac{1}{\rho g 2\mu_o}(1 - \frac{1}{\mu_r}) \qquad (3)$$

which can be rewritten to give the force ratio distribution:

$$\frac{f_{mz}}{f_g} = F_r[\frac{\partial}{\partial z}(B^2)] \qquad (4)$$

where F_r is the *ratio factor* defined as:

$$F_r = \frac{1}{\rho g 2\mu_o}(1 - \frac{1}{\mu_r}) \qquad (5)$$

Since g=9.8 m/s^2 and μ_o=12.57E-7 H/m, the factor becomes:

$$F_r = \frac{40588}{\rho}(1 - \frac{1}{\mu_r}) \qquad (6)$$

For MyOne dynabeads with ρ=1.8 g/cm^3=1800 kg/m^3 and μr =1+susceptibility= 2.4, (6) gives the factor F_r = 13.154.

To compute the magnetic flux density *B* distribution for various geometries and materials, finite element software is

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commonly used [6]. Here the free software Maxwell SV (Student Version) is used, available by free download from Ansoft Corp. at www.ansoft.com. The Maxwell postprocessor has a calculator which can be automated by means of easily written macro commands. A macro was written to compute the force distribution ratio of (4) and to display it in color over a region of the microplate of Fig. 2. The macro prompts the user to enter the factor F_r and the maximum value of the ratio, which is plotted in red, with lower force values plotted in other colors.

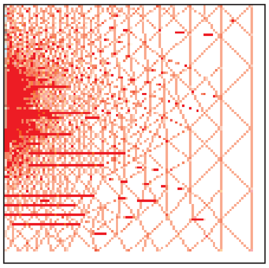

Figure 3a. Flux line plot of single ferrite magnet above well along with adjacent well, obtained using the axisymmetric magnetostatic solver of Maxwell SV.

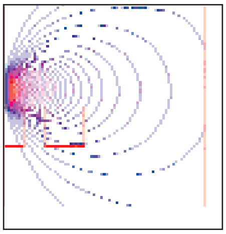

Figure 3b. Finite element model, containing over 8,000 adaptive triangular finite elements.

For a ferrite (ceramic 5) axially-magnetized cylindrical permanent magnet placed above one well of the microplate, Figure 3 shows the computed flux line plot along with the finite element model used to compute the plot. Over 8,000 triangular finite elements have been automatically generated by Maxwell in several adaptive passes. The permanent magnet diameter is 2 mm and its length is 5 mm. The computed force distribution ratio of (4) is displayed in Figure 4. Note that the magnetic force ratio is less than unity over most of the well, and thus the ferrite magnet is not powerful enough to pull dynabeads out of the entire well.

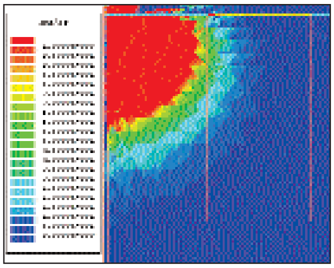

Figure 4. Force ratio distribution computed for a well top with ferrite magnet above it. Note that the ratio is less than 1 across the width and depth of the well top.

When the ferrite magnet is replaced by a neodymium iron boron magnet (of the same size but with a coercive H = 8.9E5 A/m) the force distribution computed is shown in Figure 5. Note that the magnetic force ratio now exceeds unity over most of the well, and thus most of the dynabeads will be pulled out of the well. Note also that the force ratio exceeds unity across the entire well of interest but is very low (less than 5 percent) in the adjacent well, as desired for proper magnetic separation. In actual microplate separation, it is known that neodymium iron magnets are required, thus agreeing with the computed force distributions.

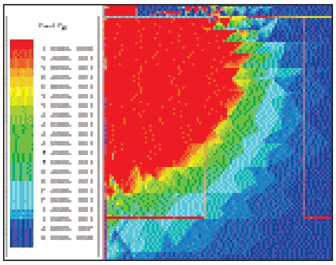

Figure 5. Force ratio distribution computed for a well top with Neodymium magnet above it. Note that the ratio exceeds 1 across the entire well top, but is below 5 percent in the adjacent well at right.

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