Thales: an instrument to measure the low field magnetophoretic mobility of microscopic objects

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Abstract. An instrument, Thales, was designed and constructed to measure the induced motion of magnetic microspheres in a low magnetic field strength environment. Results show that Thales can be used to precisely measure the speed of microspheres (± 0.08 µm.s⁻¹). We evaluated the motion of magnetic microspheres induced by an inhomogeneous magnetic field, and developed models for the microsphere magnetophoretic mobility, a parameter determining the speed attained by the microsphere in a given static low strength magnetic field environment. The data suggested that the magnetic material was located at the surfaces of the microspheres rather than being distributed evenly through the microspheres. With suitable calibration microspheres, Thales will be capable of directly measuring the low field magnetophoretic mobility of microscopic objects.

Introduction

Magnetic carriers range from particles of a similar size to cells to nano-scale colloids [1]. The surfaces of these carriers are easily modified to target particular cells, and so can be employed in biomedical procedures such as cell isolation and purification [2]. Such procedures separate one or more types of cells from a heterogeneous population, achieved by exploiting the induced motion of magnetic objects in an applied magnetic field. In a magnetic field, a magnetic carrier or a cell labelled with magnetic carriers will experience a magnetic force given by

\[ F_m = \mu \cdot \nabla H. \]

As the carriers are superparamagnetic, in low strength magnetic fields magnetisation will vary proportionately with applied field strength, and so the force on the object is best approximated by

\[ F_m \propto \nabla (H^2). \]

An object in a viscous medium of viscosity \( \eta \) will move according to the laws of low Reynolds number hydrodynamics, so the speed \( \nu \) the object attains in an inhomogeneous magnetic field will be related to the force by the low field magnetophoretic mobility \( \zeta \):

\[ \nu = \zeta \cdot \frac{F_m}{\eta}. \]
Thus, the low field magnetophoretic mobility $\zeta$ represents a measure of the dynamic response of a magnetic microsphere or a magnetically labelled cell to a given magnetic field environment. Magnetic cell sorting [3] does not provide a quantitative measure of magnetophoretic mobility on an cell-by-cell basis, which can yield valuable information on the heterogeneity of cell Antibody Binding Capacity within a population [4]. Other instruments developed measure magnetophoretic mobility in a field of approximately 1.7 Tesla [5], where the magnetisation of any superparamagnetic materials will be saturated. Thales has the unique ability to examine the motion of particles with diameters ranging from approximately 1 to 10 $\mu$m in a strictly low strength magnetic field. Such a magnetic field environment is of particular relevance in procedures such as rare cell isolation and the proposed use of magnetic microspheres in targeted drug delivery [6].

**Experiment**

Three sets of polystyrene microspheres containing superparamagnetic magnetite particles, with nominal mean diameters of 2.9, 4.5 and 5.9 $\mu$m, were obtained from Spherotech Inc. We determined the size distributions via scanning electron microscopy and measured their $M$ vs. $H$ properties at room temperature via DC magnetometry. Two possible models for the magnetophoretic mobility of the microspheres were postulated. The first model assumed that the magnetic material was distributed evenly throughout a polystyrene core, giving

$$\zeta \propto R^2$$

where $R$ is the radius of the microsphere. The second model assumes that the magnetic material forms a shell around a polystyrene sphere, and so the magnetophoretic mobility also increases with radius, but in this model, according to the formula

$$\zeta \propto R.$$

The induced speed of the microspheres was measured using Thales, which is able to manipulate a single microsphere in a region of space with fixed $\nabla(\mathbf{H}^2)$, illustrated in figure 1.

**Figure 1.** Thales, as viewed from above. Inset shows circuit diagram.

It was estimated that the field strength in Thales did not exceed 70 Oe. An accurate measure of the magnetic field gradient (and hence, the magnetic force on the microspheres) could not be made, but is expected to be approximately one order of magnitude smaller than the magnetic field gradient of 0.131 T.mm$^{-1}$ of another instrument used to measure magnetophoretic mobility [5]. Samples of microspheres suspended in fluid were placed in a perspex sample holder and viewed using an optical microscope in conjunction with a computer linked via digital camera and image capture software. Mu-metal rods, shaped to produce a magnetic field with a large gradient, were inserted into the fluid. The rods were alternately magnetised by solenoids controlled by a signal generator (figure 1 - insert). When magnetised, the magnetic field produced by each rod exerted a force on the microspheres directed
towards the tip of the rod, and so the direction of the force alternated with a frequency controlled by the square wave signal generator.

Measurements of the time taken for a microsphere to traverse a fixed distance of approximately 25 µm between the rod tips enabled us to determine the (mean) speed of each microsphere. The frequency of the square wave current was varied from 0.1 to 0.3 Hz, and it was shown that the time constant τ of the solenoids was negligible on this time scale. All measurements were made at room temperature (approximately 23ºC).

Results

Magnetisation versus field measurements of the three sets of microspheres confirmed that in fields of less than 100 Oe, it is reasonable to assume that magnetisation increases linearly with applied field strength at room temperature. Figure 2 (a) shows the repeated measurements of the speed of a single microsphere and (b) shows the speed of eleven microspheres from a sample of 5.9 µm microspheres. The speed of individual microspheres could be measured with a precision of 0.08 µm.s⁻¹, indicating that the majority of the variation in speed within the sample of microspheres represents the magnetophoretic mobility distribution within the ensemble.

![Figure 2](image)

**Figure 2.** Speed distribution from (a) repeated measurements of a single microsphere and (b) eleven microspheres from a single batch.

The mean and standard error of the speed as measured by Thales was calculated, and a theoretical mean and standard error of the magnetophoretic mobility was evaluated using both the shell and sphere models for each of the three sets of microspheres. The variation in magnetophoretic mobility represents only the standard error measured from microsphere size distributions, as no estimate in variability of magnetic properties was made. A comparison of the magnetophoretic mobility and speed for the three sets are displayed in figure 3.

As speed measurements were all obtained over the same region of space and thus experienced the same mean \( \nabla (H^2) \), it was expected that the speed of the microspheres increases proportionately with magnetophoretic mobility. The measured size distributions and magnetophoretic behaviour of the microspheres were in better agreement with a model of the magnetic material being in the shell of the microspheres rather than distributed evenly through the spheres.
Figure 3. Theoretical magnetophoretic mobility evaluated using (a) sphere model and (b) shell model, versus speed as measured by Thales. The line fitted to the data was constrained to pass through the origin.

Conclusions
Thales enables measurements on individual microspheres, allowing determination of both the mean and range of microsphere speeds within a sample. Once calibrated, Thales will be used to directly measure the magnetophoretic mobility of microspheres, which will enable refinement of microsphere production and assist in determining the experimental procedures for which they are most suitable. Additionally, Thales is an instrument that examines the motion of magnetic objects in low strength magnetic fields, and will be adapted for use in measuring cell antigen expression [7].

Acknowledgements
'And Thales, according to what is related of him, seems to have regarded the soul as something endowed with the power of motion, if indeed he said that the lodestone has a soul because it moves iron.' Aristotle: de Anima, i.2; 405 a 19.

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