MAGNETO-OPTICAL DETECTION OF MAGNETIC NANOBEBADS IN A MICROFLUIDIC CHANNEL

Marco Donolato1,2, Paolo Vavassori3, Mikkel F.Hansen2
1 CIC nanoGUNE Consolider, Tolosa Hiribidea 76, 20009 San Sebastian, Spain
2 DTU Nanotech, Building 345 East, DK-2800 Kongens Lyngby, Denmark
3 IKERBASQUE, Basque Foundation for Science, 48011 Bilbao, Spain

ABSTRACT
We report on the measurement of the Brownian relaxation frequency of a magnetic nanobeads suspension in microfluidic system using a novel magneto-optical method. We demonstrate that by lock-in analysis of the signal produced on a photodetector by the light transmitted through the particle suspension excited by an uniaxial AC magnetic field, it is possible to precisely record the frequency response of commercial magnetic nanobeads in a microfluidic channel.

KEYWORDS: magnetic nanobeads, optical biosensing

INTRODUCTION
In the last few years a large amount of work has been carried out by several research groups toward the development of a miniaturized microfluidic biodetection platform based on the use of magnetic nanobeads (MNBs). The possibility of using the same tags both for sample preparation, and analyte detection has produced a large amount of technical implementation[1,2]. In particular, the possibility of realizing homogeneous immunoassays exploiting the dynamics properties of magnetic nanobeads has recently attracted the attention of several groups. A promising detection scheme is based on the measurement of the change of the magnetic nanobeads hydrodynamic properties resulting from their binding to target analytes. In this detection scheme, usually referred to as Brownian magnetorelaxometry approach, one measures the decrease in the magnetic bead Brownian relaxation frequency (or, in the time domain, of the Brownian relaxation time) caused by the increase of the bead hydrodynamic size upon probe–target coupling[3].

In this paper we show that it is possible to measure the Brownian relaxation frequency of commercial magnetic nanobeads in a microfluidic channel using a simple and inexpensive optical platform, in contrast to the method commonly used (i.e. bulky magnetometers).

EXPERIMENTAL
Figure 1 shows a schematic of the system employed. The setup consists of a laser source (λ = 650 nm or λ = 405 nm), a transparent microfluidic fluidic channel, having, in the central part, a diameter variable from 2 to 5 mm and height, corresponding to the thickness of the liquid sheet, of 1 mm. The readout chamber, having a capacity of roughly 10 μl, of liquid, is surrounded by two electromagnets for generating a AC field parallel to the laser beam. Finally a photodetector (Thorlab PD36A) is used to record the transmitted beam intensity. The laser spot size can be expanded up to ~ 5 mm diameter by means of an adjustable beam expander in order to interact with the largest possible number of particles.

In both cases the applied magnetic field intensity range is from 1 mT to 3 mT. The AC magnetic field is measured in real time by a high-speed Hall probe, whose output signal provides the reference for a lock-in amplifier used to filter and detect the different harmonics of the photodetector voltage output. The signal is then analyzed by a computerized platform.

THEORY
The upper part Fig.2 shows the basic mechanism at the base of the measurements of Brownian relaxation of magnetic nanobeads. The individual MNBs show negligible optical anisotropy and does not show any significant agglomeration in
zero applied magnetic field as verified by dynamic light scattering. Therefore, under magnetic actuation, it is the collective behavior of the particles that modulates the light transmission measured by the photodetector.

When no magnetic field is applied, particles are randomly oriented as shown in Fig. 2(a). The transmitted signal changes when a magnetic field is applied, due to formation of magnetic particles chains along the light path that decrease the geometrical scattering cross-section of the suspension. If an alternated magnetic field is applied, after positive or negative field saturation when the field is back to zero, the chains break up or become loosely bound due to thermal agitation and the system turns back into an isotropic disorder distribution.

Therefore, schematically the dynamic processes involved are: for (1) field approx. 0, disruption of MNB chains due to thermal agitation and/or the sign change of the magnetic field, (2) low field but away from 0, rotation of the individual MNBs to align with the magnetic field, and (3) high field, reforming of MNB chains.

Hence, the time scale for the rotation of the individual MNBs sets the time scale for the reforming of MNB chains that gives rise to a modulation of the optical signal that is revealed by the photodetector.

The rotation dynamics of individual MNBs with hydrodynamic volume $V_h$ is characterized by the Brownian relaxation frequency

$$f_B = \frac{k_B T}{6 \pi \eta V_h}$$

where $k_B$ is Boltzmann’s constant, $T$ is the absolute temperature and $\eta$ is the dynamical viscosity of the fluid. Therefore, by measuring the light transmission modulation, without the need of extra optical elements it is possible to characterize the dynamic behavior of magnetic nanobeads and extract $f_B$.

RESULTS AND DISCUSSION

Figure 2(c) shows the complex signal measured by lock-in technique vs. frequency of the applied magnetic field for a suspension of 100 nm BNF starch Micromod beads having a concentration of 200 $\mu$g/ml and actuated using a AC field having a maximum intensity of 1 mT. Since the bead dynamics does not depend on the magnetic field direction, the strongest component of the measured signal is at the double frequency with respect to the excitation one. Therefore the graph shows the recorded 2nd harmonic signal, where $V_2^+$ and $V_2^-$ represent the in-phase and out-of-phase component of the signal. $V_2^+$ has a clear peak near about 120 Hz, resembling the Brownian relaxation frequency peak recorded by standard techniques, whereas the out-of-phase signal shows a smooth step-like transition with saturation at low frequencies and a value close to zero at high frequencies.

By data analysis using a more detailed model the value of $f_B$ extracted from the data is in agreement with what expected from other techniques.[4]
Fig 3(a) show a picture of the setup where the curves can be measured while flowing the magnetic nanobeads; the laser beam is applied vertically through a mirror, in order to reduce the effect on the signal of bead sedimentation at the bottom of the microfluidic channel. A more compact setup is shown in panel (b) where a blue laser (λ=405 nm) and miniaturized electromagnetic coils are used. Different chambers can be measured sequentially using an optical stage (c), paving the way to multiplexed detection of analytes.

**CONCLUSION**

In conclusion, we have been presented a novel approach to magnetorelaxometry, based on the measurement of the relaxation behavior of magnetic nanobeads by light scattering. Without exploiting any magneto-optical effect based on the particles induced light polarization rotation, is possible to characterize and distinguish the dynamic behavior of different population of magnetic nanobeads. This methodology is of easy integration with modular microfluidic systems and holds great potential toward the realization of a miniaturized homogeneous assay based on the relaxation behavior of cluster of magnetic nanobeads.

**REFERENCES**


**CONTACT**

*marco.donolato@gmail.com*