Invited Paper

Micro manipulation of superparamegnetic particles using magneto-optic tweezers

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ABSTRACT

We have developed a magneto-optic tweezers that offer new experimental possibilities when laser tweezers were traditionaly used. The magneto-optic tweezers combine a multi-trap optical tweezers based on acousto optic deflectors and homogeneous magnetic field which direction and magnitude can be time modulated in arbitrary fashion. Superparamagnetic beads that are readily available from several commercial sources are used as trap handles. They can be manipulated using optical tweezers in a well known way. By applying magnetic field additional repulsive or attractive interaction between the particles can be induced, giving rise to new micromanipulation possibilities. Several examples of how magneto-optic traps can be used in colloidal physics reasearch and potential applications in biophysics and microfluidic systems are presented.

Keywords: laser tweezers, magnetic tweezers, micromanipulation, micro fluidics

1. INTRODUCTION

Since their discovery [1] laser tweezers have proved to be an excellent tool for micromanipulation of microscopic particles and a precise force gauge. They have been successfully used in many fields of science. With recently emerging commercial high end laser tweezers systems that support multiple traps with sub nanometer positioning resolution and precise trap stiffness control combined with ease of use a broader proliferation of laser tweezers and their wider use by non-specialists is expected. These are the signs that the technique is becoming mature and will hopefully become a standard experimental tool in soft matter physics, biophysics, biology and medicine. In spite of the huge progress made in the development of different types of optical tweezers in the past, new ideas are still needed to solve new challenges in the field of micromanipulation. One possible direction of the future development is to combine laser tweezers with some other micromanipulation technique. Magnetic tweezers are obvious candidates and particularly attractive because the magnetic field and optical tweezers couple to different type of induced dipole moments which potentially means greater experimental versatility. In this paper we will present a magneto-optic tweezers instrument and a few experimental examples that demonstrate, how a combination of advanced laser tweezers system and magnetic tweezers using time and space modulated homogeneous magnetic field can offer many interesting experimental possibilities not available by laser or magnetic tweezers alone.

2. OPERATING PRINCIPLES

Magneto-optic tweezers use super paramagnetic beads as handles. Super paramagnetic beads are commercially available from several sources with a range of magnetic susceptibilities. For use with magneto-optic tweezers the beads must have low absorption for the laser radiation in order to prevent catastrophic damage during laser trapping. When the super paramagnetic beads are exposed to the external magnetic field the induced dipole moments interact via dipole-dipole interaction given by

$$U_{ij} = -\frac{\mu_0}{4\pi\, r^5}\left(3(\vec{p}_i \cdot \vec{r})(\vec{p}_j \cdot \vec{r}) - \vec{p}_i \cdot \vec{p}_j r^2\right) \qquad , \tag{1}$$

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where $\vec{p}_i$ and $\vec{p}_j$ are magnetic dipole moments and $\vec{r}$ corresponding radius vector. The force between the dipoles can be calculated using

$$\vec{F}_{i,j} = -\nabla U_{i,j} \tag{2}$$

and has in general a complicated dependence on the dipole orientations and positions [2]. However, in two cases that are of particular interest for experimental application of magnetic tweezers the dependence becomes rather simple. Those two cases are (shown in Figure 1): (i) External magnetic field is perpendicular to the sample plane. The induced magnetic moments are parallel to each other giving rise to isotropic repulsive interaction in the imaging plane described by

$$\vec{F}_{i,j} = 3\frac{\mu_0}{4\pi}\frac{p_i p_j}{r^4} \tag{3}$$

(ii) External magnetic field is rotating in the sample plane. If the frequency of rotation is faster than the dynamic response of the particles they feel an average interaction between induced magnetic dipoles which is in this case isotropic, attractive and given by

$$\vec{F}_{i,j} \cong -\frac{3\mu_0}{4}\frac{p_i p_j}{r^4} \tag{4}$$

By switching between the two modes of magnetic field modulation one can easily induce either attractive or repulsive interaction between the super paramagnetic beads. In the above discussion we assumed that the particles are confined to the 2D sample plane. This is required in most experiments in particular the case when repulsive interaction is used in order to prevent, the particles jumping on top of each other. However this constraint is usually not limiting and can be experimentally realized either by using multi beam laser tweezers to hold particles at a certain position or by using a thin sample cell with cell thickness slightly bigger than the diameter of the particles.

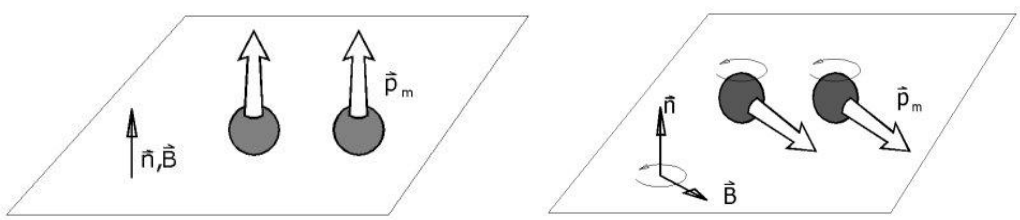


Fig. 1. Interaction between the induced dipole moments of super paramagnetic beads in external magnetic field can be either repulsive (left image) or attractive (right image) depending on the orientation of the magnetic field. If the in-plane magnetic field is rotated fast enough, the average interaction between the beads is attractive and isotropic within the sample plane.

3. DESIGN OF MAGNETO-OPTIC TWEEZERS

Magneto optic tweezers were realized by integrating laser tweezers and magnetic tweezers subsystems into a single versatile instrument. Laser tweezers and magnetic tweezers can be used as a stand alone unit. However, when used in combination they provide complementary functionality with many new exciting experimental possibilities.

3.1 Laser tweezers

Laser tweezers were build around a commercial inverted microscope (Zeiss Axiovert 200M) equipped with a water immersion microscope objective (Zeiss Achroplan 63/0.9W). Diode pumped Nd:YAG CW laser operating at 1064nm with maximum output power of 2W (Coherent, Compass 2500MN) was used as a laser source. Multiple trap generation and precision beam steering was accomplished by using accousto optic deflector (AOD) pair (Intraaction, DTD-274HA6) driven by control electronics and PC software for laser tweezers systems (Aresis, Tweez). Setup schematic is shown in figure 2.

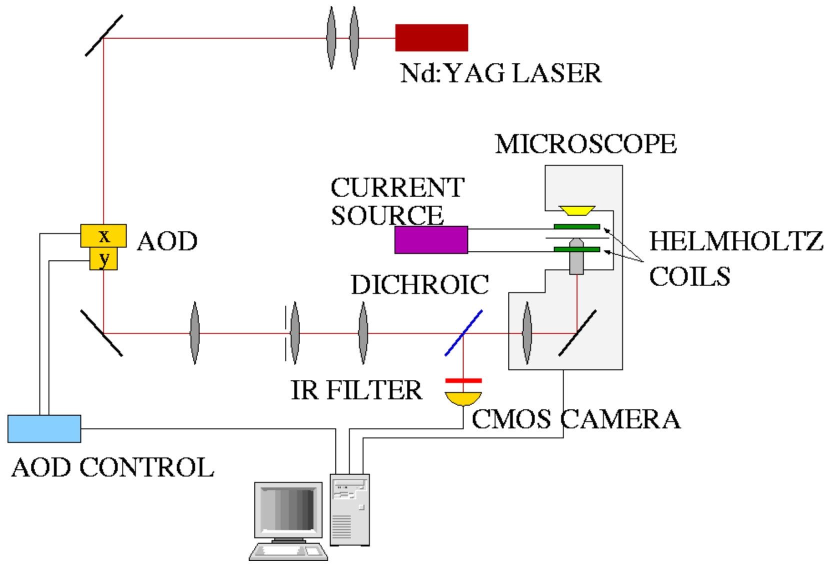


Fig. 2. Schematics of laser tweezers setup. Laser beam from a diode pumped Nd:YAG laser is expanded and deflected used for generating laser traps. Laser trap positions and strengths are controlled using acousto optic deflectors driven by dedicated electronics.

The laser tweezers can generate hundreds of time shared traps which can be controlled individually or grouped in a user defined patterns for easier manipulation. The minimum switching time between two consecutive traps was 10 µs. The resulting refresh rate was fast enough that the effective trapping potential was quasi-static even when a large number (e.g. 400, see figure 3) of micron sized particles were trapped simultaneously. In addition to the large number of traps, AOD based laser tweezers support sub-nanometer positioning resolution combined with a precise (14 bit) laser trap intensity control.

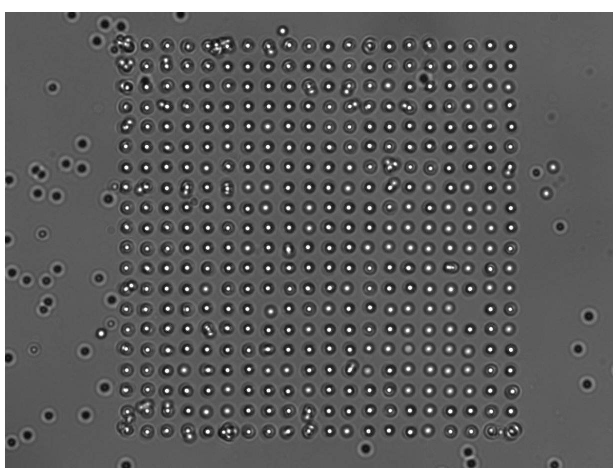


Fig. 3.Snapshot of 400 simultaneously trapped 1.5 µm diameter silica particles dispersed in water, demonstrating multi-tweezing action. Trap switching frequency was 80 kHz giving 200 Hz trap refresh rate. Average laser power was approx. 0.5 mW per trap.

3.2 Magnetic tweezers

Magnetic tweezers consist of control software that runs on a standard PC and two hardware building blocks: (i) Magnetic head and (ii) Six channel microprocessor controlled current generator. Magnetic head is assembly of six water cooled solenoids grouped into three Helmholz coil pairs. Due to the requirement that the coils are as close together as possible and the geometrical constraints imposed by the size of the microscope objective only the two horizontal solenoids were in a true Helmholz configuration (see figure 4) while the distance between the solenoids in the other two pairs was slightly bigger. Nevertheless, a very homogenous magnetic field could be obtained well beyond the viewing area of a microscope objective (approx 300 μm) with magnetic field density inhomogenieties bellow the measuring limit of our experimental setup. The maximum achievable magnetic field was 30 mT. The magnetic head was attached directly to the microscope with custom made holder and adjustable height control along the optical axis of microscope objective. Current in each coil was controlled by one channel of a custom made six channel arbitrary current generator. Current waveform of each channel can be updated with a maximum update frequency of 50 kHz and can source maximum current of 8 A per channel with perfect phase coherence between the channels. Multi-channel phase coherent arbitrary current controller is more complicated to build than using standard DC or sine wave current sources. However, the additional effort is compensated by much higher modulation flexibility. This turned out to be particularly important in experiments that required a homogeneous rotating magnetic field for inducing isotropic attractive interactions between magnetic particles. If a sine and cosine current sources are used for driving the coils torque is introduced into the measuring system which may result in unwanted experimental side effect. By using arbitrary current controller such side effect can be completely eliminated by reversing the direction of the filed rotation after each full turn.

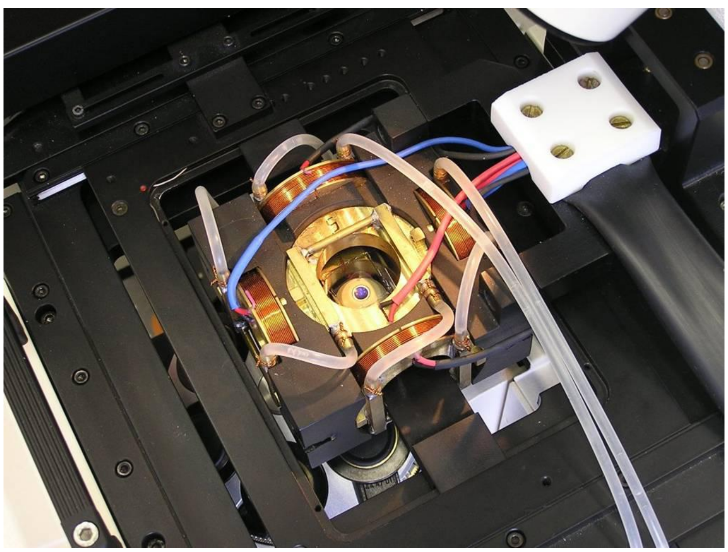


Fig. 4. Image of a magnetic tweezers head. Three orthogonal pairs of Helmholz coils are assembled into a compact design that fits around Zeiss 63x /0.9 water immersion microscope objective. Coils are water cooled to prevent excessive temperature rise during continuous operation.

Additionally, independent current control in each coil allows for fine tuning of magnetic field amplitude needed for elimination of residual magnetic field gradients due to the asymmetries in coil geometry and positioning.

4. APPLICATIONS

Magneto-optic tweezers can be used in a wide range of experiments. In some cases they are alternative to the existing micromanipulation techniques and give some additional flexibility while in the other they offer entirely new experimental possibilities. In the following a few experiments where magneto-optic tweezers proved to be a very powerful experimental tool will be presented.

4.1 Active microrheology in liquid crystals

Active microrheology is an experimental technique used for measuring local visco-elastic properties of soft matter [3]. It uses colloidal particles that are actively manipulated as a source of local stress in the material. By analyzing the positions or trajectories of tracer particles and/or a probe particle one can deduce local visco-elastic properties of the material. Standard laser tweezers are often used as a micromanipulation tool. Magneto-optic tweezers can improve sensitivity and precision of microrheological measurements in two ways: (i) increase maximum available force and thus give higher sensitivity in stiffer materials and (ii) in certain materials high electric fields in the focus of a trapping beam can lead to considerably changed local structure of a material. Example are liquid crystals where high electric fields can lead to significant distortion of the local director field (i.e. Fredericks transition) making experimental results less reliable and much more difficult to interpret. In this case the problems can be avoided by using magnetic tweezers since low magnetic fields used in magnetic tweezers have no influence on the orientation of director field.

In the following we will present the outline and the results of the measurements of liquid crystal mediated forces between colloidal particles in a thin homeotropic cell filled with a nematic liquid crystal (5CB, Aldrich). The embedded colloidal particles were super paramagnetic beads with a diameter of 4.5 μm (Dynabeads, M-450 Epoxy, Dynalbiotech). The details of the force dependence on the particle separation depend on the anchoring of liquid crystal molecules on the particle and sample wall surfaces. In our case the orientation of director field was parallel to the colloidal particle surface as shown in figure 5.

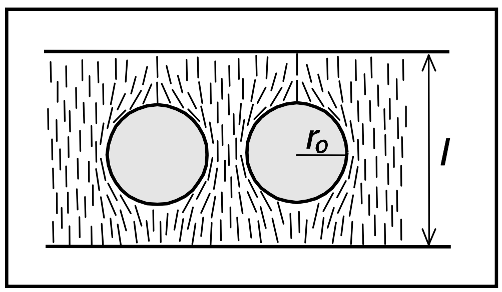


Fig. 5. Schematically side view of a thin homeotropic cell filled with nematic liquid crystal 5CB sample and embedded colloidal particles of radius r_0. Cell thickness l of 8 μm was less then twice the bead diameter to prevent stacking of the beads on top of each other. The orientation of director field at the colloidal particles surface was tangential which resulted in repulsive liquid crystal mediated force between the particles.

Such geometry induced repulsive interaction between the particles. In principle repulsive force as a function of a distance could be measured by using a force calibrated two beam laser tweezers [4]. However, due to a significant distortion of a local director field induced by strong electric field of the tweezing laser beam the results at small interparticle separations become unreliable and difficult to interpret. The problems can be avoided if magnetic tweezers are used because applied magnetic field densities are well below the values where any influence on the local liquid crystal structure could be expected.

The experiment was performed in the following sequence: (I) two super paramagnetic beads were brought together to a distance of a few micrometers using laser tweezers, (ii) the laser tweezers were switched off and the attractive force of magnetic tweezers was used to bring the beads into the initial position x_0, (iii) magnetic field was switched off and the beads started to move apart due to the liquid crystal mediated repulsive force. The trajectory of the particle movement was recorded using a high speed CMOS camera (section A in figure 6), (iiii) when the beads were separated at distance where the liquid crystal's repulsive force become negligible, calibrated repulsive magnetic force was switched on in order to measure the drag coefficient of the beads (section B in figure 6).

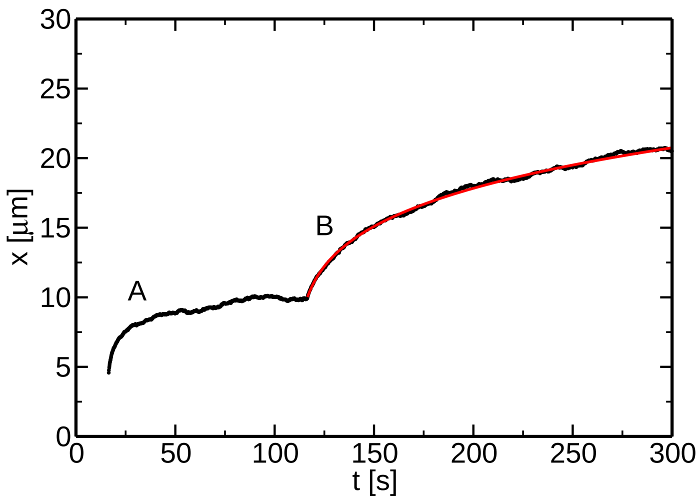


Fig. 6. Measured bead separation as a function of time. In section A, the beads were pushed apart by liquid crystal mediated repulsive force. External magnetic field was switched off during this step of the experiment. When the bead separation was large enough that the liquid crystal forces become negligible, external magnetic field was switched on (section B) forcing the beads to move apart again this time due to the repulsion between the parallel induced magnetic dipoles. The second measurement was used for a precise magnetic force calibration.

From the measurements it was possible to determine all parameters needed for the determination of interparticle interaction strength as a function of particle separation. We would like to point out that in each experiment all needed parameters were measured on the same pair of beads as used for measuring interparticle interaction thus significantly reducing systematic errors. The details of the data analysis and theoretical models used in data interpretation can be elswhere [5]. The experiments have revealed that the repulsive force between colloidal particles in nematically ordered liquid crystal cell decays as an inverse sixth power of the particle separation for a wide range of particle separations, most notably, including very close distances (fig. 7). Results were in very good agreement with theoretical predictions except at bead separations larger than the bead diameter. The later can be contributed to the surface effects not taken into account within the model.

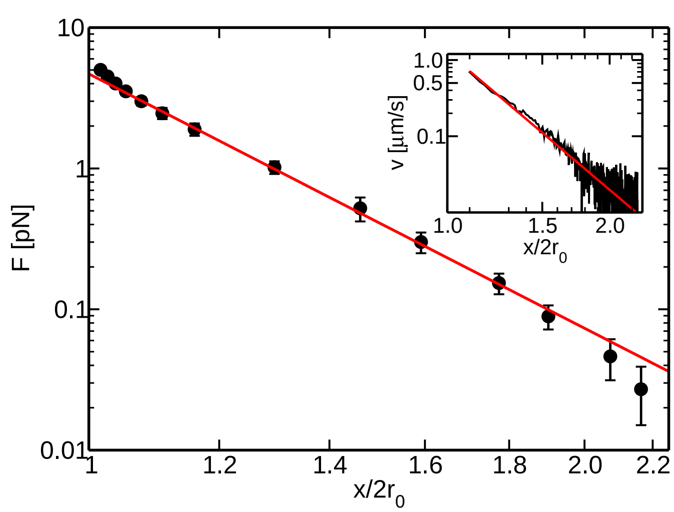


Fig. 7. Measured and calculated force and bead velocity dependence as a function of normalized bead separation showing very good agreement between measured values (squares) and theoretical predictions (red lines).

4.2 Model systems for exotic interactions studies

Magneto-optic tweezers offer an elegant way for experimental realization of some types of exotic potentials that are difficult to create in other ways. An interesting family of core softened potentials can be realized by confining super paramagnetic colloidal particles in a thin sample cell with a thickness between one and two particle diameters. Those potentials are characterized by the softening of the pair potential at small interparticle separations [6]. The degree of softening can be controlled by the cell thickness and can range from a more or less pronounced sub power law repulsive behavior to the crossover from repulsive to attractive interparticle interaction regime at small distances. The functional dependence of the core softened potential is given by equation (5)

$$U_{ij}(r,z) = K\frac{r^2 - 2z^2}{\left(r^2 + z^2\right)^{5/2}} \quad , \tag{5}$$

where *r* and *z* are in plane and vertical separations of the spheres. In figure 8 are measured and calculated pair interaction force shown as a function of in plane particle separation *r*.

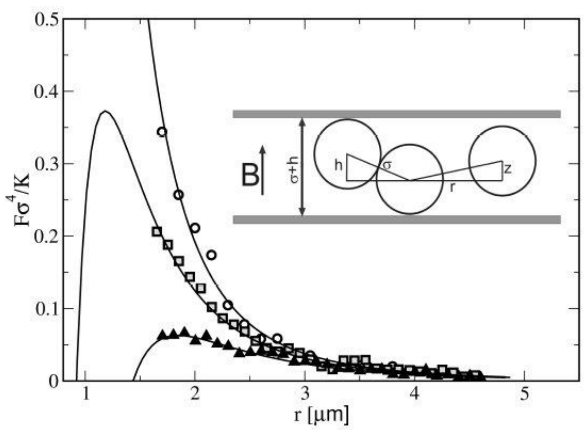


Fig. 8. Measured and calculated (solid line) dependence of pair interaction force as a function of in plane pair separation *r*. Measurements were performed with σ = 0.89 μm diameter super paramagnetic beads in three different cells. Solid lines are fits for *h* = 0 μm (open circles), *h* = 0.46 μm (open squares), and *h* = 0.72 μm (triangles).

Measurements were made using super paramagnetic beads with a diameter of σ = 0.89 μm in three cells of different thicknes. Solid lines are calculated fits for *h* = 0 μm (open circles), *h* = 0.46 μm (open squares), and *h* = 0.72 μm (triangles).

Isotropic core softened potentials are interesting because in dense colloidal systems they lead not only to usual hexagonal phase but have much richer phase diagrams. Examples of different experimentally observed phases are presented in figure 9. It should be pointed out that all phases were generated under the same experimental conditions with isotropic softened repulsive interaction. The only parameter that was varied was particle density. Details can be found elsewhere [7].

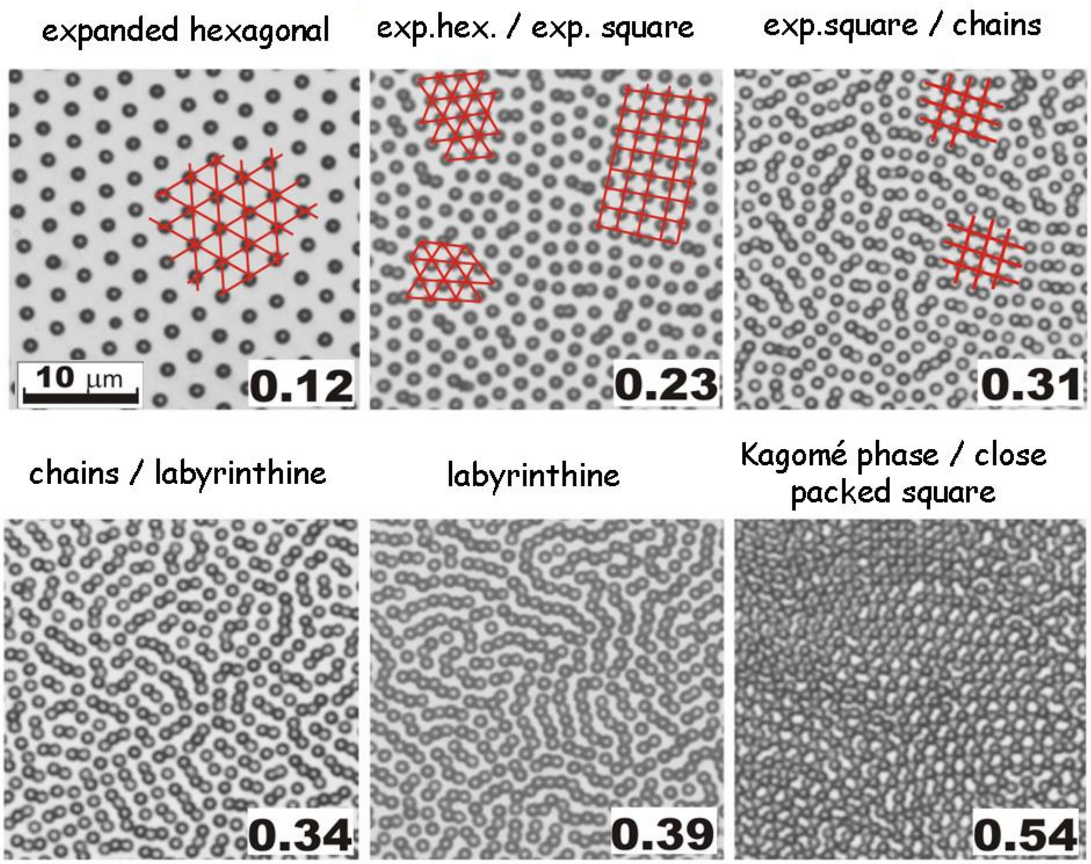


Fig. 9. Experimental realization of different phases of a dense colloidal system with a softened isotropic pair interaction. At low densities (filling fraction 0.12) a usual hexagonal phase that is characteristic for isotropic interaction is observed. At higher densities particles start to feel potential softening and more complicated phases emerge.

4.3 Micromanipulation and microfluidics

Time shared laser tweezers and magnetic tweezers are complementary micromanipulation techniques in a sense that laser tweezers exert force on one particle at a time while magnetic tweezers simultaneously interact with all particles within the working volume. Both techniques can be applied independently which gives rise to numerous interesting ways for either micromanipulation or for driving micro devices in microfluidic systems. In the following a few examples will be presented.

4.3.1. Rotation of trapped particle

Particles in optical traps can be rotated by optical means exploiting spin or orbital momentum carried by the photons in the laser beam. To transfer the angular momentum from light to particles the photons need to be absorbed or scattered by the particles that are anisotropic either optically (i.e. birefringent) or in shape (i.e. non-spherical). Alternatively magneto-optic tweezers can be used to induce particle rotation with some important advantages over all optical approach. Main advantages are: (i) Better control over torque and angular speed. Both can be continuously varied from zero to the maximum value determined by particle's magnetic susceptibility and magnetic field strength. (ii) The rotation axis can be in arbitrary direction. (iii) There are no constraints regarding particle shape or optical anisotropy.

In figure 10. are presented the results of angular velocity measurement of a super paramagnetic bead (Dynabeads, M-450 Epoxy, Dynalbiotech) held in an optical trap. Magnetic field with strength of 10 mT was rotated in the plane perpendicular to the laser beam with a frequency varying from 0.6 Hz to 500 Hz. The particle rotation followed the rotation of the external magnetic field up to the frequency of 10 Hz. At higher drive frequencies the rotation of the particles started to lag and saturated at approximately 23 Hz. The maximum achievable torque can be estimated from the maximum particle rotation frequency using [8]

$$M = 8\pi\eta R^3 \omega\left(1+\frac{1}{8}\left(\frac{R}{h}\right)^3+\frac{1}{64}\left(\frac{R}{h}\right)^6+\ldots\right) \quad , \tag{6}$$

where M is torque, η is viscosity of the medium, R sphere radius, h the distance of the sphere center from the cell wall and ω angular velocity. In our case the maximum torque corresponding to the maximum rotation frequency of 23 Hz was approximately $M = 45pN\mu m$.

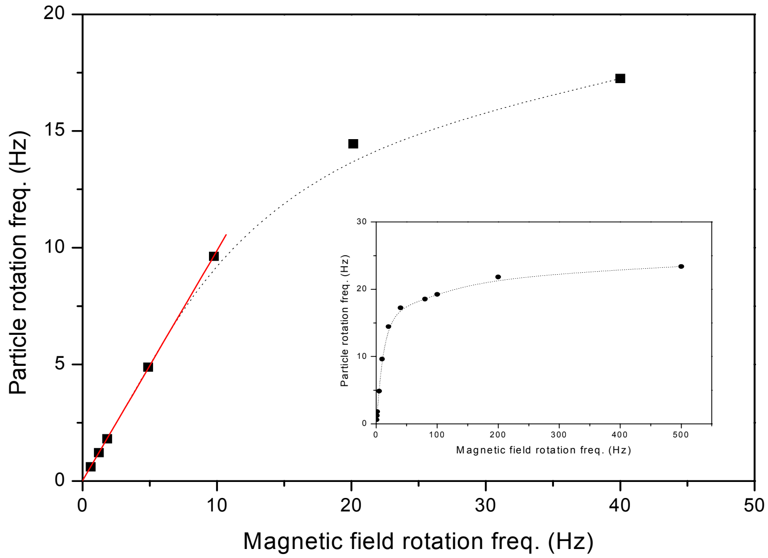
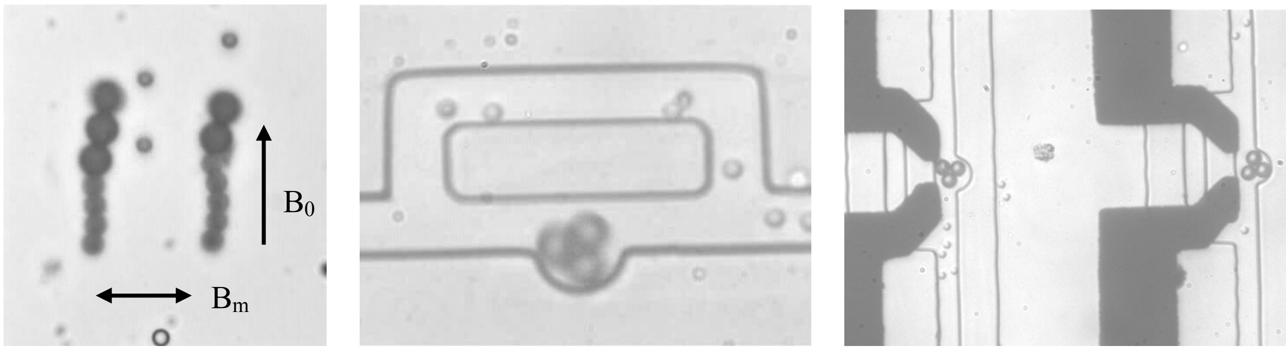


Fig. 10. Rotation frequency of a super paramagnetic sphere driven by rotating magnetic field. Rotation of the sphere follows external magnetic field up to the frequency of 10 Hz (red line) and then starts to saturate due to the increasing viscous torque that can not be compensated by magnetic torque.

4.3.2. Swimmers and micro pumps

Magneto-optic tweezers are ideal tool for assembling, driving and controlling of microswimmers and micropumps. Working of many of those structures was already demonstrated by other methods [9]. However, the use of magneto-optic tweezers offers some distinct advantages: (i) They provide simple simultaneous drive of many pumps or swimmers [10]. (ii) Attractive interaction between super paramagnetic particles keeps structures stable and to some extent works as a self repair mechanism. (iii) Optical tweezers can be used either for positioning or individual control of each element. Alternatively, a dielectrophoretic force generated by low (< MHz) frequency electric field between micro structured electrodes which are part of a microfluidic system can be used for controlling the pumps. In figure 11 are shown examples of micro structures actuated and controlled by magneto-optic tweezers.



A B C

Fig. 11. Examples of micro structures actuated and controlled by magneto-optic tweezers: (A) Two sperm like structures that are held together by a static magnetic field B_0. If a small perpendicular magnetic field component B_m that is sine modulated is added, the sperms start to swim. Alternatively if they are held at spot using laser tweezers they induce flow in the surrounding liquid. (B) Micropump composed of three superparamagnetic beads in a microfluidic channel driven by a rotating magnetic field. Channels are approx. 6 μm wide and high. (C) Two pumps as in figure B with added micro structured electrodes. Both pumps are driven simultaneously by rotating external magnetic field. Dielectrophoretic force produced by low frequency AC electric field between the electrodes is used for independent control of rotation speed of each pump. Laser tweezers could also be used for the same purpose.

5. CONCLUDING REMARKS

Magnetic tweezers can significantly enhance utility of any laser tweezers system. Compared to laser tweezers they are technically less demanding to build and thus worth considering as an upgrade of an existing laser tweezers system. As has been presented in this paper magneto-optic tweezers can be used in many different ways ranging from micromanipulation of super paramagnetic particles to generation of simple dipolar type interparticle interactions to more exotic interactions that are difficult to realize by any other experimental approach. In many cases magnetic tweezers are just an alternative to the existing micromanipulation techniques and give some additional flexibility while in the other cases they are providing new experimental possibilities that are not available by either technique alone and are thus essential for a successful realization of experiments. With further development of micro fluidic systems and growing demand for different types of micro-actuators and pumps, the prospects for magneto-optic tweezers looks bright.

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