Novel Magnetic Tweezer for Tissue Stimulation and Rheology

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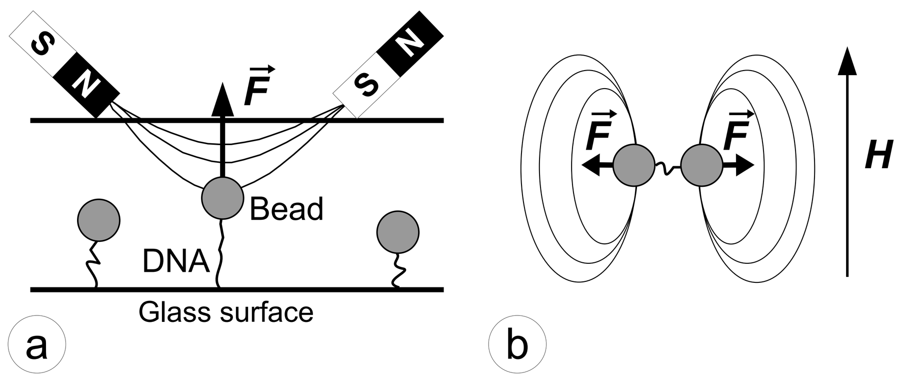
State of the Art:

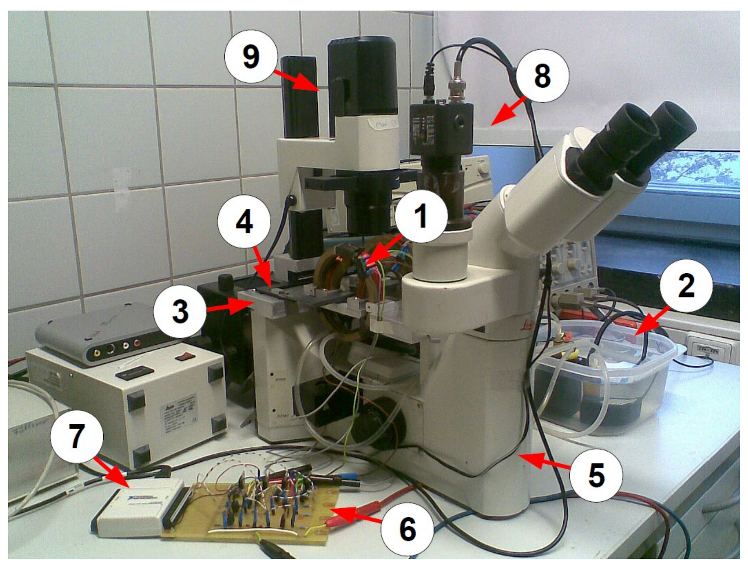
A magnetic tweezer is a technique based on the principle that a force can be applied on a magnetized microparticle when in the presence of a magnetic field gradient.



A possible configuration is shown in the figure (a). The micro particle is hold in the magnetic field gradient generated by the two permanent magnets. Macromolecules are then bond to a glass surface and to the surface of the particle. The molecule is then pulled by translating the magnets, increasing or decreasing the gradient and the force.

Our system differs from this configuration in the way that no glass surface is needed, see figure (b). The macro molecule is bond at both ends to two different magnetic particles. These particles float freely in the solution. The magnetic field produced by a pair of Helmholtz coils induces a stray magnetic field on both magnetic particles and these will then spread apart due to the forces derived from the local inhomogeneous magnetic field.

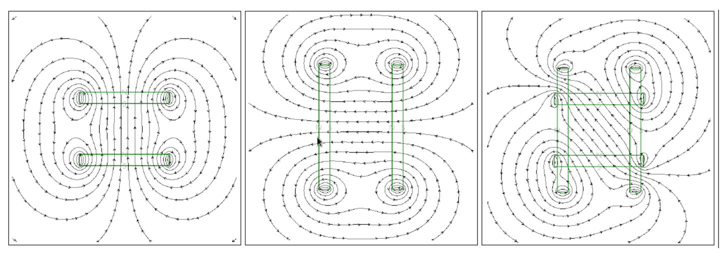
Design of the System:

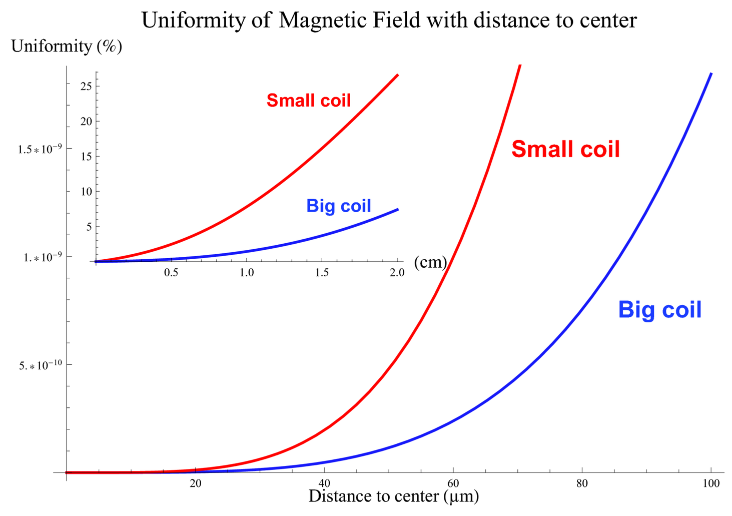


Overall view of the system:

(1) Two Helmholtz coils
(2) Cooling system
(3) Supporting table
(4) Moving table and Sample holder
(5) Microscope
(6) Electronic controlling circuit
(7) Computerized control
(8) Video camera
(9) Lighting system

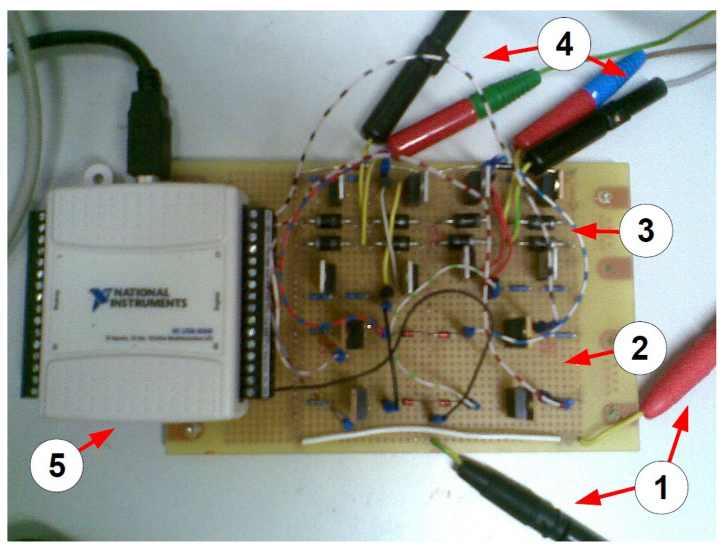
	Small coil	Big coil	
Turns	300	320	
Radius	3,5	5,0	**cm**
Resistance	10,5	11,0	**Ω**
Inductance	8,7	18,7	**mH**
Power dissipated	94,5	99,0	**W**
Magnetic Field (single)	14,1	10,0	**mT**
Magnetic Field (pair)	18,2	12,3	**mT**





Control of the System:

The control of the system is made with the help of an electronic circuit which is controlled by an electronic device, namely a USB-6008 from National Instruments, that is by its turn controlled by LabVIEW software.

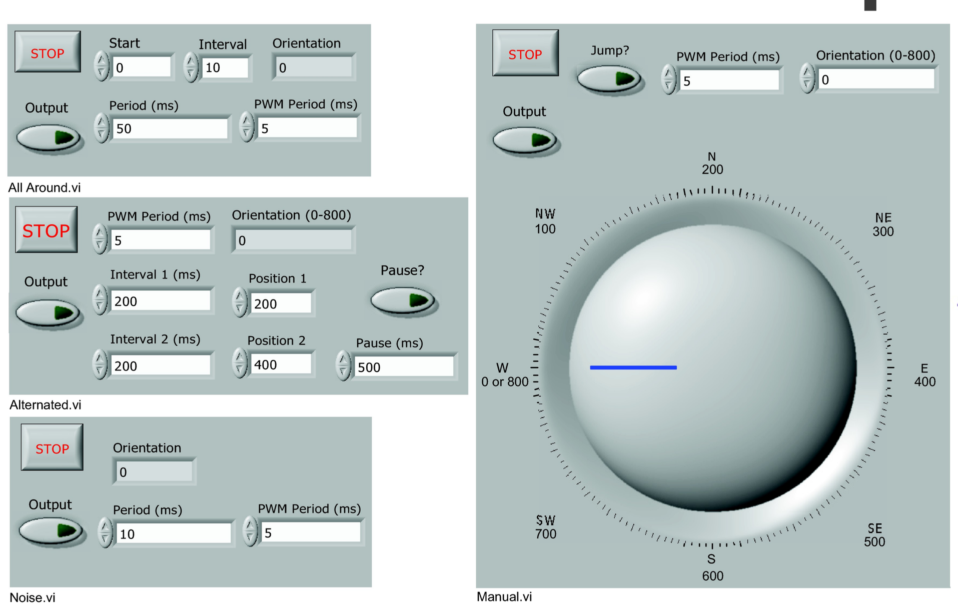


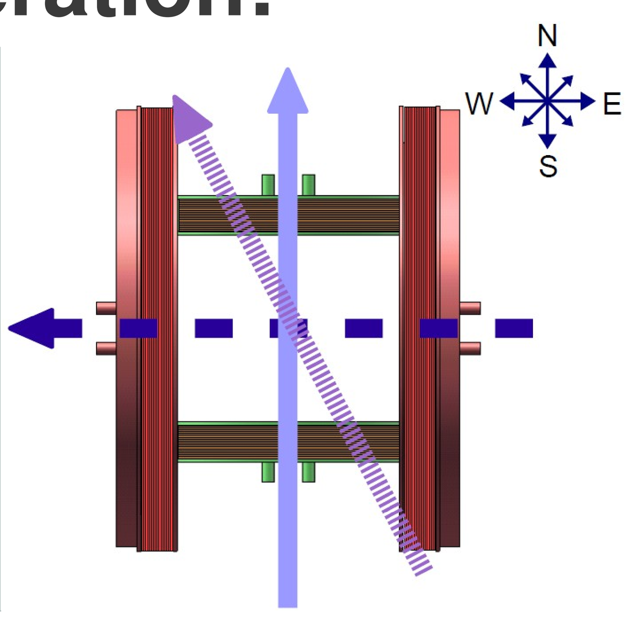
Coil's current controller:

(1) Power cables
(2) Four converter circuits
(3) Two Half-Bridge circuits
(4) Connections to the coils
(5) NI USB-6008 controller

The USB-6008's digital signals permit us to control the gates of the MOSFETs of the electronic circuit, allowing us to control the direction in which the current flows through the coils and thus the field's direction. Allied to this we used a special technique called Pulse Width Modulation, PWM, which allows us to reduce the average current flowing through the coils, using square waves with different periods, maintaining the MOSFETs in the saturation zone. And allowing us to more finely vary the magnetic field's direction.

Modes of Operation:





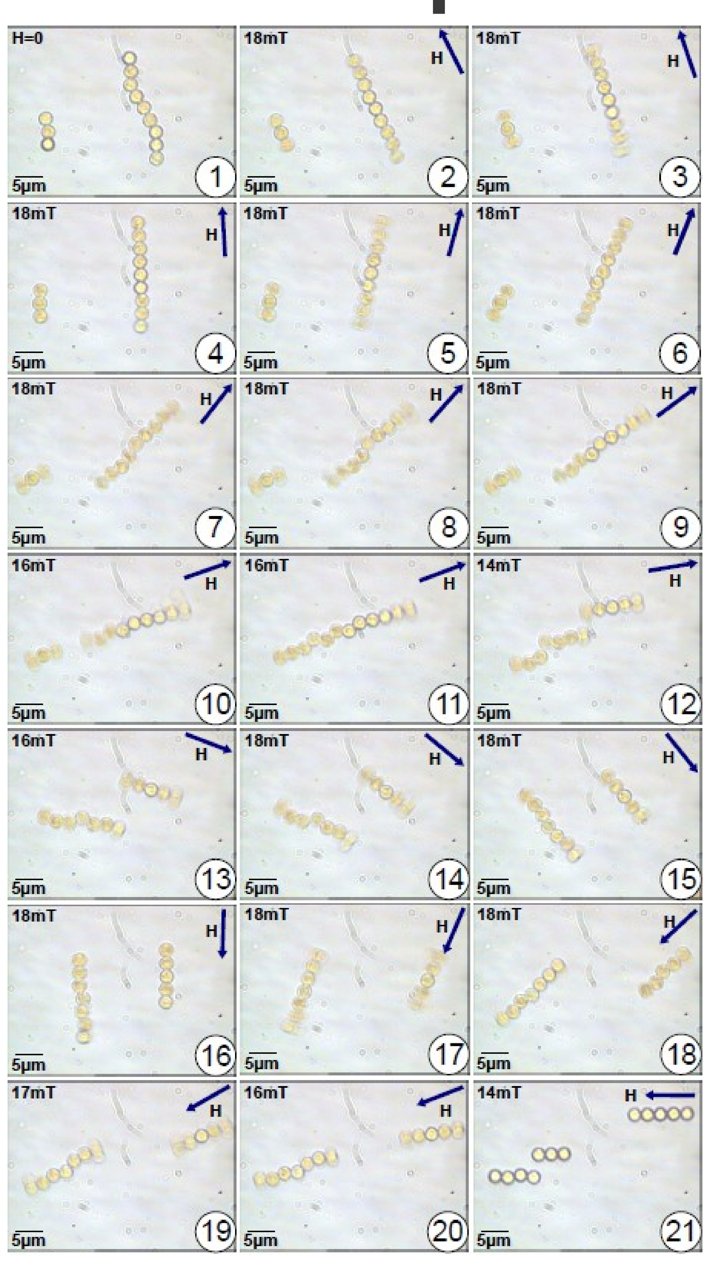
The **All Around Mode** automatically rotates the columns of beads, choosing the rotation frequency, direction of rotation and the interval of angular variation (see panel in left figure. The PWM technique is here used to permit the minimal angular rotation of 5º. This is achieved by turning one of the coils always on, and changing the period of the square wave that controls the passing of the current through the other. As an example (see right figure) to have the field between North and Northwest, we will have the vertical pair of coils always on, and the other pair of coils, intermittently on and off at a specific frequency.

The **Alternated Mode** allows us to select two different orientations magnetic field, **Position 1** and **Position 2**, and the period in which the magnetic fields stay in that position is independently controlled.

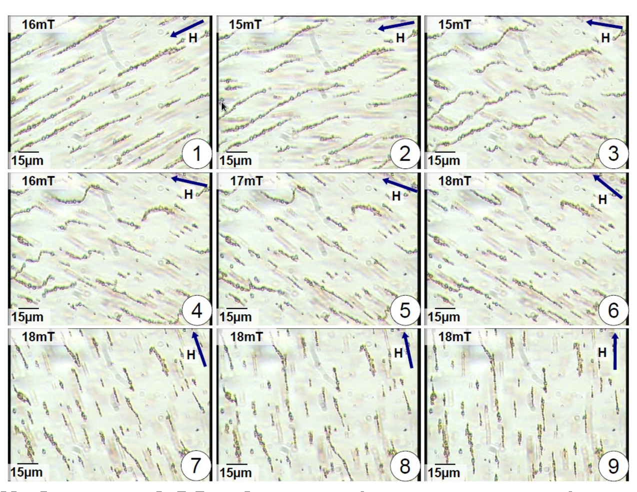
The **Manual Mod**e, provides manual operation and selection of the orientation of the magnetic field by means of the manipulation of the knob showed in the left figure.

The **Noise Mode** randomly selects an orientation for the magnetic field, at a chosen frequency.

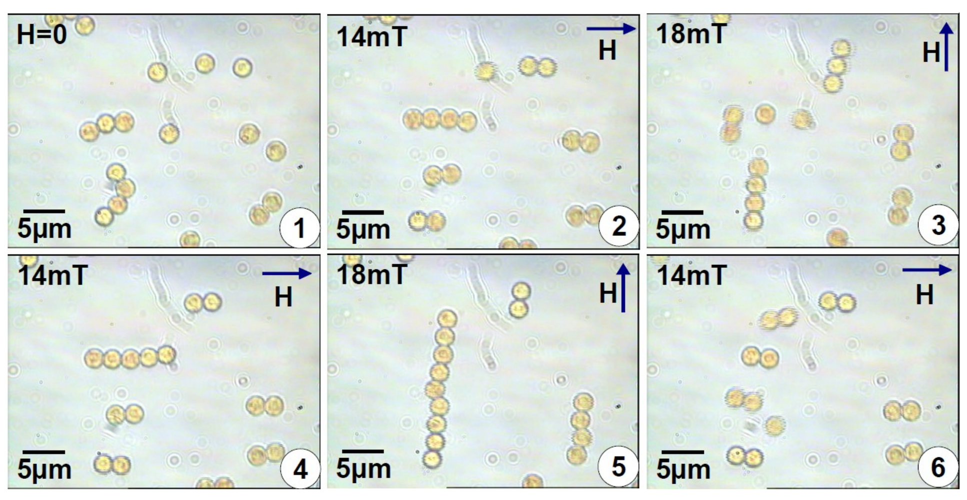
Experiments and Results:



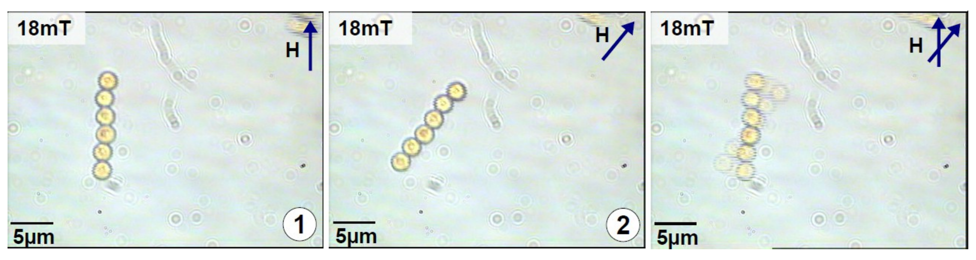
Manual mode with 2.8µm particles. At picture 12 a variation on the direction of the field induces a bigger jump than desired and consequently breaks the column.



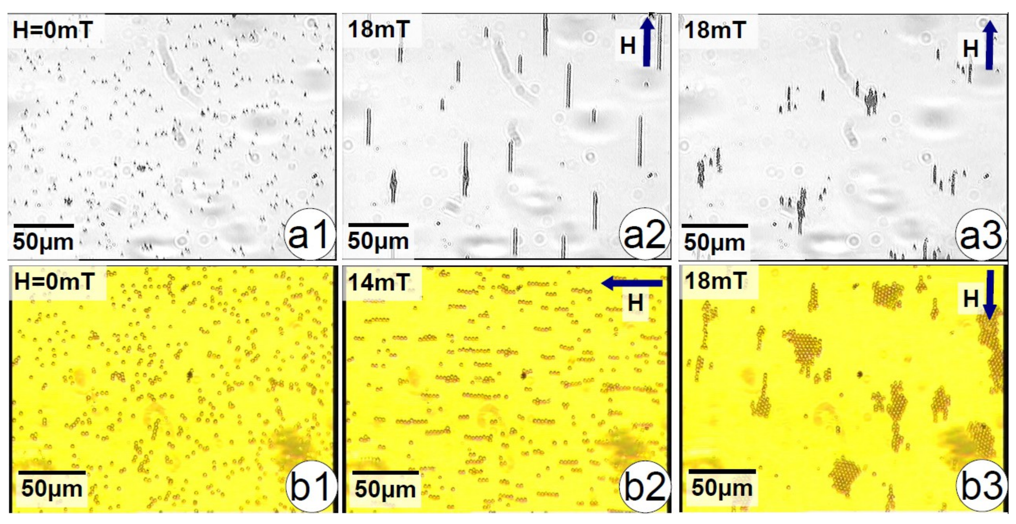
All Around Mode used to rotate columns of Epoxy Beads. The twisting and bending originated what we called the agglomeration of beads and the formation of sheets of beads.



Alternated Mode with 2.8µm. The sequential images show the separation of the particles when the direction of the magnetic field alternates between North and East (90º).



Alternated Mode vibration of 2.8µm particle columns. The first two images show the vibration of a column of beads. The direction of the magnetic field is changed 45º.



On the upper sequence we start with the 1.0µm particles with no magnetic field applied. After applying field (**Alternated Mode**) in figure **a2** the beads approximate one another and start forming columns. Figure **a3** shows what happens after some minutes of operation. The bead columns will attract each other and begin to form sheets.

A similar behavior can be seen in sequence **b** (**Noise Mode**). The beads form linear columns in the direction of the field applied, figure **b2**, and after some minutes sheets start to form in figure **b3**.

Future Work:

The future work and future developments intended include the design and construction of a new system while improving and experimenting with the present one. Improvements to the present system include adding a third pair of coils to have control in the three spatial dimensions. This way we can rotate cells and have a view of them in all intended directions. And not only on one plane.

Wanted is also the implementation of a different control device that allows PWM frequencies up to tens of kHz. With this capability the parasite vibration of the rotation operation modes will be greatly reduced and the precision of rotation increased. This also implies the reprogramming of all software in a new, more robust, language.

The design of the new system will focus on the minimization of the limitations and of the major problems of the present system while trying to maintain the strength of the generated magnetic fields. With this new design we pretend to redo the whole system on a new microscope specifically designed for it. With that, the space limitations and focusing system will not be so strict and may be adapted to our requirements.

We pretend to spread apart the coils to have a system composed of identical coils. A cube can then be constructed with a coil in each surface. This will permit the consolidation of the system and eliminate the need for having a supporting table. A negative side of this idea is the decrease of the field's intensity and uniformity, but as seen above (graphic in 'Design of the System'), the work area is small enough to have a good uniformity.

Parallel to this the implementation of video analysis in order to measure forces, cell and DNA strand deformation and velocities and displacements will be initiated. A video analysis software will be developed.

The connection of the beads to the macromolecules and DNA strands will be deeper studied and implemented.

The study of the beads behavior and the formation of columns and sheets will be quantified.

Finally the experiments with macromolecules as DNA strands or with cells, early stage fish eggs and protein filaments and every biological system that is in the order of some micrometers, will continue.