Optimization of delivery systems for biomedical applications

Julie Chang, Jennene Fields, Seyoung An, Joshua Sautner, Vitali Metlushko

University of Illinois at Chicago, Department of Electrical and Computer Engineering

ABSTRACT

Magnetic drug delivery systems use externally applied magnetic fields to guide magnetic nanoparticles to the destination. With presence of specific targeting mechanism (Magnetic field gradient), it improved overall target reaching efficiency and side effects concerns when compared to non-magnetic drug delivery systems. Many earlier studies have experimented placing magnetic fields externally. However since magnetic field strength decreases exponentially with increase in distance from the source, it only provided surface treatment to those magnetic nanoparticles. An improved magnetic nanoparticle drug delivery system utilizes strong localized magnetic field built in to the system to guide magnetic nanoparticles within the magnetic structures to prevent any unwanted delivery. However this system is also heavily depended on the working distance, to further increase the delivery efficiency, we have considered transporting magnetic nanoparticles from outside environments onto the magnetic structures individually using Atomic Force Microscope. By placing magnetic nano-particles close to regions where strong localized magnetic field can properly deliver them ultimately leads to 100 % delivery of nanoparticles, minimizes unwanted delivery of drug bearing nanoparticles to locations which can cause serious side effects. In addition to the improved efficiency, a possible solution to eliminate the surface sticking problems of nanoparticles outside of the magnetic structure was carefully studied. Nanomanipulation technique allows atom by atom movement of nano-sized magnetic particles, and by using Atomic Force Microscope, high resolution imaging and nanometer precision of manipulation can be achieved. This exciting method of nano-delivery system is not only limited to drug delivery applications, but it can be extended to any biomedical applications in need of manipulation of nanometer sized molecules.

Methods and Materials

•Magnetic structures provide localized magnetic fields which can directly influence magnetic nanoparticles close to the structure (Fabricated at UIC)

•Gold Nanoparticles Fabricated at the University of New Mexico and University of Illinois using Interference Lithography and lift off technique.

•Atomic Force Microscope's contact force to push gold nanoparticles near strong magnetic fields. (Proof of Concept done in Air)

•Nanomanipulation was performed in liquid environments to provide solutions to nanoparticle sticking problem to the surface.

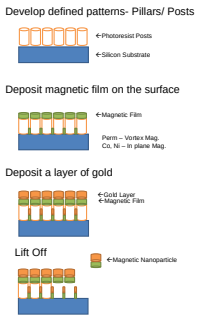

Figure 1. Fabrication process of gold magnetic nanoparticles

Figure 2. Photoresist Pillars fabricated at the University of New Mexico

Figure 3. Optical image of fabricated magnetic nanoparticles after Liftoff Process

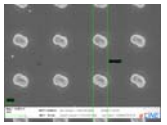

Figure 4. Scanning Electron Microscopy image of gold magnetic nanoparticles

Atomic Force Microscope

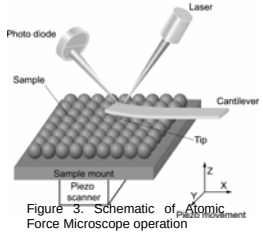

Figure 3. Schematic of Atomic Force Microscope operation

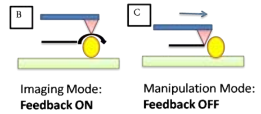

Figure 4. Schematic of Atomic Force Microscope operation for imaging and manipulation

RESULT/DATA

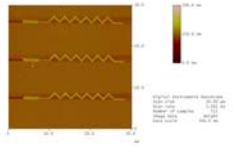

Figure 5. AFM Image of the magnetic structures using e-beam lithography

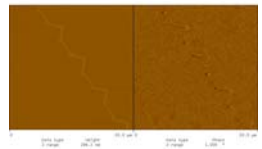

Figure 6. Magnetic Force Microscope image of the structure Indicating strong local magnetic fields.

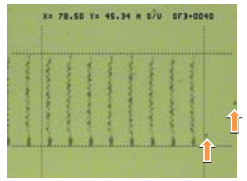

Figure 7. Introduced magnetic nanoparticles on the magnetic structures.

Nearly all magnetic nanoparticles introduced to the surface landed on the surface where strong localized magnetic fields exist!

Nanomanipulation in Air

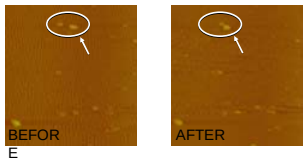

Figure 8. Nanomanipulation using Atomic Force microscope to individually move particles on the surface.

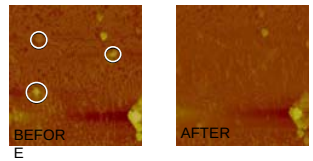

Figure 9. Nanomanipulation of multiple particles using Atomic Force Microscope

Using Atomic Force Microscope's scanning probe, our group was able to move magnetic nanoparticles from one position to another in nanometer precision!

Nanomanipulation in Liquid

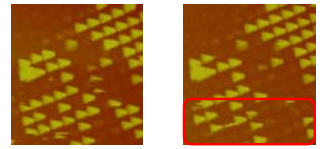

Figure 10. Nanomanipulation using Atomic Force microscope in liquid environment (Acetone)

•Biomedical applications require nanomanipulation in liquid environment.

•Au magnetic nanoparticles bound to the surface via Photoresist layer.

•By using Acetone as our liquid environment, we have found a solution to the particle sticking problem to the surface.

Mechanically Push "Stuck" nanoparticles Using AFM to place them near the structure.

Summary

Currently, gold is one of the material that is widely used to functionalize Superparamagnetic beads that are used for molecule **molecule carriers** or **labels** for molecule studies. Such particles can serve as "Little Engines", and our magnetic structures as "Tracks", this offers applications in many different fields as "Universal Delivery System".

Also, using nanomanipulation technique and Atomic Force Microscope, one can precisely calculate the dosageto be used by the simple formula, Because it ensures no waste particles, therefore minimized side effects, and ultimately achieve 100% delivery efficiency

Dose required = (Dosage per nanoparticle)* (number of nanoparticles)

References

1.Arruebo,Manuel, " Magnetic nanoparticles for drug delivery"Nanotoday 2 (2007):22-32

2.R. Resch *et al., "Manipulation of nanoparticles* using dynamic force microscopy: simulation and experiments", *Applied Physics A, Vol. 67, No. 3,* pp. 265-271, September 1998.

3.A.A.G.Requicha, "*Manipulation of Nanoscale Components with the AFM: Principles and Applications" , Laboratory for Molecular Robotics*

Acknowledgements

Special thanks goes to our collaborator Professor S. Brueck (University of New Mexico)

And Robert Lajos (Nanotechnology Core Facility)