CPS: A Cyber-Physical Framework for Magnetic Resonance Imaging (MRI) Guided Magnetic NanoParticles

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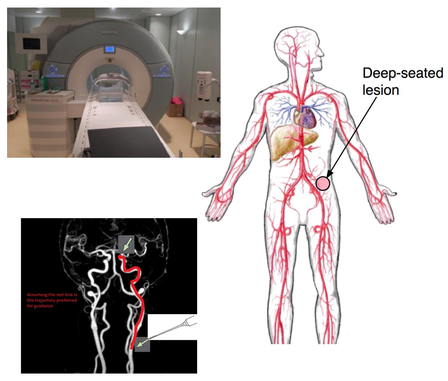
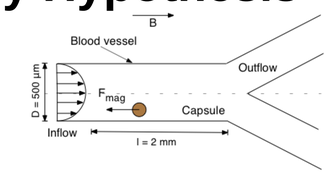
DAPS Directed Assembly of Particles & Suspensions

Project Goal

The goal of this project is to study the fundamental principles (dynamics and control) in using clinical techniques for accurately guiding agglomerations of magnetic nanoparticles in targeted drug delivery. The innovative technology component of this study is the dual use of clinical magnetic technology as an imaging modality for both diagnostics and feedback control signal purposes and as a propulsion modality that generates the control forces to accurately guide agglomerations of magnetic nanoparticles.



Key Hypothesis

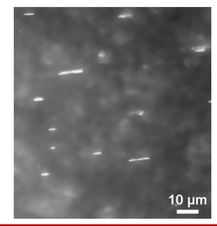


Against the flow

Bz > 500 mT/m

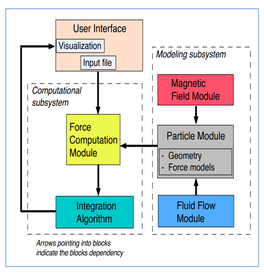
Diameter > 100 µm

Magnetic targeting of nanoparticles in drug delivery applications can be enabled even in the presence of Brownian motion through a controlled aggregation of the magnetic nanoparticles.



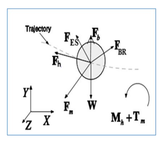
Computational Platform

In this work, Mutual Dipolar Model is utilized to get a better description of magnetic interaction between particles and in order to study the mobility of particles better, hydrodynamics interaction and Brownian dynamics are implemented.



$$\frac{\partial^2 \mathrm{r}_i}{\partial t^2} = \frac{1}{m_i}\vec{F}_i(\vec{r}_j, \vec{v}_j, \vec{\varphi}_j, \vec{\omega}_j)$$

$$\frac{\partial^2 \varphi_i}{\partial t^2} = \frac{1}{J_i}\vec{M}_i(\vec{r}_j, \vec{v}_j, \vec{\varphi}_j, \vec{\omega}_j) \quad (j = 1, \cdots, N)$$



Brownian Dynamics

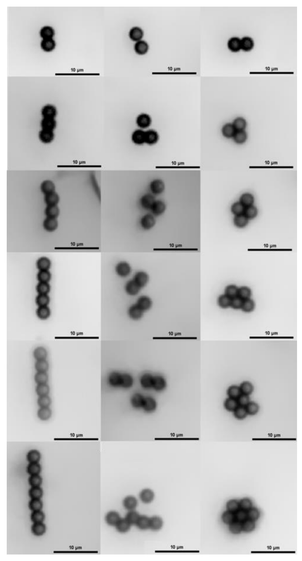
$$r_i = r_i^0 + \sum_j \frac{D_{ij}^0 F_j^0}{kT}\Delta t + \sum_j \sigma_{ij} X_j$$

Mutual Dipolar Model

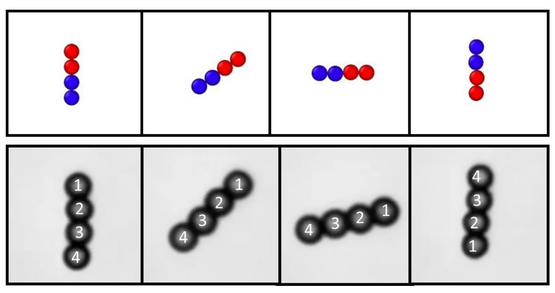
$$m_{i,x} = \chi V_p \left(H_{0,x} + \sum_{j \neq i}^{N} \frac{3}{4\pi {r_{ij,m}}^5} \left(({r_{ij,x}}^2 - {r_{ij,m}}^2/3) m_{j,x} + r_{ij,x} r_{ij,y} m_{j,y} + r_{ij,x} r_{ij,z} m_{j,z} \right) \right)$$

Validation of Model

Behavior of magnetic colloidal suspensions in the presence of dynamic magnetic fields is very complex but in the simplest classification there exist 3 regimes. Below a critical frequency where particles stay chained and act as a rigid body. Above a critical frequency where chains break into smaller fragments and finally way above the critical frequency where crystallization is induced in the particle suspension. In this section, a very detailed study on the behavior of a 4 particle chain is presented. It is seen that there exist 2 critical frequencies in the system. The first critical frequency is showing the transition from chain to a periodic slipping behavior and the second critical frequency is showing the transition from the periodic slipping behavior to a transient chaotic behavior. This transient chaotic behavior will eventually lead to formation of a cluster.



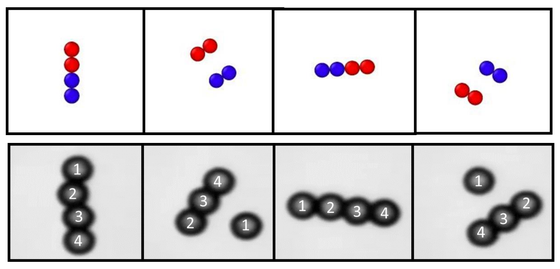
Chained Behavior (Rigid Body)



Simulation

Experiment

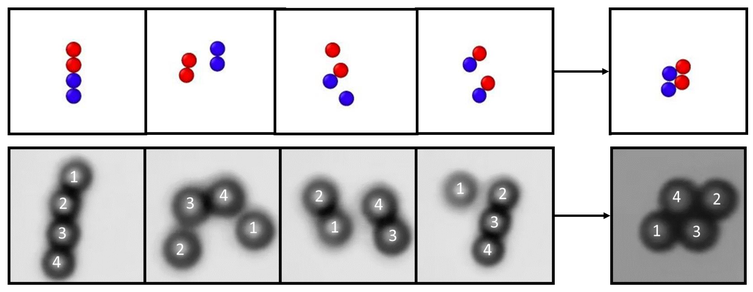
Periodic Slipping Behavior



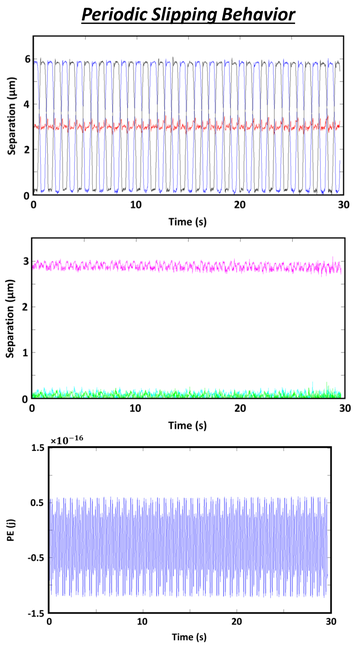
Simulation

Experiment

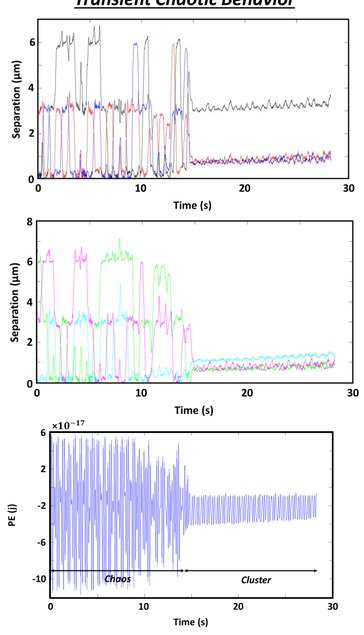
Transient Chaotic Behavior → ***Cluster***



Periodic Slipping Behavior

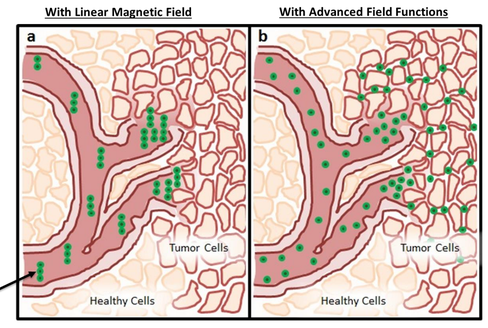


Transient Chaotic Behavior



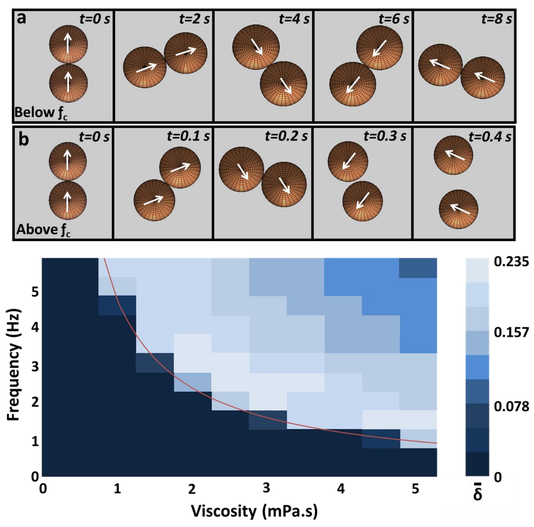
Towards Magnetic Targeting

Instead of simple linear magnetic fields that lead to aggregation, we employ advanced field functions (in this case rotating magnetic fields that allow the MNPs to be concentrated locally while utilizing inter-particle force dynamics to continuously drive separation events, thus preventing aggregation.

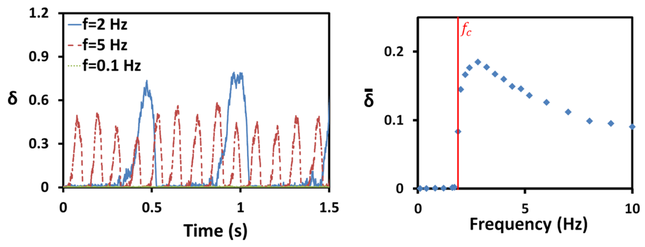


Matlab Simulation

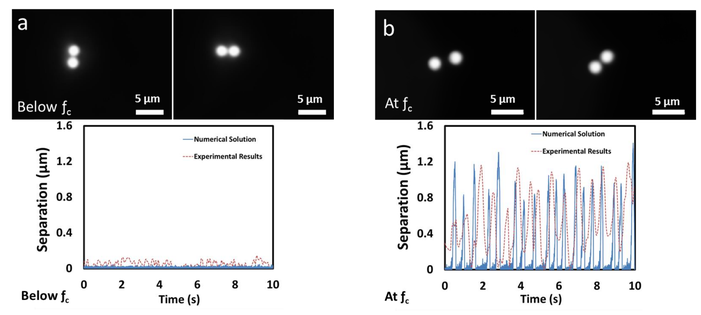
Separation vs. time for a micro-particle with χ=0.163 and η=2.5 mPa s. Critical frequency solved analytically and numerically for different viscosities.

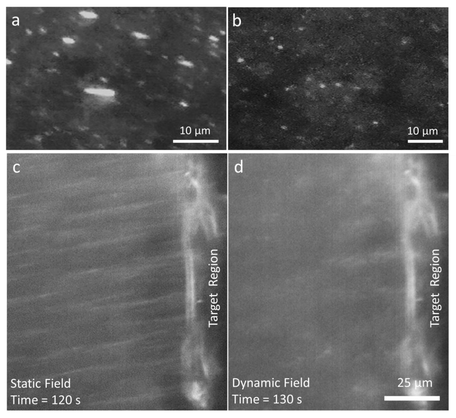


Critical frequency is the frequency that gives the highest separation possible between particles. This non-linear response shows the importance of tailoring the field characteristics to the specific system

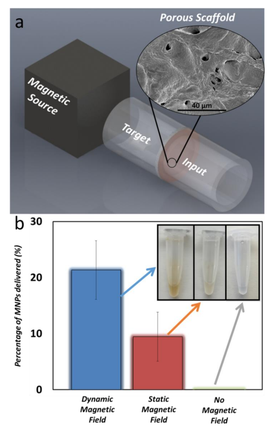


Experimental Results



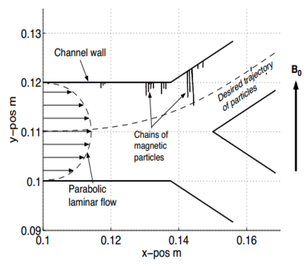


Experimental dark-field micrographs of 150 nm magnetic particles under rotating fields of (a) 0.1 and (b) 2.5 Hz frequency. (c) Significant aggregation in 150 nm magnetic nanoparticles under static fields after 2 min. The magnetic field gradient was 60 Oe/cm, and the applied magnetic field was 165 Oe. (d) Dynamic fields studied here immediately de-aggregate nanoparticles while maintaining 165 and 60 Oe/cm.



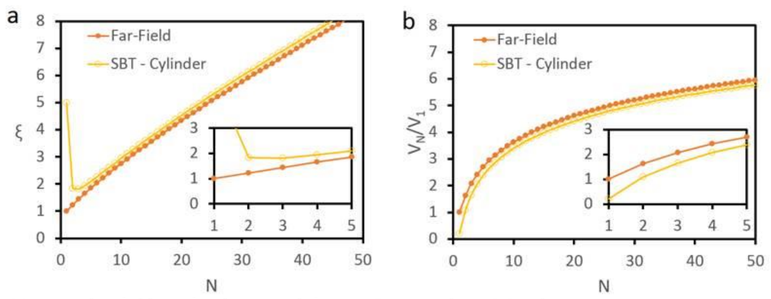
(a) Schematics of the in situ setup. (b) Percentage of delivered 150 nm MNPs after applying dynamic and static magnetic field for 1 h.

Magnetic Transport *in situ*



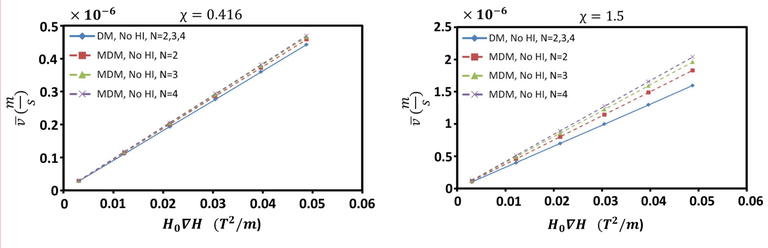
Capillary systems are designed in order to study the ability of guiding magnetic particles through a porous membrane in the presence of a flow. Observations from both experiments and simulations show that aggregates of magnetic particles are moving faster compared to single particles.

Far Field Hydrodynamics vs. Slender Body Theory

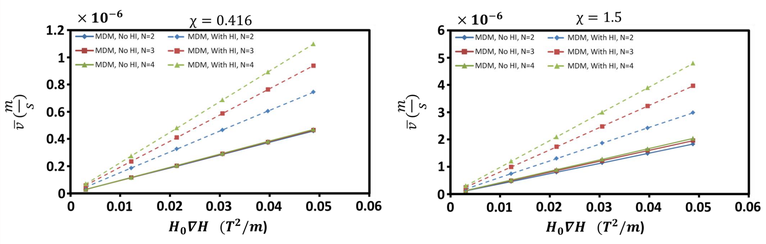


Numerical Simulations without Brownian Motion:

Mutual Dipolar Model vs. Dipolar Model

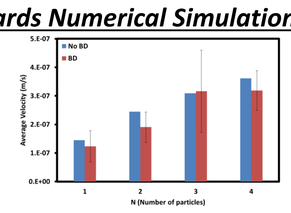


Mutual Dipolar Model with Hydrodynamics Interaction vs. Simple Stokes

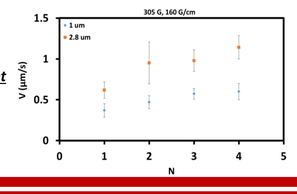


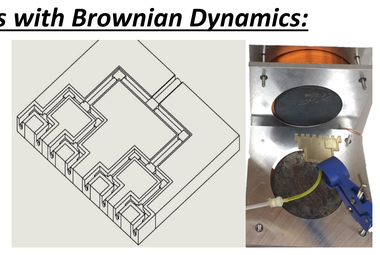
Towards Numerical Simulations with Brownian Dynamics:

Theory



Experiment





Mobility of different size particle chains in the presence of a magnetic field gradient in a quiescent flow. Experimental setup for studying the transportation of magnetic nanoparticles through a designed capillary system.

Conclusions

Here we suggest a method for using magnetic particles in drug delivery applications. In order to elucidate the interaction of magnetic particles, computational models were developed. It is seen that these models are effective in describing the experimental observations. Both experiments and numerical simulations verify that aggregates of magnetic particles move faster compared to single particles. Finally, *in vitro* studies are designed to be done in order to prove the ability of controlling magnetic particles in biological systems.

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