

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

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## Motivation

Cancer is one of the most acute health issues in our society nowadays and almost 30% of all deaths each year are due to cancer [1]. In the past decades, chemotherapy has been the only way to treat cancer but there are issues related to this method such as side effects and not being able to destroy all cancer (neoplastic) cells [2]. It is depicted that drug-laden magnetic nanoparticles can improve the efficiency of the drug delivery [3]. These particles can be guided through human's body by using a magnetic source which has a strong field and also a high field gradient.

However, Using such a source will cause the nanoparticles to form chains and aggregations that are larger than the size of the tumor pores. It is believed that the aggregate sizes are too large to effectively permeate the pores in the tumor cell network. This effect is going to lower the efficiency of drug delivery. In this work, we demonstrate that by using advanced field functions for our magnetic fields we can manipulate the field and gradient to break up this magnetic nanoparticles.

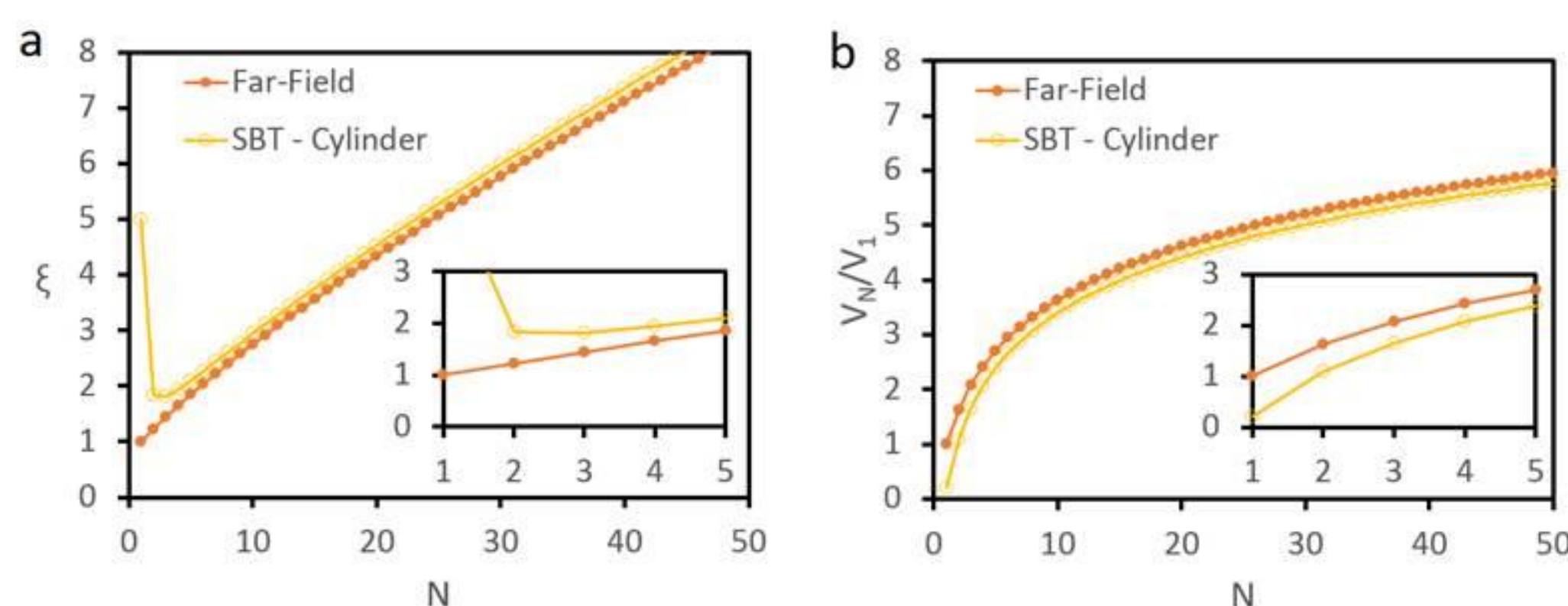
## Project Goal

The goal of this project is to study the fundamental principles (dynamics) in using magnetic fields for accurately guiding agglomerations of magnetic nanoparticles in targeted drug delivery. The innovative technology component of this study is the use of advanced field functions for achieving a higher drug delivery efficiency. In this work, Instead of simple linear magnetic fields that lead to aggregation, dynamic magnetic fields are employed that allow the MNPs to be concentrated locally while utilizing inter-particle force dynamics to continuously drive separation events, thus preventing aggregation.

## Magnetic Transport *in situ*

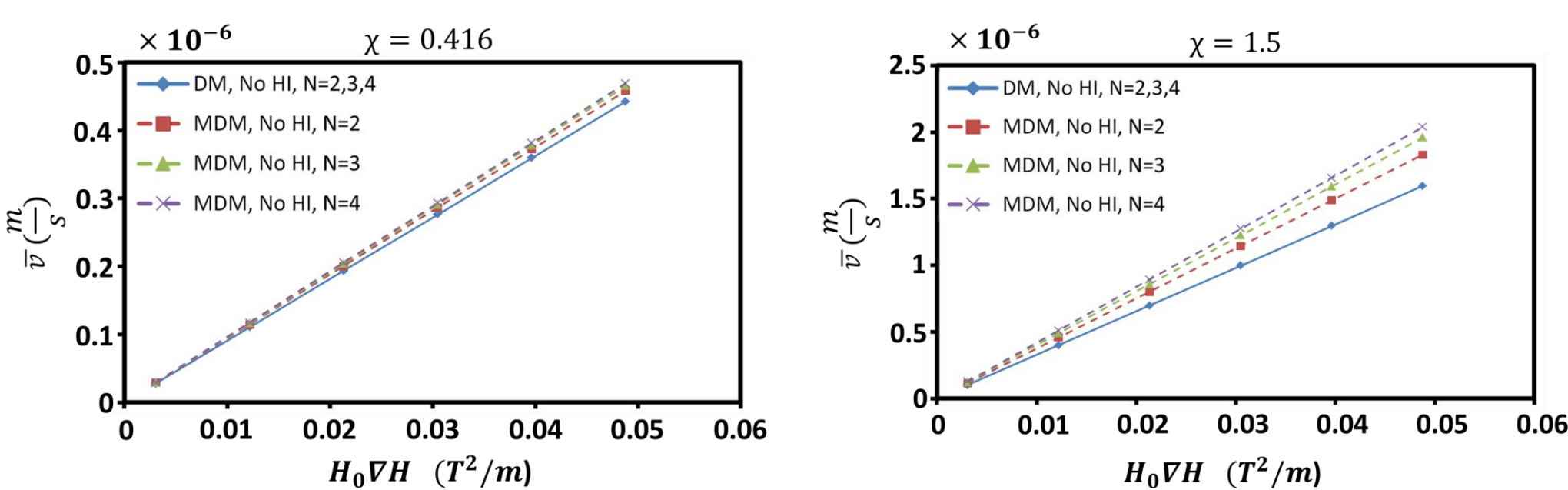
Numerical models have been developed to capture the effects of hydrodynamics and magnetic interactions between particles. It is observed that at high magnetization for particles, accurate description of magnetic interactions is necessary but compared to hydrodynamics interactions these effects are minimal and can be neglected.

### Far Field Hydrodynamics vs. Slender Body Theory

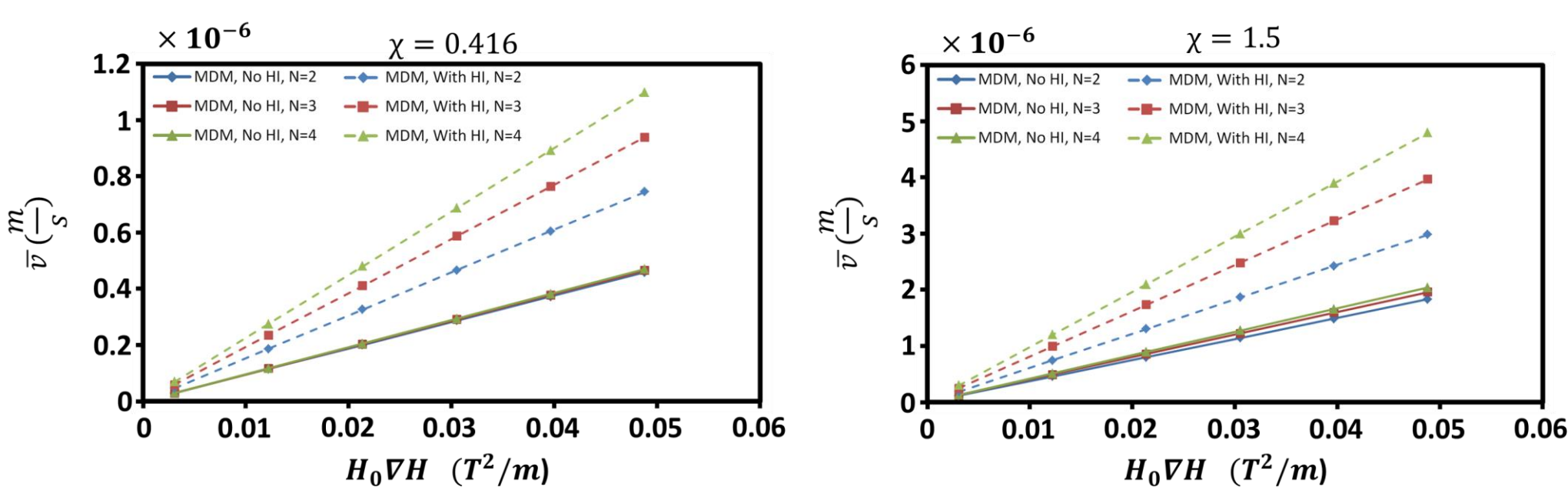


### Numerical Simulations without Brownian Motion:

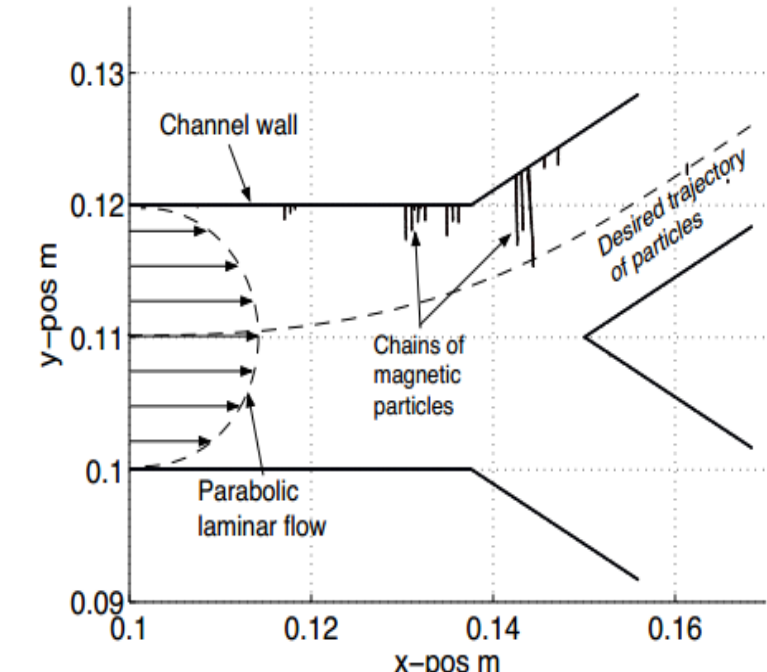
#### Mutual Dipolar Model vs. Dipolar Model



#### Mutual Dipolar Model with Hydrodynamics Interaction vs. Simple Stokes



### Toward magnetic transport in capillary systems:

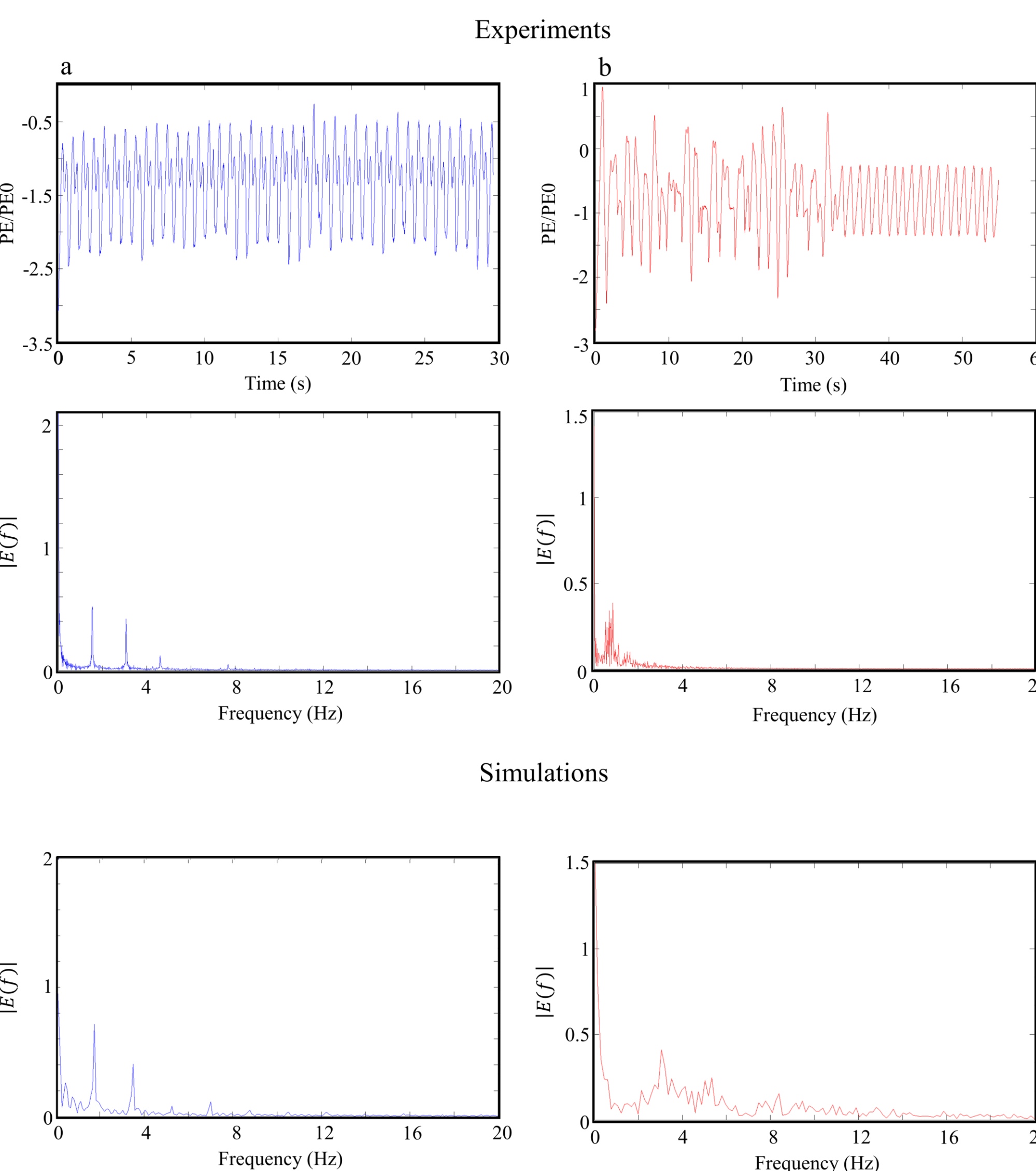
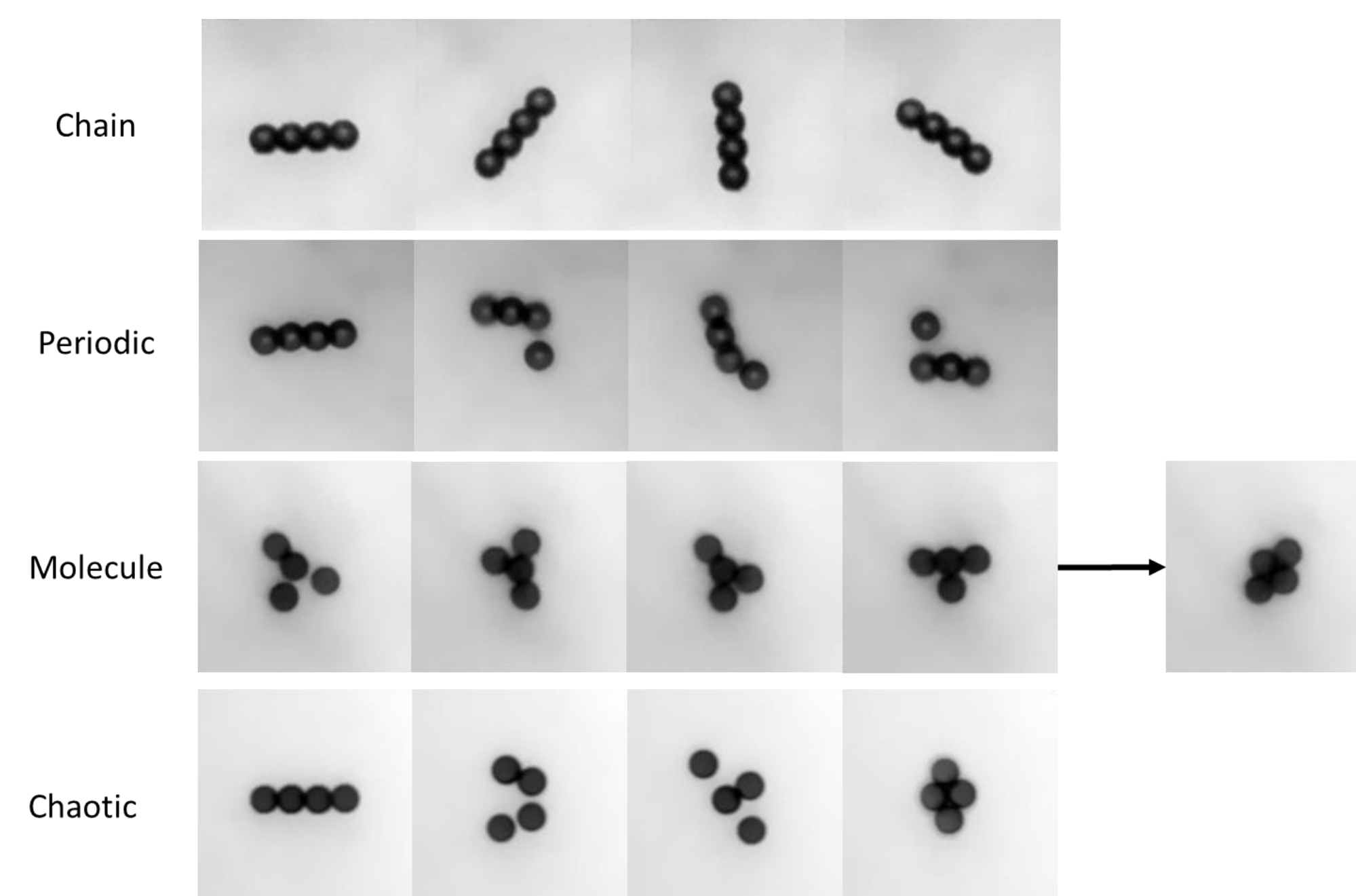


Capillary systems are designed in order to study the ability of guiding magnetic particles through a porous membrane in the presence of a flow. Observations from both experiments and simulations show that aggregates of magnetic particles are moving faster compared to single particles but these aggregations are not favorable for drug delivery purposes since they have limited movement in porous tissue.

## Different Regimes

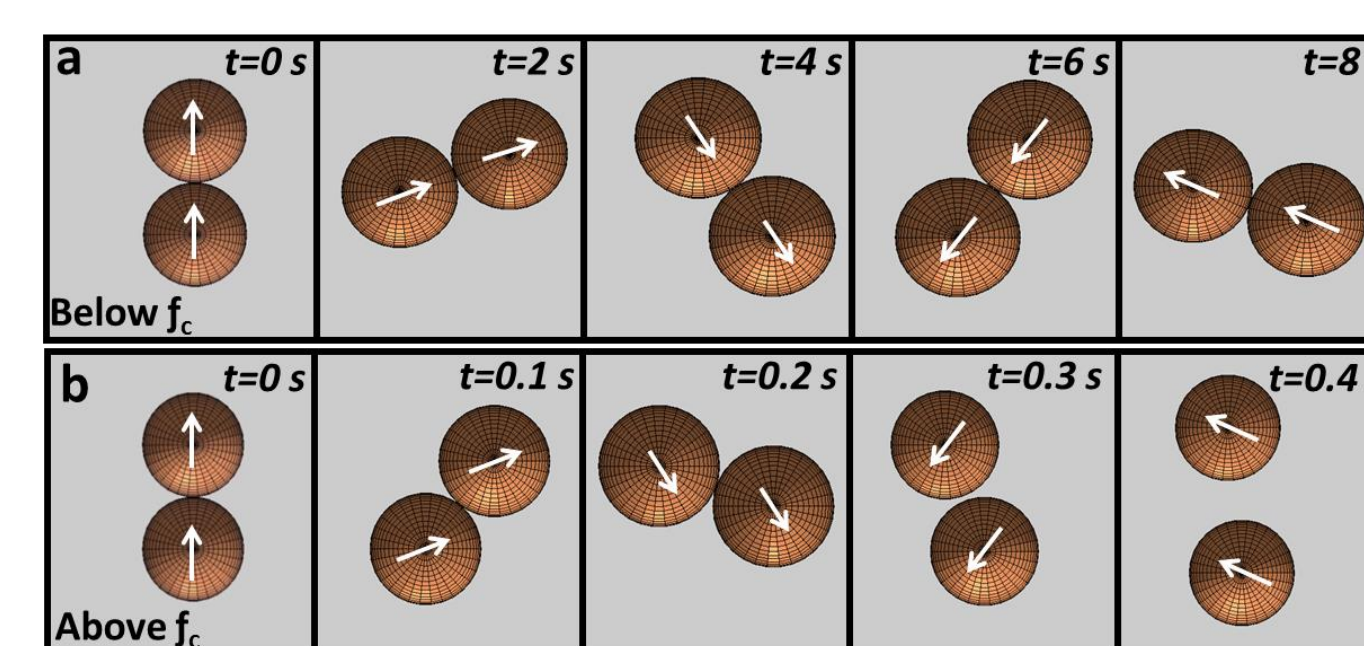
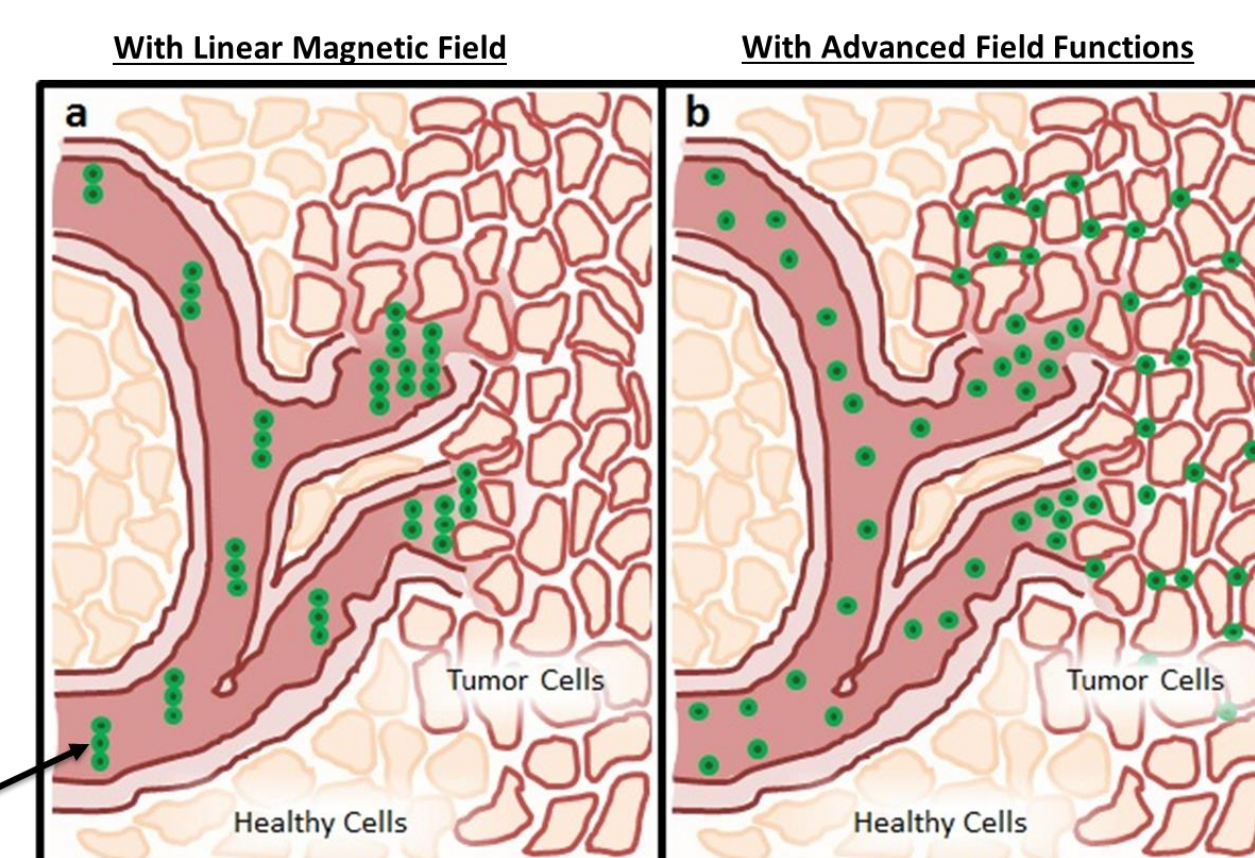
Behavior of magnetic colloidal suspensions in the presence of dynamic magnetic fields is very complex but in the simplest classification there exist 3 regimes. Below a critical frequency where particles stay chained and act as a rigid body. Above a critical frequency where chains break into smaller fragments 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.

In Collaboration with Hamed Abdi & Craig Maloney

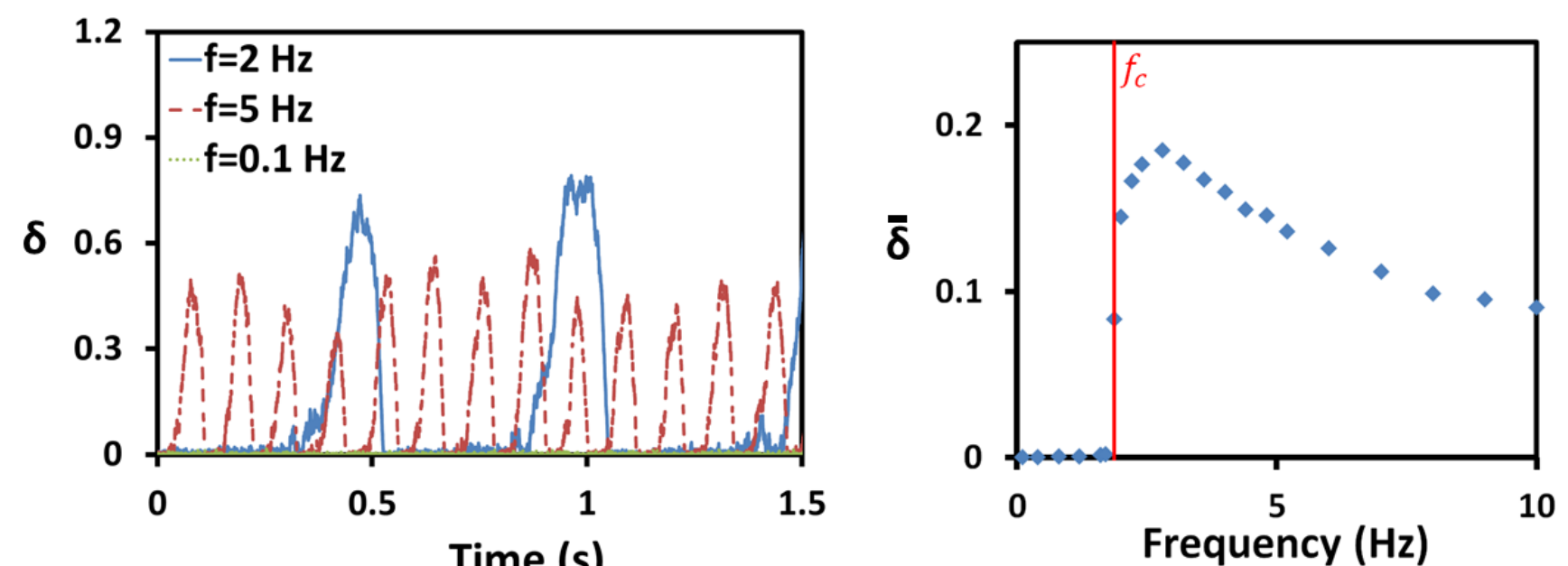


## Toward Magnetic Targeting

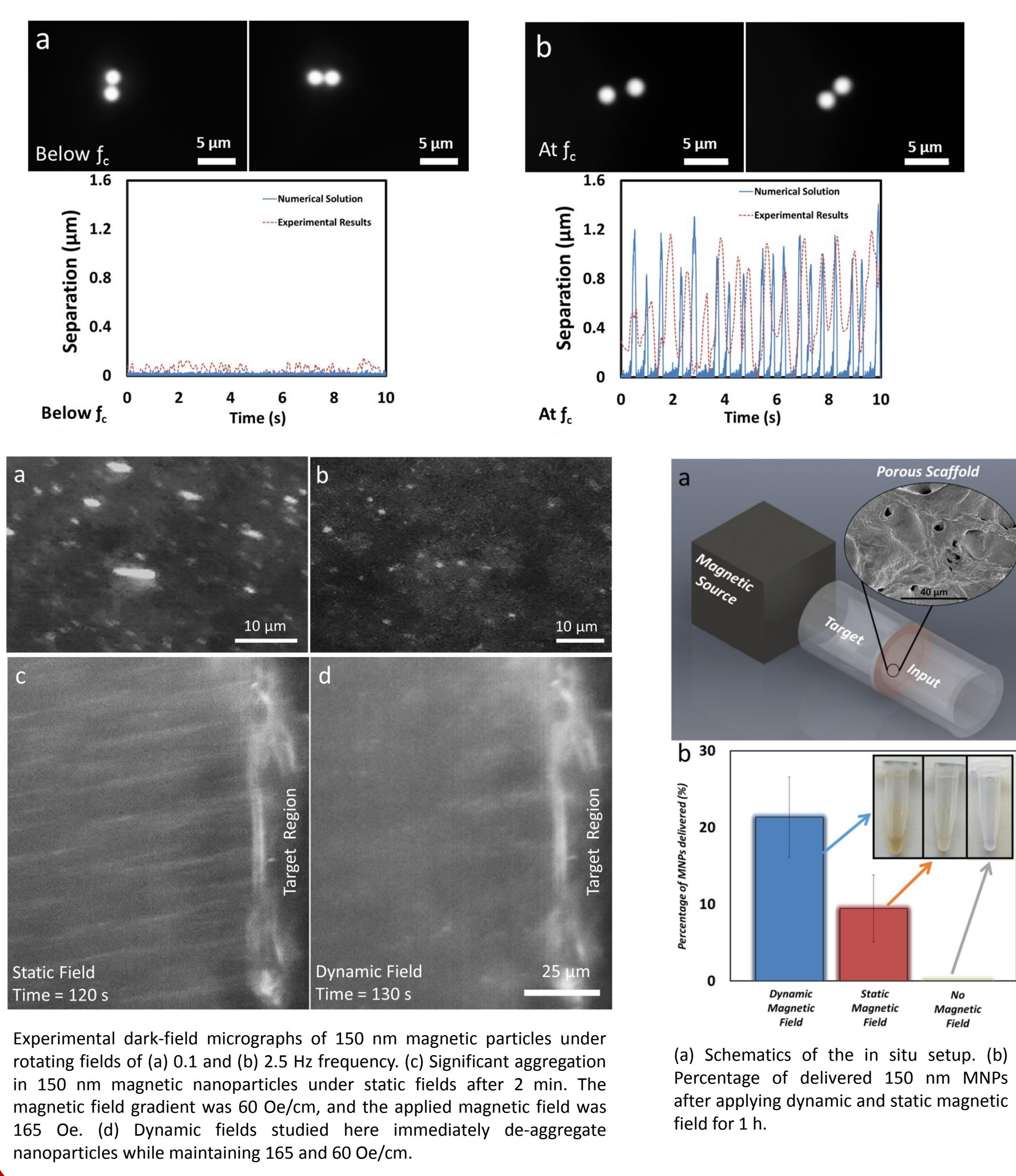
Instead of simple linear magnetic fields that lead to aggregation, we employ advanced field functions (in this case rotating magnetic fields that allow the MNPs to be concentrated locally while utilizing inter-particle force dynamics to continuously drive separation events, thus preventing aggregation.



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



## Conclusions

Here we suggest a method for using drug laden magnetic nanoparticles under applied rotating magnetic fields. This technique is going to resolve the issue of particles aggregating during magnetic targeting that has been previously observed. By implementing advanced field functions like rotating magnetic fields a dynamic energy landscape causes the particle aggregates to break up so that they may enter the smallest capillaries such as tumor pores. *In-vitro* experiments show that penetration of the MNPs is enhanced by 2-fold with dynamic magnetic fields compared to static fields. This result suggests that dynamic fields could indeed provide a large enhancement to the efficiency of magnetic targeting.