CHAPTER-6.0

HYDRODYNAMICS OF SUPERPARAMAGNETIC IRON OXIDE NANOPARTICLES
6.1 BRIEF INTRODUCTION

The flow behavior of iron oxide nanoparticles becomes critical in many applications. For instance, for effective targeting, it is imperative that the applied magnetic field is to be strong enough to hold the nanoparticles in place against the advective and drag forces of blood flow. Since, these studies will be supportive for practical application during clinical trials and treatment. Such mechanisms were investigated using simulation and Ex-vivo experiments.

The problem is still highly complex; while it is understood that large applied fields on small particles with high saturation magnetization will retain the particles well for good targeting, a clear, quantitative picture of the relative effects of external field strength, particle size, and its saturation magnetization is yet to be determined. A hydrodynamics set-up has been developed as discussed in chapter.3 under section 3.3 and visualized the hydrodynamic behavior of iron oxide nanoparticles in the absence and presence of external magnetic fields. The effects of chelating the nanoparticles with citric acid are also studied. MATLAB® software was used to determine the area of nanoparticles occupied in that region under various conditions and the results are discussed in this chapter.

6.2 RESULTS AND DISCUSSION

Magnetite nanoparticles synthesized were found to have a mean size of 6.5 nm diameter in particle size analysis, and a narrow size distribution. In our earlier study [107], these nanoparticles have been found to be spherical in shape, with a saturation magnetization of ~ 75 emu/g. When chelated with citric acid, there was neither a significant change in size nor a significant reduction in magnetization (~ 71 emu/g). All hydrodynamics experiments were carried out in water medium. Figure 6.1a depicts the flow patterns observed for a velocity of 1 cm/s with an injection of 0.2 ml of ferrofluid containing 0.8 μl of magnetite nanoparticles at time t = 0 in the absence of an external magnetic field.
Figure: 6.1. CMOS images of magnetite nanoparticles in the region of visualization for the three systems studied. (a) magnetite nanoparticles, (b) nanoparticles chelated with citric acid, and (c) nanoparticles in the presence of a magnetic field (at 1 mm distance)

It is apparent that the attractive magnetic dipole interactions between the nanoparticles are not strong enough to withstand the advective shear forces arising from flow. To obtain a quantitative estimate of the hydrodynamics, the obtained CMOS images were processed in MATLAB to first convert them into BW images, with the particles (threshold = 0.7) displayed in white color in a black background. Then, the area of the region occupied by the particles was estimated, and this is presented in Table 6.1 as a function of time, after normalization (area at time t = 0 is taken as 100%). It is seen that, relative to the area occupied by the nanoparticles at t = 0, only 35% is occupied at 10 minutes. Thus, the majority of the particles are washed away.
An applied external magnetic field significantly enhances the attractive forces between the nanoparticles as well as with the magnet placed at the bottom of the tube. Thus, most of the nanoparticles are attracted to the wall of the tube closest to the magnet and are retained for longer durations. Yet, it is also seen that the hydrodynamic forces are able to gradually remove the retained nanoparticles. This is seen in Figure 6.1c.

Table 6.1. Relative (%) of area in the field of visualization occupied by the nanoparticles

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>w/o field</th>
<th>Field @ 1 mm distance [Magnetite]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Magnetite</td>
<td>Magnetite – citric acid</td>
</tr>
<tr>
<td>0</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>2</td>
<td>76</td>
<td>76</td>
</tr>
<tr>
<td>4</td>
<td>66</td>
<td>58</td>
</tr>
<tr>
<td>6</td>
<td>65</td>
<td>45</td>
</tr>
<tr>
<td>8</td>
<td>50</td>
<td>34</td>
</tr>
<tr>
<td>10</td>
<td>35</td>
<td>18</td>
</tr>
</tbody>
</table>

Chelating the nanoparticles with citric acid disperses the nanoparticles more effectively due to stabilization arising from electrostatic repulsion between the citrate anions decorating the surface of the nanoparticles. This further reduces the attractive dipole interactions, and works in conjunction with the advective shear forces to enhance the removal of the nanoparticles from the region of visualization, as indicated from the time-lapse images in Figure 6.1b. After 10 minutes, only 18% of the original area is occupied by the nanoparticles, indicating nearly doubling of the wash away. The flow behavior was monitored with velocity of 1 cm/s, flow rates below this value is not sufficient to undergo the required studies using the existing setup.
6.2.1 Effect of magnetic field and citric acid on aggregates

Figure 6.2 (a and b) shows the effect of two different magnetic field strength [1 mm and 20 mm distance] and citric acid on aggregates. The average magnetic field exposed on nanoparticles inside the tubing is around 340 G at 1 mm distance and 40 G at 20 mm distance.

![Figure 6.2](image)

Figure: 6.2. (a) Effect of magnetic field on aggregates at 1 mm distance and citric acid, (b) 20 mm distance and citric acid

The magnetic fields were carefully chosen to observe the effect of aggregates in hydrodynamics; similar magnetic fields were chosen to investigate suspension stability of iron oxide nanoparticles under static condition. The shedding of aggregates strongly relies on flow rate of medium and effect of magnetic field. Alicia et. al. reported similar studies with two magnetic fields [1507 G and 3015 G], with Reynolds number ranging from 100 to 1000 at gradual steps [68]. We have studied this mechanism with Reynolds number: 33 [Laminar flow]. These parameters can be varied to analyze the behavior of aggregates for various applications. Figure 6.3 shows the aggregate level at
intermediate stage at 6 mins and final stage at 10 mins. This data indicates that distance of magnetic field at 20 mm has capacity to hold the particles for longer duration with the effect of citric acid than the effect at 1 mm distance. This part indicates that magnetic field at a very closer distance may disrupt the stretching of aggregates and initiates shedding of particles.

Figure: 6.3. Aggregate levels for (a) SP1 and SP1-C, (b) SP1 with magnetic field at 1 mm distance and effect of citric acid and (c) SP1 with magnetic field at 1 mm distance and effect of citric acid.

It is clearly observed in the Figure 6.2 (a) that the aggregates were stretched due to repulsive force between nanoparticles caused by citric acid and shedding occurs in faster rate than samples without the effect of citric acid.

The washaway of aggregates are rapid compared to previous case at 1 mm distance. The effect of magnetic field is reduced by increasing the distance up to 20 mm from the aggregates as shown in Figure 6.2 (b), but with the effect of citric acid the aggregate level at 6 mins and 10 mins are larger compared to samples without the effect of citric acid at 20 mm distance. The studies clearly indicate that effect of citric acid and magnetic field plays key role in controlling the magnetic nanoparticle fluidic systems under different conditions. Several reports have investigated the flow studies of magnetic nano particles that is
procure from industries. In this study, we have synthesized magnetic nanoparticles with tunable magnetic properties and analyzed the behaviour in hydrodynamic condition. Most of the studies involved with magnetic drug targeting require spherical magnetic nanoparticles for effective transport in fluid medium, but it is also important to undergo the flow studies with different morphology, particle size, and magnetization to acquire a broad picture for effective magnetic drug targeting.

6.3 CONCLUSION

An experimental setup has been developed for studying the hydrodynamics of superparamagnetic iron oxide nanoparticles. Experimental results were obtained to validate the ability of the test setup in order to effectively capture the hydrodynamic behavior of the nanoparticles. A preliminary quantitative analysis has been developed for determining the fraction of the nanoparticles retained in the visualization region. Taken together, a quantitative picture would emerge relating the relevant structural parameters of the nanoparticles and the process parameters such as flow velocity and magnetic field strength with the hydrodynamic behavior of the magnetic nanoparticles. A systematic study is also proposed to analyze the flow behavior of magnetic nanoparticles under different flow rates similar to human veins and capillaries.

Further, in the following chapter the same setup has been used to study the release of magnetite nanoparticles from electrospun nanofiber under flow conditions. The following chapter specifically focuses on the release mechanism magnetite nanoparticles embedded in biocompatible nanofiber. Polymeric sandwich model is developed to shield the nanofiber sample consisting of magnetite nanoparticles during flow conditions. This model can be highly useful for controlled release of magnetite nanoparticles for real-time clinical applications. The factors for flow studies specified in this chapter were utilized to identify the suitable flow conditions to undergo the nanoparticle release studies and the outcomes were reported in the in the following chapter.