Particle dynamics in magneto-fluidic microsystems

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PARTICLE DYNAMICS IN

MAGNETO-FLUIDIC MICROSYSTEMS

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SUMMARY

PARTICLE DYNAMICS IN MAGNETO-FLUIDIC MICROSYSTEMS

The trend in microfluidics and lab-on-a-chip is to miniaturize and integrate many functions in a single chip, while achieving a high functional performance. To reach fast processing and a high sensitivity at the same time, recent lab-on-a-chip approaches use high-surface-area elements together with micro-scaled detection techniques. One of the related challenges is to solve transport limitations within microfluidic processes. Using superparamagnetic particles as actuation vehicles in lab-on-a-chip systems appears to be a promising approach. However, the full control of particle motion in direction and velocity remains complicated. In this thesis we investigate the interactions between neighboring particles, surrounding fluid and nearby walls. We found that these effects highly influence the dynamics of the particle loaded fluid.

First, particle dynamics in open fluid volumes was studied using an experimental setup containing a sub-microliter fluid volume surrounded by four miniaturized electromagnets for particle actuation. On the basis of optical velocity measurements, the induced motion of single particles and ordered particle chains was analyzed. Experiments on single particles revealed velocities that highly vary between particles and also the average measured velocity was found to deviate from theoretical predictions, which we attributed to non-uniform magnetic particle properties. Equations for the influence of particle chain formation on magnetization and hydrodynamics have been established, and show an increasing logarithmic dependence of the velocity on the chain length. Experimental studies on rotating particle chains showed transient regimes for the chain shape including chain rupture events, which could be reconstructed with a mechanistic pin-joint model based on magnetic and hydrodynamic inter-particle forces.
Furthermore, within the spatial confinement of a microsystem, we studied the interactions between particles, fluid, and nearby walls. An experimental setup was built providing a constant magnetic force on individual particles dispersed in a microchannel. The hydrodynamic particle interactions appeared to generate unforeseen self-organization phenomena. Superparamagnetic particles aligned on the channel axis successively organize towards a stable poly-twin system, which could be explained by a 1-dimensional model based on the superposition of particle induced flow profiles along the channel axis. In addition, particles traveling close to a channel wall show complex rotation transitions that result in s-shaped trajectories while focusing towards the channel center, which could be explained by local self-induced fluid velocity gradients within the channel. Additionally, using micro-scaled flux guides to locally generate high magnetic field gradients, the particles reached amplified velocities and could be forced and controlled in circular pathways within the channels.

On system level, the fluid driving efficiency of the observed particle configurations were evaluated with numerical simulation models. Axially aligned particles appear to be very efficient for fluid pumping through channels. The efficiency can be tuned by the channel-to-particle radius and the particle spacing. The off-axis counter-rotating particles appear to enhance near-surface mixing. Integrated fluid actuation by magnetic particles is demonstrated in micro pore systems, where pressure-driven techniques are ineffective for the exchange of fluids. Our experimental investigations and theoretical analyses lead to a better understanding of particle dynamics, in order to improve the functional performance of magneto-fluidic microsystems.
Chapter 1

INTRODUCTION

Miniaturizing traditional large-scale fluidic devices to microfluidic systems poses many challenges. How could systems be designed, fabricated and used? Starting from the fields of microfluidics, lab-on-a-chip and biosensor systems, this chapter will discuss a selection of important miniaturization aspects. The challenges faced for integrated fluidic actuation are discussed, and the use of superparamagnetic particles in lab-on-a-chip systems is introduced.
1.1. **MICROFLUIDICS AND BIOSENSOR SYSTEMS**

Microfluidics is a rapidly evolving area that has received a lot of interest in the last decades [1]. Miniaturizing fluidics to micro-scaled systems with dimensions in the order of tens of micrometers offers advantages such as fast reaction rates and reduction in required fluid volumes [2], which is of interest for fields such as chemical and molecular analysis. Early examples for fluid manipulation on the micro-scale are miniaturized capillary systems for chromatography and electrophoresis [3]. These devices showed the possibilities of integrating fluid manipulation and processing on a single microfluidic chip of only a few square centimeters, now commonly referred as lab-on-a-chip (LOC) systems. With these first successful proofs of concept, various other technologies were combined with microfluidics to develop new applications, for instance in the field of micro-electro-mechanical systems (MEMS) [4]. On the other hand, researchers in biochemistry, molecular biology and medical diagnostics also showed interest to develop microfluidic systems for detecting bio-materials on-chip [1].

1.1.1. **LAB-ON-A-CHIP BIOSENSORS**

In medical diagnostics, lab-on-a-chip devices have the potential to bring point-of-care (POC) tests to the patient [2]. One of the most successful examples of such a device is the glucose meter for diabetes patients. With a hand-held device diabetes patients are now able to measure their glucose level in a full-blood finger-prick sample [5]. Glucose in full blood is present in relatively high concentrations (mmol/l), which can be detected without any advanced fluidic manipulation steps. However, other markers in the blood are typically present at much lower concentrations. For example, life threatening cardiac conditions can be revealed by the detection of troponin proteins, but this requires a detection technology that is able to measure concentrations down to pmol/l [6]. Many examples can be found in literature that demonstrate technological concepts for sensitive detection, but commercial and ready-to-market lab-on-a-chip devices are still not widely available [1]. Testing of markers in body fluids at picomolar concentrations is still performed in large central laboratories using large and expensive instruments that require large sample volumes and long process times.

1.1.2. **HIGH SURFACE AREA SUPPORTS**

Bio-analytical systems often contain high-surface-area elements with a high binding capacity allowing for high reaction rates. For instance, porous hybridization micro arrays allow for the analysis of a large collection of different target analyte simultaneously. Examples of such systems are shown in Figure 1.1 [7]. The capture surface can consist of
porous aluminium-oxide \cite{7,8}, silicon or a polymer \cite{9}. In order to allow for efficient binding, the fluid needs to be actuated through the high surface-area elements. Miniaturized detection of molecules at low concentrations demands for an accelerated and a precise control of the reaction conditions \cite{10}. For these systems, the key challenge is to integrate fluidic actuation which is suited for small samples of complex biological fluids.

Figure 1.1 An example of a porous hybridization micro array. The overview (panel a) shows the different spots for different sorts of target analyte \cite{7}. Panel b) shows a detail of a single spot, consisting of a porous structure made with MEMS technology \cite{9}.

1.2. FLUID ACTUATION IN MICROSYSTEMS

This section will discuss several challenges for fluid flow on the micro-scale. The Navier-Stokes equations theoretically describe fluid motion \cite{11}. The set of equations consist of several parts. The first part describes acceleration terms arising from Newton’s second law. It assumes that the fluid stress is induced by the summation of viscous effects (velocity gradients) and pressure gradients. The fluid is assumed to be incompressible and Newtonian (stress versus strain is linear). On the micro-scale the surface-to-volume ratio is high and surface forces dominate over volume forces. Inertial forces are negligible, reducing the Navier-Stokes equations to the so-called Stokes equations \cite{11}:

\[
\nabla p = \eta_f \nabla^2 v_f + F_{\text{ext}} \\
\nabla \cdot v_f = 0
\]

1-1

Here, \( p \) is the applied pressure, \( v_f \) is the fluid velocity, \( \eta_f \) is the fluid viscosity and \( F_{\text{ext}} \) any external applied body force. To illustrate the consequences of downscaling a fluidic
system and the related surface-to-volume effects, a simple Poiseuille pipe-flow is considered.

![Figure 1.2](image)

Figure 1.2 Two different fluid flows around passive obstacles, where the design is the same but only scaled. The macro regime (panel a), diameter 0.1m and fluid velocity 0.1m/s, \( Re = 10^4 \) shows a turbulent flow with vortices after the obstacles. In the micro regime (panel b), diameter 0.1mm and fluid velocity 100\( \mu \)m/s, \( Re = 0.01 \) no visible disturbances are introduced after the obstacles because of the laminar flow conditions.

In Figure 1.2, two similar looking simulation results of channels with circular shaped obstructions are shown; however they differ in their scale. Panel a) shows a fluid flow with a velocity of 0.1m/s in a big channel of 0.1m in diameter. The fluid shows very irregular patterns and exhibits a chaotic velocity profile after the circular obstructions, including vortices that indicate turbulence. In panel b), the channel is scaled down to 100\( \mu \)m in diameter with a fluid flow velocity of 100\( \mu \)m/s. In this micro-scaled example, the flow is laminar and regular as indicated by the parallel streamlines. The fluid velocity displays the same profile after the obstructions. The shown transition from turbulent to laminar flows is one of the most characteristic fluidic phenomena introduced by downscaling. In a highly laminar regime, viscous forces dominate over inertial forces. This is described by the dimensionless Reynolds number \( Re \), according to \[12\]:

\[
Re = \frac{\rho_f v_f I}{\eta_f}
\]

Here, \( \rho_f \) is the fluid density. For a given fluid, the Reynolds number is mainly dependent on the characteristic flow velocity \( v_f \) and a typical length-unit \( I \) such as the channel diameter. Going from a turbulent \( (Re \gg 1) \) to a laminar regime \( (Re \ll 1) \) is a very smooth transformation process without a clear transition point. Moreover, local fluid dynamics can be influenced by the shape of the volume or integrated obstacles and is not included in the Reynolds number describing the overall fluid behavior \[12\]. As a consequence of a high surface-to-volume, this is of special concern for micro-scaled fluidic systems.
1.2.1. FLUID PUMPING IN LAMINAR FLOW CONDITIONS

In traditional macro-scaled systems, a fluid flow through pipes is generally induced by a pressure gradient over the channel. Pressure-driven system examples also exist for performing fluid actuation on the micro-scale. Most of these pumps apply external forces on the fluid by means of a moving membrane on one side of the system, which creates the required pressure gradient. The membrane can be actuated by for example piezoelectric, electrostatic, pneumatic or even shape-memory alloy drivers \(^{13}\). For a pressure-driven system, the average fluid velocity \(v_{f,\text{avg}}\) is calculated using the Hagen-Poiseuille law (derived from the Navier-Stokes equations), according to \(^{11}\):

\[
v_{f,\text{avg}} = \frac{\Delta p R^2}{8 \eta L}
\]

As shown in equation 1-3, linearly downsizing the channel radius \(R\) results in a quadratic increase of the required pressure drop \(\Delta p\) in order to maintain the same fluid velocity; therefore a pressure-driven system does not scale favorably for micro-sized fluidic systems. Another problem arises by the laminar flow conditions that generate a parabolic velocity profile, where the fluid near the walls moves very slowly. To illustrate these effects, a simple microchannel with length \(L = 0.1\text{mm}\) and \(R = 5\mu\text{m}\) is considered as shown in Figure 1.3, assuming no molecular diffusion (see section 1.2.2).

![Figure 1.3](image_url)  
**Figure 1.3** A flow of two different fluids (top and bottom) entering from the left of a microchannel \((L = 0.1\text{mm}\) and \(R = 5\mu\text{m}\)). As shown on the top, replenishment from a colorized to a transparent fluid is obstructed by the laminar flow conditions.

Initially the channel is filled with a colored fluid (black). The top part of the microchannel is then replenished over time by a transparent fluid (white) from left to right. First of all, the laminar flow condition (in this case, \(Re=1\)) results in only axial motion of the fluid and therefore obstructs mixing between the colored (bottom) and transparent (top) fluid. Moreover, the local no-slip conditions obstruct the fluid elements near the wall to move along with the main flow, which therefore experience a much higher residence time compared to the elements in the center of a fluid volume. In the absence of molecular diffusion, fluidic replenishment is therefore very difficult to reach, where the laminar flow...
condition creates (unwanted) concentration gradients perpendicular to the main flow direction.

A trend in microfluidic pumping is to perform volume-based fluid forcing. Instead of applying a pressure gradient that arises by applying a force on only one surface of the fluid, external forces can be applied on the whole fluid volume. Volume force based techniques receive attention because of their advantageous downscaling properties over the more traditional pressure-driven systems. For example, actuation by electrophoresis (electrokinetic migration of charged elements due to an applied potential difference) is widely used for DNA separation in gels \cite{14}. Electro-osmotic fluid actuation is based on the surface charge that develops when a fluid comes in contact with a solid wall, which forms an electric double layer. The counter-ions in the working fluid can be set into motion by applying an electric field parallel to the channel. The flow rates by EOF are not very high, but micro-sized electrodes can be efficiently used for local fluid actuation near channel walls, as shown in Figure 1.4. However, most electrokinetic systems require high currents or high potential differences that may affect a biological sample, for example generate unwanted electro-osmosis of cells. As the electrokinetic fluid flow is dependent on the ionic content of the fluid, the performance is highly sample dependent and difficult to control \cite{13}.

![Figure 1.4](image.png)

Figure 1.4 A home-built microfluidic pump based on electro-osmotic forcing. Two different colored fluids are introduced at the two different inlets on the top and bottom of the picture. The approach of volume forcing prevents a depletion layer as was observed in Figure 1.3, but the two fluids remain separated due to the laminar flow conditions.

1.2.2. MIXING IN LAMINAR CONDITIONS

In microchannels the high surface-to-volume ratio hinders the generation of fluid flow and also complicates the mixing or replenishing of fluid elements near no-slip boundaries. In practice, fluids have to undergo a sequence of stretching and folding to increase the interfacial area of the fluids, known as the Bakers transformation. In macro-scaled systems
with high Reynolds numbers, this mechanism is self-induced by the turbulent motion creating vortices that arise by velocity and pressure variations in space and time \[^{15}\]. The stretching and folding of fluid elements is obstructed in miniaturized systems by the strong viscous effects. The mixing mechanism that is still present in Microsystems is molecular diffusion. The time \( t \) required to overcome a certain distance \( l \) with a fluidic substance with molecular diffusivity \( D \) can be calculated with \[^{14}]^{16}]^{17}:

\[
t = \frac{l^2}{2D}
\]

1-4

Diffusion limited transport is very slow and highly dependent on the temperature and substance properties. For instance, spreading proteins or DNA molecules \((D=10^{-11}\text{m}^2/\text{s})\) over only 1mm with molecular diffusion already takes hours of time. Therefore, in laminar flow, mixing has to be artificially enhanced by passive or active elements such as obstructions or external transient volume forces. Passive approaches require long mixing lengths. For more efficient mixing, multi-layered fluid manipulation elements are required, but these require even higher pressure drops.

The challenge in the micro-scale is to create efficient mixing everywhere in the volume and especially at locations where convection is normally obstructed \[^{18}\]. Similar to the field of microfluidic pumping, active mixers based on volume forcing are therefore preferred in micro-scaled systems. One way to characterize these mixers is to compare the values of induced convective fluid motion over the diffusion rates, which are quantified by the Péclet number \[^{17}]^{19}:

\[
P_{p} = \frac{v_{f} l}{D}
\]

1-5

The Péclet number shows that in addition to long waiting times also long transport lengths need to be overcome if mixing is based on molecular diffusion only. For instance, if a two-flow system such as in Figure 1.3 and Figure 1.4 needs to mix over a channel diameter of 100\(\mu\)m, a flow-velocity of 0.1mm/s requires a mixing length of at least 50mm to generate a homogeneous mixture of the two different fluids.
1.3. **MICRO-SIZED PARTICLES IN FLUIDIC SYSTEMS**

The above discussion on fluid motion on the micro-scale shows that the use of high surface-to-volume ratio elements hampers efficient fluidic actuation. Instead of passive and solid elements, also mobile supports can be used in microfluidic systems by using bio-activated micrometer-sized particles \[^{[20]}\]. Fluidic actuation benefits from the mobility of the particles, while preserving a high surface-to-volume ratio on the particles within the system. For example, using particles with a size of 1μm in a 0.1% volume concentration offers a total available reactive surface of 30mm\(^2\) within a sample of only 1μl ( = 1mm\(^3\)). There are a variety of surface modifications available on these particles, which introduce multiple functionalities to a single microfluidic design.

Moreover, the detection sensitivity in biological systems is increased by the mobility of the particles due to a higher efficiency of interactions between samples and reagents. For instance, the Biosite Triage\(^{®}\) system based on lateral flow assay technologies uses a mixture of reagents with mobile nanoparticles \[^{[21]}\]. The immunoassay is driven by passive capillary forces that are tuned by hydrophobic and hydrophilic areas within a micro-capillary system. The device determines different protein levels at picomolar concentrations from a full blood sample within 15 minutes, performing the following sequence of steps: sample addition, filtering, reagent dispersion, antibody / analyte incubation, capillary transport and detection.

1.3.1. **SUPERPARAMAGNETIC PARTICLES AS ACTUATION VEHICLES**

In addition to the benefits of a high total surface area, particles can also be mobilized by means of external applied forces. Superparamagnetic particles are only magnetized in the presence of an applied magnetic field, and are therefore controllable in their motion direction and velocity \[^{[22],[23],[24]}\]. In combination with their self-assembly to larger agglomerates, the particles appear to be efficient for fluidic actuation and analyte manipulation in many ways, which could address the challenges on fluidic actuation in laminar regimes. As biological materials are essentially non-magnetic, magnetic particles can be applied in complex samples with high reproducibility \[^{[25]}\].

As an example, the company Spinomix (a spin-off company of the Swiss Federal Institute of Technology in Lausanne) developed their MagPhase platform with superparamagnetic particles as mobile antibody supports and mobile carriers within a microfluidic assay system \[^{[26],[27]}\]. The key element of the technology is that the particles are manipulated in a specific way to form a dynamic sweeping structure, allowing optimal exposure and enhanced mixing with the surrounding liquid medium as shown in Figure 1.5. The binding
reaction of the analyte is enhanced by the particle motion induced by the external magnetic actuation.

![Image](image.jpg)

Figure 1.5 The concept of using functionalized particles as mobile carriers in assays a). Panel b) shows the Spinomix MagPhase microfluidic chip that allows for 4 process steps in parallel. By magnetic actuation, a dynamic cloud of magnetic particles is efficiently moved through the sample to enhance mixing and catching performance on chip c).

Several other examples can be found that use superparamagnetic particles in lab-on-a-chip systems. Functions such as sample filtering, analyte transport, mixing, labeling and detection have been demonstrated using magnetic particles. Lehmann et al. have used magnetic particles as micro-carriers in a droplet to purify DNA on chip. Todd et al. used magnetic particles for purely catching and up-concentration steps before detection in micro-capillaries. Bruls et al. employed the dynamic control of magnetic particles to shorten process times, enhancing assay control and integration of the total test. Other approaches use large-volume preparation steps together with micro-scaled analysis techniques to reach fast processing and a high sensitivity at the same time.

1.3.2. PARTICLE DYNAMICS AND INTERACTIONS

A full control of particle motion in direction and velocity is an important challenge for optimal system performance. However, research on magnetic particle dynamics in microfluidic environments has often followed a single particle approach, or has described the particle ensemble as a continuum. Both approaches do not take into account any interaction effects that could occur between particles and their surroundings. The complete set of particle forces and interaction effects could highly influence the dynamics of the particle loaded fluid. In addition to magnetic actuation and interaction forces, the hydrodynamic interaction effects between neighboring particles, surrounding fluid and nearby walls have to be considered over longer distances.

The Mason number originates from early magnetorheological studies and it compares the ratio of hydrodynamic and magnetic forces within a system. Magnetorheological systems
having the same value of Mason number will behave similarly regardless of the actual geometrical dimensions \[33\]. The Mason number can be used for describing particle translations, rotations and interaction effects, according to the general formulation:

\[
Ma = \frac{\text{hydrodynamic (interaction) forces}}{\text{magnetic (interaction) forces}}
\]

The above dimensionless number \( Ma \) will be used together with the other dimensionless numbers given in this chapter (such as \( Re \) and \( Pe \)) to characterize the typical regimes of our investigations on “particle dynamics in magneto-fluidic Microsystems”.

1.4. THESIS OUTLINE

This thesis provides a series of experimental investigations and theoretical analyses by which we explore the dynamics and interactions of superparamagnetic particles. Studies are performed on different scales, from open fluid volumes towards confined system geometries wherein the particle radius and channel radius are in the same range.

Chapter 2 describes the properties of superparamagnetic particles, including their material composition and magnetic behavior, along with a first discussion on magnetic and hydrodynamic forces acting on the particles. Chapter 3 deals with the design and fabrication of several magneto-fluidic Microsystems that are used in our studies on multiple scales. To understand the influence of local magnetic and hydrodynamic particle interactions, we subsequently describe in Chapter 4 our experiments and analyses performed on the particle dynamics effects in open fluid volumes, such as velocity measurements, the influence of chain formation and related manipulation possibilities.

Our further study on the dynamics of particles confined in microchannels is described in Chapter 5. We focus on new interaction phenomena that are analyzed with the help of established analytical and numerical models, and discuss a more application oriented system with soft-magnetic flux-guides for local particle manipulation. Chapter 6 discusses our numerical studies in a more system level approach, where the fluid driving efficiency of the observed particle configurations is evaluated on the basis of fluid actuation and near surface mixing. All conclusions are listed in Chapter 7, which is finalized by an outlook containing new research questions for further studies.
Chapter 2

SUPERPARAMAGNETIC PARTICLES: PROPERTIES AND FORCES

Superparamagnetic particles are studied for the application in lab-on-a-chip systems as multifunctional manipulation vehicles. This chapter describes the properties of these particles, with respect to their material composition, magnetic response, shape and size. First, the literature on the dynamics of superparamagnetic particles will be reviewed. Next, the magnetic and hydrodynamic particle-particle interactions are discussed for a two-particle configuration by analytical calculations and numerical simulations. These serve as the starting point for our research on the particle dynamics and interplay effects in the subsequent chapters.
2.1. SUPERPARAMAGNETIC PARTICLE PROPERTIES

Superparamagnetic particles usually consist of a large ensemble of nano-sized ferromagnetic grains in the order of 5-15 nm, embedded in a non-magnetic matrix. The magnetic material is generally an iron-oxide (such as magnetite, Fe₃O₄) because of a high saturation magnetization. The non-magnetic matrix is often a polymer such as polystyrene (PS), in order to evenly distribute and encapsulate the grains to prevent further chemical reactions and degradation. The polymer shell ensures that the superparamagnetic particles are compatible with biological materials. Two examples of particles are given in Figure 2.1. The smaller Dynal MyOne superparamagnetic particles show a very narrow distribution in size with a mean diameter of 1.05 μm [34], but show a high surface roughness. The Spherotech superparamagnetic particles are bigger with a mean diameter of 22.3 μm, but their surface is much more smooth (in relative and absolute way) [35].

![Figure 2.1](image-url)

Figure 2.1 Two examples of superparamagnetic particles that are used in upcoming sections and chapters: a) A picture (SEM) of the Dynal MyOne 1 μm particles [34] and b) a microscope image of the Spherotech 22 μm magnetic particles [35].

2.1.1. THE NATURE OF SUPERPARAMAGNETISM

Magnetism in materials is only occurring when the orientations of microscopic magnetic dipole moments are aligned. These dipole moments are induced by running currents that are present in electron-conducting wires or, on a more local scale, due to freely spinning and revolving electrons around a nucleus. The process of magnetic alignment is called magnetization and can be categorized in several classes. The most common class of magnetism is called ferromagnetism, which occurs in materials that have a very strong internal magnetic interaction that results in a net attractive magnetic moment even after the removal of the external applied magnetic field. This is shown in the hysteresis curve in
Figure 2.2 (left panel). In case of diamagnetism, the magnetic dipoles tend to oppose the applied magnetic field alignment, which is generally a very weak effect and loses its opposing magnetization after removal of the applied magnetic field. In the class of paramagnetism, the dipoles will tend to align with the applied field, resulting in a net magnetic moment in the direction of the applied field. However, the dipoles do not interact with one another and are randomly oriented in the absence of an external field due to thermal agitation, resulting in zero net magnetic moment as shown in Figure 2.2 (right panel), where the magnetization curve intersects with the origin.

Figure 2.2 Two magnetization curves for a ferromagnetic material (left) and a (super) paramagnetic material (right). Ferromagnetism shows hysteresis resulting in a remanent magnetic moment $M_{\text{rem}}$ after removal of the external applied magnetic field. Pure (super) paramagnetism shows no hysteresis.

Superparamagnetism is a special form of magnetism with characteristics from both ferromagnetism and paramagnetism, which is present in the particles shown in Figure 2.1 due to their unique material composition. The in essence ferromagnetic grains within the particle are generally so small, so that these can be considered to be individual magnetic domains. Every grain has a preferred state of magnetization along its easy-axis, but its magnetization can easily flip because of thermal fluctuations $^{[36]}$. The time between two flips is called the Néel relaxation time. Due to the high number of grains in the particle with independently and fast flipping magnetizations, the net magnetic moment of the particle is zero in the absence of an applied magnetic field. However, if an external magnetic field is applied, the grains within the superparamagnetic particle preferably magnetize along the direction of the applied magnetic field. A net magnetic moment is created, similar to the mechanism in paramagnetism. The magnetic susceptibility of a superparamagnetic material is however much higher.
2.1.2. Magnetization of Superparamagnetic Particles

At low magnetic fields, the magnetization $M$ of a superparamagnetic particle is assumed to increase as function of the external applied magnetic field $H$ as shown in Figure 2.2 (right panel). The increase of the particle magnetization is characterized by the proportionality factor called the effective magnetic susceptibility $\chi_p$. The magnetic moment per particle $m_p$ is calculated with the use of $V_p$ as the volume of the particle, according to $^{22}[37]$:

$$m_p = V_p \chi_p \vec{H}$$  \hspace{1cm} (2-1)

Equation 2-1 assumes that the particle magnetization completely vanishes after removal of the field as in the case of perfect paramagnetic behavior. The magnetic susceptibility of the particle $\chi_p$ is determined from the linear part of the magnetization curve as shown in Figure 2.2 (right panel). Although $\chi_p$ is a dimensionless material property, it takes into account the effect of demagnetizing fields. In fact, $H$ in equation 2-1 is the applied magnetic field and does not account for any of these effects. For any given object shape, free surface poles induce a demagnetizing field $H_d$ that opposes to the applied magnetic field, according to:

$$\vec{H}_d = -N_d \vec{M}$$  \hspace{1cm} (2-2)

Here, $N_d$ is the demagnetization factor. This factor or related demagnetizing fields are difficult to calculate or measure directly. Demagnetization effects are therefore related to the already defined effective susceptibility $\chi_p$ and the intrinsic material susceptibility $\chi_{mat}$ (excluding demagnetizing effects), according to $^{36}[37]$:

$$N_d = \frac{\chi_{mat} - \chi_p}{\chi_{mat} \cdot \chi_p}$$  \hspace{1cm} (2-3)

The demagnetization factor $N_d$ can have different values for different object orientations, which is called shape or magnetic anisotropy. For an object being magnetized in its long direction, the free surface poles are very few ($N_d$ approaches 0). However, if the same object is magnetized perpendicular to its long direction, demagnetization effects are much more present ($N_d$ approaches 1). For a perfectly spherical particle, the demagnetization factor $N_d$ is exactly 1/3 and not dependent on its orientation. However,
superparamagnetic particles could show anisotropy effects by for instance an elliptical shape or irregular grain distribution within the particle itself (also see Chapter 4).

2.1.3. PARTICLE MAGNETIZATION MEASUREMENTS

The two different types of magnetic particles given in Figure 2.1 will be examined in this section on their magnetic response by means of VSM measurements. The vibrating sample magnetometer (VSM) has become a widely used instrument for determining moment of magnetization as function of an external applied magnetic field [36][38] and is also used for studying the magnetic properties of the superparamagnetic particles.

For both curves, the magnetic moment per particle \( m_p \) was calculated by dividing the measured magnetic moment to the number of particles present in the sample. In order to detect any hysteresis or remanent magnetization, the particles were fixed in their orientation by freezing the sample during the measurement \( (T = 269 \text{K}) \). The number of particles within the sample was estimated from a density measurement. Although very dilute samples of particle solutions (0.1% volume) were used, the effect of magnetic particle-to-particle interactions that occur during the measurement is unknown. Moreover, a VSM measurement also conceals a variation in magnetic properties between individual particles, which could be polydisperse in magnetic content (shape, size, volume) [39]. The presented values may therefore not reflect the exact single particle properties, but will nevertheless give reasonable starting values for further analysis.

From the VSM measurements presented in Figure 2.3 for the Dynal MyOne particles [34], the average particle susceptibility is calculated to be \( \chi_p = 1.52 \) and is in agreement with the values found by Fonnum et al [38]. Compared to other commercially available particles this value is relatively high, mainly owing to a high iron-oxide content [34][38]. No hysteresis or remanent magnetization could be found in the measurement and is therefore assumed to be smaller than the VSM accuracy, resulting in close-to-perfect superparamagnetic behavior. However, recent rotation studies on the same particles revealed that there may exist a very small remanent moment of about 1% of \( m_{sat} \) [40]. The VSM measurement performed on the superparamagnetic particles from Spherotech, presented in Figure 2.4, shows a high magnetic moment per particle as a consequence of its size (average diameter 22.3\,\mu m). However, the calculated effective susceptibility of these particles is only \( \chi_p = 0.06 \), which is a result of the low iron-oxide content distributed only within a thin layer just below the particle surface [35]. A small remanent magnetic moment is measured at about \( 2 \cdot 10^{-13} \text{Am}^2 \), which is 2.5% of the saturation magnetization of \( 8 \cdot 10^{-12} \text{Am}^2 \).
Figure 2.3 Results of a VSM measurement of a dilute sample of the Dynal MyOne particles\textsuperscript{[34]}. The magnetization is back-calculated to the magnetic moment per particle. The measurement curve shows no hysteresis or remanent moment at all.

Figure 2.4 The results of the VSM measurement of a dilute sample of the Spherotech superparamagnetic particles\textsuperscript{[35]}. The magnetization is higher for one particle due to a larger volume, but the calculated susceptibility is lower because of a low iron content.
2.2. **Forces on a Single Particle**

This section will describe analytical models found in current literature to calculate the magnetic particle velocity as a function of its properties. In the following case, the particle is actuated in an open fluid volume and is not influenced by the motion of other particles. As a start, the magnetic force is calculated by the following integral over the volume \( V_p \) of the particle \([41]\):

\[
\vec{F}_m = \mu_0 \int (\vec{M} \cdot \nabla) \vec{H} \, dV_p
\]

Parameter \( \mu_0 \) is the magnetic permeability of vacuum. The magnetic force is called a gradient force, which includes the gradient of the applied magnetic field multiplied by the magnetization of the particle. The applied magnetic field \( H \) is altered by the presence of the particle. Moreover, as the applied magnetic field needs to vary in space to apply a force on a particle; the magnetization of the particle will also vary in space. It is however difficult to calculate the exact result; therefore literature often introduces a simplified form of equation 2-4 using an ideal magnetic point-dipole approximation, according to \([42]\):

\[
\vec{F}_m = \mu_0 (\vec{m}_p \cdot \nabla) \vec{H}
\]

The magnetic moment of the particle \( m_p \) is calculated with equation 2-1, where demagnetization effects are taken into account by using the effective susceptibility \( \chi_p \) out of the VSM measurements instead of using a material susceptibility \( \chi_{mat} \). Note that the effects of a varying magnetic field \( H \) in space and the influence of the presence of the particle are still not taken into account by this point-dipole approximation. Next to this approach, literature also often uses the symbol \( B \) to indicate the applied magnetic field instead of \( H \) as in equation 2-5, which is actually the most correct way to express the value for the applied magnetic field. However the units of \( H \) in \([A/m]\) are often not so meaningful over the units of \( B \) in \([T]\) that are usually used in literature. Note that if \( B \) is used to indicate the value of the applied magnetic field, it should be calculated as \( B = \mu_0 H \) as will be used in this thesis also \([41]\).

The magnetic attraction force given in equation 2-5 generates particle motion in a fluid, which causes a counteracting hydrodynamic drag force. For a single particle without surface roughness, the drag force \( F_d \) in open volumes is calculated with Stokes’ law \([11]\):

\[
\vec{F}_d = -6 \pi \eta_f r_p \vec{v}_p
\]
The dynamic viscosity of the surrounding fluid is given by $\eta_f$. The hydrodynamic radius of the particle is assumed to be equal to the material radius $r_p$ of the particle. Equations 2-5 and 2-6 can now be combined to calculate the velocity of the particle $v_p$ [42]:

$$v_p = \frac{\chi_p r_p^2}{9 \mu_0 \eta_f} \vec{B}^2$$ \hspace{1cm} 2-7

Important to note is that the magnetic force on the particle $F_m$ is proportional to particle magnetic susceptibility $\chi_p$, as already explained in section 2.1.3. However, in case of high fields the particle magnetization is no longer dependent on the applied field as shown in the VSM measurements in Figure 2.3 and Figure 2.4 and becomes constant in a saturated state expressed as $m_{p,sat}$. In this case of a moving particle in magnetic saturation, the velocity of the particle $v_p$ is calculated as [43]:

$$v_p = \frac{2 \overline{m}_{p,sat} r_p^2}{9 \eta_f} \vec{B}$$ \hspace{1cm} 2-8

Both equations calculate only the terminal velocity of the particle, which is allowed as the time to reach terminal velocity is negligible ($\tau < 10^{-6}$ s). Important to note is that the force direction is given by the gradient direction of the applied magnetic field. Both equations are valid if gravitational or buoyancy forces can be neglected (also see section 4.1.1). For both variants of micrometer-sized particles discussed in section 2.1, Brownian motion leads to superimposed velocities in random directions below 100nm/s and can also be neglected [39].

### 2.3. MAGNETIC PARTICLE-PARTICLE INTERACTIONS

In case of particle ensembles, the magnetic force as described by equation 2-5 is not the only actuation forces present, as the superparamagnetic particles also interact by inter-particle forces. Therefore, the magnetic interaction forces between two particles aligned in their magnetization direction are analyzed here (for sketch of this model see the inset of Figure 2.5). The magnetic interaction force $F_{m,\text{int}}$ on a particle caused by another particle at interspacing $s$ can be calculated using a first order point-dipole approximation [31] [37]:
As further analysis will involve full body to body calculations, the interspacing $s$ between two particles is defined as the distance between the two adjacent particles surfaces (instead of the core-to-core distance that is generally used). The above equation shows that this force is a strong but short-range interaction which falls off very strongly as a function of the particle interspacing ($1/s^6$). The magnetic interaction force can be attractive in the case the two particle structure is aligned with the field lines, or can be repulsive in the case the two particle structure is oriented perpendicular to the field lines.

The above equation assumes a homogeneous magnetization of the particles that is independent of the particle interspacing and it assumes the particles to be point-dipoles, which may be a source of error if the particles are close. As an example, the magnetic interaction forces between two particles are calculated as a function of the surface-to-surface interspacing under the action of an applied field of $B = 10\text{mT}$, aligned with the particle couple easy axis. The closest distance calculated for the two particles is given by twice the polymer shell thickness given by the manufacturer, which is $100\text{nm}$ for the Dynal MyOne particles$^{[34]}$ and $1\mu\text{m}$ for the Spherotech particles$^{[35]}$.

Several curves for different magnetic interaction force calculations are plotted in Figure 2.5 for the case of the Dynal MyOne particles ($r_p = 0.5\mu\text{m}$ and $\chi_p = 1.52$). In the simplest case, a homogeneous particle magnetization $m_p$ is assumed calculated with equation 2-1, where the interaction force is calculated with equation 2-9. However, if a particle approaches another particle, the magnetic field is changed, which influences the magnetization of the other particle and gets enhanced. This effect is difficult to calculate analytically and has to be analyzed numerically (see for the full model description section 5.2). Taking this effect into account, $m_p$ in equation 2-9 will be larger as a function of the particles interspacing and therefore the magnetic interaction force calculated by this way is 24% higher.

Moreover, nearby particles do not exert their interaction forces from and to only the centers of the particles as is assumed by the point dipole approximation, but these are distributed from out and within the whole volumes of the particles. This effect can also be analyzed numerically by integrating the force over the whole particles volume (see section 5.2 for the full model description), which shows even more amplified magnetic particle interaction forces. For the particles in close contact, this way of calculating the magnetic particle interaction forces can give an increase of 64%. However, this way of calculation is
rather complex to calculate and not easy to implement in models and is highly dependent on the assumed shell thickness of the particles. In fact, the calculation results are within 1% agreement after a particle interspacing of $s = 2.09r_p$; therefore the point-dipole approximation given in equation 2-9 may be used if particles are separated at least one diameter away from each other. The same analysis has been performed for the Spherotech particles ($r_p = 11.2\mu m$ and $\chi_p = 0.06$). Their low susceptibility and thicker shell both hampers a magnetization enhancement by the presence of each other and the curves practically overlap (<5%). The full 3d-simulation curve for these particles is shown in Figure 2.6.

![Figure 2.5 Simulation results of different magnetic interaction force calculations for two Dynal particles in a magnetic field intensity of 10mT. A point di-pole approximation calculates a 64% lower interaction force at the point where the particles are in contact ($s = 0.1\mu m$, twice the shell thickness).](image)

**2.4. HYDRODYNAMIC PARTICLE-PARTICLE INTERACTIONS**

In addition to magnetic interactions, particles in motion also influence each other by hydrodynamic effects. The (in this case magnetic) driving force on a particle is balanced by viscous forces from the fluid as given in equation 2-6, which transfers momentum from the moving particle to the fluid. In the case of nearby particles, this momentum will also affect their motion, similar to the case of magnetic interactions. An axi-symmetric fluid
dynamics simulation model (for full description see section 5.2) has been used to investigate the hydrodynamic interaction forces between two nearby particles with the same settings as the magnetic particle interaction analysis. Now, two Spherotech particles with \( r_p = 11.2 \mu m \) are positioned in a quiescent open fluid (no external flow) at an interspacing \( s \), which both experience an actuation force of \( F_m = 1.33 \times 10^{-11} N \) as a consequence of an external applied magnetic field with \( B = 10 \text{mT} \) and \( \nabla B^2 = 0.1 \text{T}^2/m \).

![Figure 2.6](image)

Figure 2.6 A comparison of the magnetic and hydrodynamic particle-particle interaction forces for two Spherotech particles. Hydrodynamic interactions between particles in close proximity are not as strong as the magnetic interactions, but will already dominate at an interspacing \( s = 1.18 r_p \).

Figure 2.6 shows the simulation results as the hydrodynamic particle-particle interaction force \( F_{d,int} \) as function of the particles interspacing, together with the previously calculated magnetic particle-particle interaction force \( F_{m,int} \). The hydrodynamic interactions between particles in close proximity are not as strong as the magnetic interactions. However, if the particle interspacing increases the hydrodynamic interaction forces starts to dominate over the magnetic interaction forces because of the slower decline. In this case of the Spherotech particles the point of transition is calculated at a particle interspacing \( s = 1.18 r_p \), where both interactions exert a force of \( F_{m,int} = F_{d,int} = 2.81 \times 10^{-12} N \) on each particle. Furthermore, hydrodynamic interaction forces work in the same direction as the common motion axis of both particles, where magnetic particle-particle interactions can be attractive or repulsive depending on their orientation with the magnetic field.
2.5. **DISCUSSION**

First calculations show that superparamagnetic particles in open or confined fluid volumes are heavily influenced by different particle-to-particle interactions and were studied with different calculation methods. Magnetic particle-particle interactions calculated by using a dipole-approximation can differ up to 1.64 times to the case of full numerical simulations. Simulations on the hydrodynamic particle-particle interactions show that the initially weaker hydrodynamic interaction forces start to dominate over the magnetic interaction forces already at a particle interspacing of only $s = 1.18r_p$. In fact, the longer range hydrodynamic interaction forces will have a much bigger influence on a large particle loaded fluid volume and will therefore mainly receive our attention in the upcoming chapters.

Two types of superparamagnetic particles were selected for experimental purposes. The Dynal MyOne particles are small but show a very high magnetic response ($r_p = 0.5\mu m, \chi_p = 1.52$), which can be used for analyzing the effects of magnetic particle agglomeration, as will be given in Chapter 4 and Chapter 5. The Spherotech particles on the other hand are much bigger but show a much lower magnetic response ($r_p = 22.3\mu m, \chi_p = 0.06$), which are more suitable for analyzing the hydrodynamic momentum transfer to the fluid and back to neighboring particles and will be used in Chapter 5 and Chapter 6.
Chapter 3

DESIGN AND FABRICATION OF MAGNETO-FLUIDIC MICROSYSTEMS

For experimental studies on the particle dynamics in open or confined fluid volumes, several experimental setups were designed and fabricated. Particles can be immersed in large fluid volumes without nearby boundaries, or can be studied in highly confined fluidic environments such as micro-porous structures. In the used implementation the applied magnetic field is highly configurable and can tune the particle behavior on for instance forced formation of typical structures, maximum velocities, or the (transient) direction of motion and alignment. This chapter discusses several aspects of the design and fabrication of magneto-fluidic microsystems, where the first section will give special attention to excimer-laser-based fabrication.

In condensed form, section 3.1 is in preparation for publication, section 3.2 is published in Microfluidics and Nanofluidics [44], section 3.3 is published in Applied Physics Letters [45] and in Microfluidics and Nanofluidics [46] and section 3.4 is submitted for publication.
3.1. EXCIMER-LASER FABRICATION TECHNIQUES

Microsystems can nowadays be realized using a wide variety of fabrication techniques [47][48][49][50]. In literature, options as conventional lithography and molding are frequently reported, but often require many different steps and expensive master fabrication costs. Single piece fabrication of experimental setups generally prefers rapid prototyping, demanding more direct fabrication methods such as micro milling or laser-based fabrication [51][52]. The micro-scaled components in the experimental setups discussed in this chapter are therefore mainly developed using excimer-laser-based fabrication, which will be discussed in the below sections including several examples.

3.1.1. EXCIMER-LASER BASICS

Traditional lasers continuously heat the work piece locally until its melting point and subsequently eject the melted material by for instance a gas jet. Excimer-lasers however use short pulses of much higher energy densities (typically 1J/cm² per pulse) to entirely vaporize the material. Because the time span of the pulses is short (around 5ns) and much of the energy is removed immediately by the ejected debris, the process is optimal for thermally sensitive materials that do not have a clear and homogeneous melting point or have poor thermal conduction. Most polymers are extremely useful for excimer-laser-based fabrication due to the photo-ablative decomposition that occurs at lower wavelengths (below 300nm). The typical large molecules are broken into smaller fragments, which eject from the surface due to the volume expansion induced by their lower molecular weight [51][53].

![Figure 3.1 Concept of the Optec Micro Master excimer-laser [53]. The beam (10 mJ/cm², 5ns, 300Hz) is directed through a beam shaper to optimize uniformity, an attenuator to set the energy level, and finally through the mask selector and projection lens that both are adjustable in focal distance in order to demagnify and focus the projection image on the substrate.](image)

The beam of an excimer-laser is not concentrated in a focal point but uses projection optics in order to image a user defined mask on the substrate as shown in Figure 3.1 from
left to right. A beam shaper is used to optimize the energy distribution from a Gaussian to a more top-hat profile, by cutting of the edges of the beam and superposing to its mirror side to compensate for the lower energy regions. In order to reduce the energy, an attenuator can be used that uses two symmetric dichromatic mirrors that split off a part of the beam energy as function of its mutual angle to the beam. The mask selector partly blocks the beam to end up with a certain shape such as a square / triangle / circle that can vary in size. The beam finally passes the image projection lens that can demagnify and focus the mask image on the substrate, which is fixed on an x-y motion stage using a vacuum system. For handling and positioning, a camera is installed that enables vision through the same lens. Typical feature sizes can range up to 100’s of micrometers down to a few micrometers, which is mainly limited by the optical resolution of the components and the accuracy of the motion stage\textsuperscript{[53]}.

3.1.2. Depth calibration

The required depth of the structure to fabricate is tuned by the number of shots on a single location. For shallow channels the number of shots is proportional to the acquired depth. However deeper channels will require more shots, as shown in Figure 3.2.

![Figure 3.2](image-url)

Figure 3.2 Measurement of the depth per shot using 10 mJ/cm\(^2\) with a projection image of 100\(\mu\)m by 100\(\mu\)m. At the top of the substrate every shot results in a depth increase of about 0.5 \(\mu\)m, but decreases as the projection image goes out of focus and deposited debris cannot eject and is re-ablated. Error bars are not visible in this scale.
First of all, the debris is hindered to eject away and leaves a layer of material that is ablated over and over again. Secondly, at larger sub-surface distances, the projection image will go out of focus (depth of focus is about 50µm), which lowers the effective beam energy. Refocusing is an option for compensation, but this will expand the channel dimension at the top because of the converging beam due to the low numerical aperture of the projection lens.

3.1.3 APPLYING OVERLAP

Figure 3.3 Schematic representation of ablation process for an excimer-laser applying overlap using a square mask. The top row shows the cross-section and the bottom row is a top view. The numbers in the bottom row indicate the number of shots for each location. The 3 times overlap results in a channel with depth of 3 times the shot depth, and a stair-case shaped start and end.

![Figure 3.3](image.png)

Figure 3.4 The ablation process for creating a reservoir shaped volume in a substrate using overlap in horizontal and vertical direction (top). After 6 x 6 = 36 shots the reservoir is created, which has tilted walls because of the applied overlap. The bottom pictures show two examples of using overlap with a 25µm projection image.

![Figure 3.4](image.png)
Figure 3.3 shows how shapes different than the projection image itself can be fabricated by applying overlap of subsequent pulses. If this method is used, the overlap needs to be optimized in order to minimize transition effects by subsequent projection images, which may leave unablated areas or could generate deep trenches. However, applying overlap will always leave a stair-case shaped start and end of the structure. Overlap can also be applied in two directions if areas larger than the mask size need to be structured, as shown in Figure 3.4. This way, a reservoir shaped volume can be created, which has stair-case shaped walls in all directions. The angle of the walls and step-sizes can be tuned by adjusting the mask dimensions or applying less/more overlap, but can influence the process times dramatically.

3.1.4. LASER FABRICATION EXAMPLES

The possibility of using small and big masks in combination with different demagnification factors, excimer-lasers are able to fabricate micro- and milli-scaled features in one single batch. Figure 3.5 shows two examples used in the microfluidic chips in the next sections. Panel a) shows a very big reservoir of 5mm by 2mm surrounding microchannels of only 50µm in width and depth. Panel b) shows in detail the transition from the big reservoir to a microchannel. The big reservoir has been created using the excimer as a scissor tool, only ablating the circumference of the reservoir. With standard techniques such as drilling, it is often very difficult to get a nicely defined connection between features of different sizes, which appears to be very accurate by excimer-laser fabrication.

![Figure 3.5](image-url) Panel a) shows a microfluidic chip used in section 3.3 with a big “through all” reservoir of 5mm long combined with two microchannels of 50µm by 50µm. Panel b) shows a detail of the transition from the big reservoir to the small microchannel, which is very accurate and smooth.
Printed circuit boards that contain electrode paths are generally made using etching techniques such as silk screen printing, photo-engraving or micro milling. However, these methods are favorable for bulk fabrication, but they lack the fast prototyping required for micro-scaled single-piece fabrication. The excimer-laser can also be used to fabricate similar electrode structures, starting from a base plate with a layer of conductive material sputtered on top such as copper or a multi-layer system such as chromium-gold-titanium, as shown in Figure 3.6. Only a few shots per location are needed to locally remove the conductive layer, which typically measures several tens of nanometers in height.

Figure 3.6 Electrode fabrication with excimer-laser techniques starting with a substrate containing a layer of conductive material. Because of the flexibility in control, very complex structures can be made as shown in panel a), while making an order of magnitude larger interconnects at the same fabrication step, shown in panel b).

Figure 3.7 Lettering (a) and alignment symbols (b) that are made by excimer-laser fabrication. The accuracy for positioning of structures in multiple layers can be reached within 5 μm or better.

Experimental structures in a large batch are often difficult to recognize and need a marking on the micro-scale. Using a homemade procedure, symbols or text can be written on the substrate, which is easily recognizable under the microscope. Moreover,
positioning and alignment are very sensitive jobs for micro-scaled components. The use of markers can simplify these processes and enables to create multi-layer structures that are only limited to the x-y stage accuracy (below 5µm or better), as shown in Figure 3.7.

Figure 3.8 A SEM picture of an array of micro-scaled pillars to increase the macroscopic hydrophobicity of a PDMS substrate. The final array has a size of 1cm² with more than 6·10⁴ features, which are fabricated within an hour using a projection mask containing a 10 by 10 hole array.

Micro-scaled features multiplexed to large arrays can be used to modify the material properties on the macroscopic level. For example, by adding large amounts of micro-sized pillars the hydrophobicity of a material can be increased, as often referred as the “lotus” effect in literature. In Figure 3.8, a PDMS surface is shown that contains micro pillars of 20µm in diameter, height and spacing, multiplexed on a surface of 1cm² containing more than 6·10⁴ features. The pillars are made by molding, where the inverse master substrate (containing an array of 20µm holes) was fabricated with excimer-laser ablation. Instead of using only a single-hole mask, a 10 by 10 array was created as projection mask that shortened the fabrication time to less than one hour, which is only 1% of the time needed for a single-hole mask fabrication process.

First measurements show that the hydrophobicity of the PDMS surfaces is increased. The static contact angle was measured to be 96° for a flat substrate, and 130° for the modified substrate as shown in Figure 3.8. For even better hydrophobicity, a second generation of features of an order of magnitude smaller in size (~2µm) is superposed on top with the same technique, increasing the contact angle to 155°, which is close to a super-hydrophobic material property.
3.2. **SYSTEM 1: ORTHOGONAL FOUR-SOLENOID SETUP**

To investigate particle and chain dynamics in open fluid volumes, the following experimental setup was designed and fabricated. This magnetic particle manipulator consists of a fluid container, surrounded by four miniaturized solenoids to generate a wide variety of magnetic field shapes. Because future miniaturized biosensor applications will generally consume sub-microliter volumes, the magnetic particle manipulator has a closed cylindrical fluid volume with a diameter of 1mm and a depth of 200µm. However small, this set of dimensions enables to study the dynamics of particles with diameters of at most a few micrometers without disturbance from boundaries.

3.2.1. **MAGNETIC SYSTEM DESIGN**

As a first design constraint, the inner diameter of the solenoids was chosen to have the same size as the fluid volume resulting in a diameter of 1mm, in order to suppress the influence of flaring field lines. Within the solenoids, soft iron cores were inserted that were coupled with a surrounding yoke to minimize air gaps and to increase the field intensity in the fluid volume. A solenoid length of 5mm and outer diameter of 2.5mm was experimentally determined to be large enough to force the cores into magnetic saturation. A top view of the final design is shown in Figure 3.9.

![Figure 3.9](image)

Figure 3.9  A top view of the magnetic design of the 4 solenoid setup. Panel a) shows the overview of the setup including the surrounding yoke and inserted cores (1) and the casing to align all components (2). Panel b) shows a detail of the center position where the fluid container is positioned (4) with the surrounding solenoids (3).

In order to optimize the performance of the magnetic system, numerical simulations were carried out in Comsol Multiphysics \[^{[54]}\] to investigate the strength and flexibility of possible...
magnetic fields produced by an orthogonal four-solenoid setup. In the first simulation, only the left solenoid is powered with a low current of 75mA, as shown in Figure 3.10. The maximum magnetic field intensity is 15mT at the border of the fluid volume, as illustrated by the color map (gray scale). The single particle trajectories are calculated with use of equation 2-7 and illustrated by the black arrows. A maximum velocity of 5µm/s is calculated for the Dynal MyOne particles \[34\] with a diameter of 1µm. This magnetic configuration is useful to study the motion of single particle and particle chain velocities, aligned in axial direction.

![Figure 3.10](image)

Figure 3.10  Simulation model of setup 1 applying 75mA on the left solenoid. The left panel shows the field lines and solenoids, where the right panel shows the field shape within the fluid container (gray scale is field intensity [T]). Particles travel towards the solenoid (black arrows), where formed chains will align with the field lines (white lines).

In a second simulation, the left and top solenoids are both powered by a higher current of 130mA as shown in Figure 3.11, generating 39.7mT at maximum. Two neighboring solenoids can be used this way to interpolate the field characteristics between the directions of the solenoids, preserving a particle velocity of 20µm/s. This magnetic configuration can be used to investigate the travel of particle chains perpendicular to its alignment, as the field lines (white lines) are orthogonal to the calculated particle trajectories (black arrows). Moreover, by adjusting the balance between the two currents, intermediate particle chain alignments can be studied.

In the third simulation, every solenoid is powered by a high current of 130mA as shown in Figure 3.12, generating maximum magnetic field intensities of 48.5mT. The particle trajectories show a large variation, with maximum velocities of 40µm/s due to high values of \(\vec{V}B^2\) in the order of 1T²/m. Applying a sinusoidal wave on every solenoid, the calculated vector field can be rotated to create a quasi-chaotic particle motion in the whole volume.
Many more (complex) field variations have been found by similar simulations, which demonstrate the high performance and flexibility of this magnetic particle setup.

![Figure 3.11](image1.png)

**Figure 3.11** Applying 130mA through the left and top solenoid. Calculated particle trajectories (black arrows) are perpendicular to the field lines (white lines).

![Figure 3.12](image2.png)

**Figure 3.12** Simulation model of setup 1 applying 130mA through all solenoids. A complex velocity field is calculated for the particles, which can be rotated with for instance a sinusoidal wave on every solenoid. More complex field variations can be found changing the currents on the separate solenoids.

### 3.2.2. Fabrication and Assembly

The disposable fluid containers as shown in Figure 3.13 on the left are fabricated out of molded polydimethylsiloxane (PDMS). An inversely shaped mold has been created on a silicon wafer that consists of an array of circular posts. A pre-mixture of a silicone elastomer (Sylgard® 184 base) and a curing agent elastomer (Dow Corning®) is poured over the whole wafer and placed in a sandwich curing plate to set the final height of the
containers. After curing, the PDMS slice is peeled from the wafer and laser-cut into individual containers with outer dimensions of 2 mm by 2 mm. BSA (Bovine Serum Albumin) is applied on all walls of the fluid container to increase the hydrophilicity of the PDMS surface (originally highly hydrophobic). To close the containers, glass cover sheets are used that were sawed into the same lateral dimensions. The four solenoids as shown in Figure 3.13 panel b) were constructed using a Ø 100µm bonding wire with hexagonal packing that resulted in 294 windings. These solenoids were checked to withstand the currents used for the simulations and showed a factor 2 higher performance without getting damaged (safety margin for maximum current density $10^6$ A/m$^2$).

Figure 3.13 Integrated components of setup 1. At the left, the fluid container and glass plate is shown. At the right, one of the 4 solenoids is shown made from Ø 100µm bonding wire in hexagonal packing, resulting in 294 windings.

The cores and surrounding yoke are machined out of soft-iron to minimize remanent magnetic fields and checked for tight fitting to minimize air gaps. A four channel home-built current source ($I_{max} = 250$mA) is used to power the solenoids separately. With use of a D/A converter, the current source is controlled with scripts that are written in Matlab.
A casing to assemble all components in the exact position was machined out of aluminium with a very low magnetic permeability to minimize the influence on the magnetic fields. Small insertion pills were used to push the solenoids as close as possible towards the fluidic container. The complete magnetic particle manipulator was mounted on a PCB board to facilitate the handling and to create solid electrical connection points. The complete assembly of the orthogonal four-solenoid setup is shown in Figure 3.14.

3.3. SYSTEM 2: ISODYNAMIC POLE-SHAPE SETUP

In a microchannel system the magnetic particles are in close proximity to no-slip boundaries, which changes the particle motion in terms of direction and velocity compared to the case of particles in an unbound fluid. The effects of this so-called particle confinement are complex and difficult to predict with analytical methods. A setup was built to experimentally study the motion and interplay of superparamagnetic particles in a micro channel under constant magnetic driving force conditions.

3.3.1. MAGNETIC SYSTEM DESIGN

To achieve independent observation of magnetic and hydrodynamic interactions, the magnetic field needs to be shaped according to certain requirements. The magnetic field lines must be oriented perpendicular to the channel axis to magnetize the particles perpendicular to their direction of motion, to have the least correlation with the hydrodynamic interactions in axial direction.

![Diagram of isodynamic force field](image)

Figure 3.15 The concept that produces an isodynamic force field over particles traveling through a micro channel at $x = 0$. The gradient of the magnetic field decreases along the channel (along y-axis from top to bottom), but is compensated by an increasing field amplitude, resulting in a constant particle force proportional to $B^2$. 
To study multiple particle configurations, the main condition is a constant driving force on each particle. Therefore, the value of $\nabla B^2$ has to be constant (see equation 2-7), meaning that the value of the magnetic induction $B$ has to balance with the value of the field gradient $\nabla B$ over the center of the micro channel according to:

$$\nabla B^2 = 2(\vec{\nabla} \cdot \vec{B}) = \text{constant}$$  \hspace{1cm} 3-1

For a gradient having a non-zero value, $B$ becomes a function of the channel axis that we assume as the y-axis of the system. The pole pieces shape illustrated in Figure 3.15 result in a decrease in the magnetic field and an increasing gradient along the centerline of the channel on the y-axis at $x=0$. Because the field lines are horizontal when arriving at the channel axis, only the x-component of $B$ is of influence. By integration of equation 3-1, the required magnetic field $B_x$ over the centerline of the channel can be expressed as:

$$B_x = \sqrt{\nabla B^2 \cdot 2y + B_y^{0=0}}$$  \hspace{1cm} 3-2

The pole pieces are made of high permeability, linear and isotropic material. Hence, there are no tangential components for $B$ at the pole ends and these can therefore be assumed to be equipotential surfaces. With equation 3-2, and $f$ as the ratio between $\nabla B^2$ and $B_y^{0=0}$, the shape of the pole pieces is calculated as:

$$x = \pm \frac{\sin^{-1}(e^{fy} \sin(fx_0))}{f}$$  \hspace{1cm} 3-3

Numerical simulations [54] of the above solution indicated that end-effects have a strong influence on the uniformity and length of the isodynamic force field. An iterative optimization on the tip ends was carried out numerically with equation 3-3 as initial condition, in order to extend the isodynamic force field as much as possible. Optimization resulted in a full coverage of the largest channel dimensions (length 5mm) allowing 10% variation in magnetic force, as shown in Figure 3.17 (dashed line).

### 3.3.2. Fabrication and Assembly

The assembly shown in Figure 3.16 consists of a PVC frame (80mm by 80mm), a polycarbonate (PC) fluidic chip (8mm by 8mm) and a magnetic system with a copper wire solenoid (4cm in width, bonding wire Ø 400µm, 1440 windings) and the two precisely...
shaped soft-magnetic yokes (ARMCO, AK Steel, The Netherlands). In the fluidic chip, a micro channel with square cross section was created by excimer-laser ablation [53]. The chip is exchangeable so that different channel dimensions could be studied, ranging from 1mm to 5mm in length and from 10µm to 250µm in width. The micro channel in- and outlet were coupled by two large backflow channels (total cross section 2mm²) to minimize external pressure drops. The entire chip was completely sealed using a thin lid of poly carbonate and disconnected from any external device.

The height of the pole pieces was set to 10mm, equal to twice the channel length. To be able to fit in the fluidic chip the minimum separation $x_0$ between the pole pieces was set to 10mm. The value of $\mu B^2$ was set to be around 0.1T²/m for sufficient magnetic driving forces. The value of the maximum magnetic field did not exceed 50mT to stay in the linear regime of the particle magnetization curve as given in section 2.1.3. To minimize the risk of magnetic saturation, the cross-sectional area of the yokes has been maximized where possible. The final fabricated setup was validated by means of a magnetic field.
measurement as function of position between the poles using a Gauss probe that was mounted on an x-y stage (micrometer accuracy). The final fabricated shape achieved $0.22T^2/m$ with a maximum field intensity of only 50mT using a current of 1A through the solenoid, as shown in Figure 3.17 (solid line). Moreover, the shape of the field nicely overlaps with the expectations obtained by the numerical simulations (dashed line).

![Graph](image)

Figure 3.17 Simulation results and final measurement of the isodynamic shaped pole tip setup. The numerically optimized pole-shape gives about $0.22 \ T^2/m$ with a maximum field of only 50 mT over at least 5mm, allowing 10% variation in magnetic force.

### 3.4. System 3: Micro Flux-Guide Array Setup

The previous setups apply particle forces using macro-scaled solenoids and poles that are placed externally. These systems are able to generate high magnetic field intensities over the fluidic sample, but fail to generate high field gradients because the pole tips are too far away from the channel of interest. In order to study the particle behavior in confined fluidic systems at higher field gradient values than the macro-magnetic devices, the following system has been designed. It uses micro-scaled flux guides placed near and
between the microfluidic channels, in order to focus the magnetic fields and hence creating higher gradients exactly at the point of interest.

3.4.1. **MAGNETIC SYSTEM DESIGN**

![Figure 3.18 Concept of flow-orthogonal bead oscillation by the use of shape-anisotropy. In panel a) the external field is directed at 45° from horizontal magnetizing the left bottom and right top pole, which attract the particles in the channel. In panel b) the field is rotated 135° from horizontal in order to magnetize the other poles, and the particles are attracted to the other side of the channel.](image)

The integration of flux-guides on the micro-scale is a difficult process and gives some limitations in active control of the magnetic field. In fact, it is practically impossible to fabricate a device that controls each micro-scaled element separately [57]. Therefore, the elements need to comprise a specific property that enables to manipulate the magnetic field passively in the desired way. Anisotropy is a self-induced effect that can create variation in response as function of its direction, as was already introduced in Chapter 2 discussing the magnetic behavior of the particles itself. In order to induce particle motion with the concept of shape anisotropy, the concept of having several micro-scaled flux-guide elements having a different preferred magnetization directions (easy axis) was studied, as shown in Figure 3.18. The flux-guides will practically only magnetize if the magnetic field lines are aligned with their preferred magnetization direction. Using this concept on both sides of the channel and by positioning their easy axis mutually orthogonal, the particles can be oscillated in the radial direction of the channel by only rotating the external applied magnetic field.

Instead of using the shape anisotropy concept at only one channel, for the final design an array of channels and flux-guides was chosen. The single rod-like structures were transformed into cross-shaped elements between channels as shown in Figure 3.19 panel
a). The two preferred magnetization directions of the cross shaped flux guides are aligned to maximize the magnetic field focusing. Numerical simulations were performed in Comsol Multiphysics \(^{54}\) on this design to investigate the device performance, as shown in panel b). An external magnetic field was applied over the chip that resulted in magnetic field intensities in the flux guides of roughly 100mT indicated by the grayscale. This value is still far away from magnetic saturation of the nickel material that was used, which typically occurs at more than an order of magnitude higher fields. The arrows indicate the value for \(|\mathbf{B}|^2\). Close to the tips (in the picture on the left bottom and right top location) values in the order of 5-10T^2/m were reached but these decay rapidly with increasing distance. The separation distance between the pole tips and the microfluidic channel of about 25µm prevented that the particles could be attracted to the non-preferred tips (in the picture on the left top and right bottom), which enables a switching of motion direction in the whole channel volume.

![A simulation of the final design with cross shaped flux guides between the microfluidic channels. The magnetic field is efficiently concentrated by the flux guides that are exactly aligned with their two preferred magnetization directions a). The close-up in panel b) shows the effect of the induced forces proportional to \(|\mathbf{B}|^2 = 5-10T^2/m\).](image)

**Figure 3.19**

3.4.2. Fabrication and Assembly

The fabrication of the above magneto-fluidic microchip starts with a base plate of polycarbonate (PC) of 125µm in thickness. The top was covered with a solid adhesive of 25µm in thickness, with on top a temporary protective foil. In this substrate, the microchannels and cavities for the flux-guides were made using excimer-laser fabrication as described in section 3.1. In parallel, another PC substrate of 125µm in thickness was covered with a multi-layered electrode structure containing 10nm of chromium for a proper adhesion and 20nm of gold for high conductivity, both by using sputter coating. For better visibility of the channel, excimer-laser fabrication was again used to pattern the
electrodes and remove the chromium-gold multi-layer at the locations where the microfluidic channels were located. Both substrates were cleaned by rinsing steps using isopropanol (IPA), and afterwards bonded together with the solid adhesive attached on the base-plate. As a next step, the electrode surface was connected to an electro formation system to grow the nickel flux guides in the created cavities. The fluidic interconnects were fabricated through the top substrate by again excimer-laser fabrication. A micrograph of the magneto-fluidic chip (panel a) and the complete assembly (panel b) are shown in Figure 3.20.

To confirm the magnetic properties of the electroformed nickel flux guides, hysteresis curves were measured with a vibrating sample magnetometer (VSM, for more info see section 2.1.3). Measurements were done on both a single flux-guide and an array of flux-guides as used in the chip. For an optimal flux-guide, the saturation magnetization should be high to allow for a high flux density. The hysteresis should be low so that the direction of magnetization in the flux-guides can easily be changed. The measured values corresponded well with these demands, the saturation magnetization was 430–493kA/m and the coercive flux density was only 5.5–7.2mT.

Figure 3.20 A micrograph of the magneto-fluidic chip containing an 9x9 array of cross shaped micro flux guides between the microfluidic channels (panel a). The complete assembly of the flux guide setup containing the in- and outlet tubes and the big poles for applying the rotational external magnetic field is shown in panel b).
3.5. **DISCUSSION**

Excimer-laser-based fabrication benefits from its direct single-step method and the ease of making complex structures with small feature sizes down to micrometers. Because of the flexibility of using different sizes and shapes of masks, features with different orders of magnitudes can be processed in a single batch. Complex structures can be made very fast within a single step process and can even be multiplexed by the use of arrays of features. The rapid prototyping of the micro-structures used in this chapter was therefore mainly performed with excimer-laser-based fabrication.

The design and fabrication of three magneto-fluidic systems is discussed, all having completely different properties in magnetics and fluidics. The first “orthogonal four-solenoid” setup can be used for analyzing the particle behavior in large open fluid volumes (typically 1µl) under the application of different magnetic field shapes ($B_{\text{max}} = 50\text{mT}$, $\nabla B^2_{\text{max}} = 1\text{T}^2/\text{m}$). For the analysis of particle dynamics in confined fluid volumes where the particle radius and channel radius are within the same order of magnitude ($R = 5\text{µm} - 125\text{µm}$), the “isodynamic pole-shape” setup has been built, that produces an identical magnetic actuation force on each particle in a microchannel ($B_{\text{max}} = 50\text{mT}$, $\nabla B^2_{\text{max}} = 0.22\text{T}^2/\text{m}$). The last “micro flux-guide array” setup is able to up-concentrate the magnetic field nearby the microchannels ($R = 75\text{µm}$) in order to apply very high actuation forces on the particles and locally control the particle trajectory shape ($B_{\text{max}} = 100\text{mT}$, $\nabla B^2_{\text{max}} = 10\text{T}^2/\text{m}$).

In summary, various field shapes in amplitude and orientation can be applied on different scales using the setups described in this chapter. Chapter 4 will use the “orthogonal four-solenoid” for particle and chain velocity measurements in open fluid volumes. Chapter 5 will use the “isodynamic pole-shape” setup and “micro flux-guide array” setup for the study on the dynamics and interactions of magnetic particles in more confined systems under the application of different magnetic fields.
Chapter 4

PARTICLE DYNAMICS
IN OPEN FLUID VOLUMES

This chapter discusses the dynamics of superparamagnetic particles in open fluid volumes. On the basis of optical velocity measurements, the induced motion of single particles and formed particle chains is analyzed. Equations of motion for single particles as given in Chapter 2 are validated. For the case of axially traveling chains equations of motion are derived. Chains in rotation are analyzed by means of predicting the moment of rupture to be used for input in fluidic simulations. The findings can be used to develop new techniques for accelerated transportation in lab-on-a-chip bio-assays.

In condensed form, section 4.2 and 4.3 are published in Microfluidics and Nanofluidics[44] and section 4.4 is published in Lab on a Chip[58].
4.1. **EXPERIMENTAL PREPARATION AND DATA PROCESSING**

Performing experiments with actuated superparamagnetic particles in fluids requires a set of experimental techniques in order to overcome and solve possible sources of error that could influence measurement results. This section discusses two of the most prominent experimental problems: particle sedimentation and particle (chain) tracking.

4.1.1. **PARTICLE SEDIMENTATION**

The superparamagnetic particles discussed in section 2.1 both comprise a higher specific material density compared to the carrier fluid that is used in experiments. Therefore, the particles are affected by sedimentation in the direction of the gravitational field, which can be characterized balancing the gravitational and hydrodynamic drag forces:

\[
\vec{v}_{sed} = \frac{2(\rho_p - \rho_f)g r_p^2}{9 \eta_f}
\]

If the properties for the Dynal MyOne\(^{[34]}\) particles are filled in, sedimentation velocities in the order of 400nm/s are calculated. However, the larger Spherotech particles\(^{[35]}\) are much more affected by gravitational influences by the squared radius function and experience sedimentation velocities in the order of 100µm/s. Therefore, in most experiments the influence of sedimentation has to be minimized by increasing the density of the carrier fluid to the value of the particle density. In mineral extraction processes, sodium-metatungstate (SMT, Acros Organics\(^{[59]}\), composed as Na\(_6\)[H\(_8\)W\(_{12}\)O\(_{40}\)]) is often used to densify carrier solutions without essentially affecting the other properties. This component is well soluble in water and can generate solutions with a density three times as high as water. In Figure 4.1 the obtained density as a function of the SMT concentration in water is measured in the regime of the particle densities.

To validate the influence of the density-matching process on other fluid properties, several viscosity measurements of the SMT solutions were performed (Paar Physica, MCR 300). The data in Figure 4.2 is plotted as a function of temperature, to account for possible heating by the solenoids and microscope. Despite the manufacturer’s claim of a low influence on viscosity\(^{[59]}\), the measurement at room temperature (293K) shows an increase from 1.0mPa·s (pure water) to 3.7mPa·s for the SMT solution used for the Dynal MyOne particles (57%\(_{wt}\)). A similar measurement is performed for the SMT solution used for the Spherotech particles (44%\(_{wt}\)), resulting in a viscosity of 3.0mPa·s.
Figure 4.1 Calibration curve of SMT solutions on the density as a function of the concentration in the regime of particle densities. The Dynal MyOne particles ($\rho_p = 1800\text{kg/m}^3$) require a concentration of 57%wt, and the Spherotech particles ($\rho_p = 1500\text{kg/m}^3$) only 44%wt.

Figure 4.2 Viscosity measurement of the SMT solution (solid line) used for density matching the carrier fluid to the Dynal MyOne particles, compared to a measurement for pure water (dashed line). At room temperature, the viscosity of the SMT solution with 57%wt is 3.7 times as high as pure water.
The SMT solutions will be used in magnetic setups that externally apply magnetic field over the whole sample volume. As the main component of SMT is tungsten (W) which is essentially a magnetic material, magnetorheological (MR) effects can also influence the viscosity of the SMT solution. Much research has been performed on magnetorheological fluids; however it is complicated to predict the exact fluid properties as its viscosity values, which dependent on many variables such as the material composition, particle size, concentration and the applied magnetic field, proportional to $^{[60]}$:

$$\eta_{MR} = \eta_{B=0} + \alpha_{MR} B^2$$

$$\alpha_{MR} \propto r_p^2, \chi_p, \%_{wt}$$

A typical MR fluid containing 80%wt solution of 1μm iron particles shows a 1000 fold increase in viscosity from 10mPa·s to 1Pa·s, applying a field in the order of $B = 100\text{mT}$. For comparison, a first approximation for the rate of viscosity change assumes a 57%wt solution of SMT containing particles of 10-100nm and a magnetic particle susceptibility of $\chi_p = 7$. According to the proportionality factors given in equation 4-2, the viscosity change would be $10^4$ to $10^6$ times smaller than for a typical MR fluid, resulting in a negligible viscosity change of less than 1%. For validation, the same viscosity measurements have been performed applying a magnetic field in the order of 100mT on the sample in different directions using a simple NdFeB bar magnet; no evidence of viscosity change was found.

4.1.2. PARTICLE-TRACKING

Analysis of the data obtained with particle experiments relies mainly on tracking the particle motion. Commercially available particle-tracking software could be used but is limited in their possibilities of processing the obtained motion data; therefore the tracking was performed with an image processing tool, home-developed in Matlab $^{[55]}$. To separate the moving particles from the (assumed) steady background, each movie frame is processed by subtracting an average of several surrounding frames in order to remain with only the moving pixels in the frame, as shown in Figure 4.3. The number of surrounding frames to subtract is dependent on the movie resolution, noise (motion, compression) and particle to pixel size, usually about half the number of frames per second. For particle localization, the frame is scanned and compared to a 2D Gaussian surface profile that resembles the picture of an individual particle. This way any remaining noise is suppressed as that mainly has a different shape and size compared to a particle. For sub-pixel resolution, the exact coordinates of the particle are then calculated by finding the center of mass of the correlation picture. Next to the analysis of individual
particles, the motion of formed particle chains is also analyzed with similar techniques. Each particle location found by the software is checked if another particle location is within the range of a particle diameter. If so, the particle surfaces overlap and particles are considered to be connected in a chain where the total surface area is calculated to determine the number of particles in a chain. The center of mass of the chain is again calculated to obtain the position of the chain with sub-pixel resolution. Next to these calculations, the easy axis of the surface area is calculated, in order to determine the orientation of the particle chain relative to its motion direction as shown in Figure 4.4.

![Figure 4.3](image1.png)  
**Figure 4.3** Background suppression step for particle-tracking. Every frame is averaged with a number of surrounding frames (in this case 8) to remain with only the moving pixels that are particles.

![Figure 4.4](image2.png)  
**Figure 4.4** The particle chain analysis routine, which calculates its center of mass, orientation with respect to its motion direction, and chain length in number of particles.

Finally, the obtained coordinates (and in case of a chain, the chain orientation and length) are correlated between subsequent frames in order to reconstruct the particle or chain trajectory, including its motion direction and velocity. Typical examples of the above particle-tracking routine can be found in the following sections.
4.2. DYNAMICS OF SINGLE PARTICLES

For magnetic actuation, the experimental setup described in section 3.2 is used, containing a sub-microliter fluid volume surrounded by four miniaturized solenoids. By only analyzing the particles in the center of the fluid volume, any possible influence from the container walls is minimized to resemble the open fluid volume condition. In the upcoming experiments, a current of 75mA is applied on only the left solenoid, generating a magnetic field shape as illustrated in Figure 3.10. The Dynal MyOne particles [34] with a diameter of 1μm are used (see section 2.1). Because the maximum magnetic field intensity is far below the particles magnetic saturation, the magnetic susceptibility of the particles can be assumed to be constant. A low concentration of 200μg/ml (≈ 2·10^8 particles/ml) minimizes chain formation, suitable to study the travel of single particles. This solution is density matched as described in section 4.1.1 to avoid out-of-plane traveling of the particles.

4.2.1. SINGLE PARTICLE VELOCITY MEASUREMENT

![Several particle trajectories obtained with the particle-tracking routine described in section 4.1.2. Note that the camera was focused on the left top area of the fluid container and was not aligned with the magnetic setup, hence the angle of the different paths.](image-url)
In a first experiment, the path of single particles is tracked using the routine described in section 4.1.2. The paths without sufficient data points or a high signal-to-noise are neglected, where the particles are tracked until they move out of focus (field of depth in the order of 10\(\mu\)m). This explains the different lengths of trajectories, which are plotted as function of its x and y position in Figure 4.5. For each single particle position located with the movie processing software, the actual velocity is calculated by using the movie frame rate of \(f = 10\)Hz. Using the simulation values from section 3.2.1, the particle velocities are compared to the corresponding local values of \(|B|^2\). In Figure 4.6, this data is plotted (121 trajectories) together with a theoretical prediction from equation 2-7 using the magnetic field simulation data from Figure 3.10.

![Figure 4.6](image)

Figure 4.6 Several calculated particle velocities as function of the gradient of the squared magnetic field \(|B|^2\). The experimental data (grey dotted points) contain much more data than visualized here; only a few are given here for clarity. The black curved line shows the running average of all experimental points. The theoretical expected value is given by the solid bold line on the top, calculated with equation 2-7.

4.2.2. VELOCITY ERROR AND VARIATION

Equation 2-7 calculates theoretical velocity values between 2.5\(\mu\)m/s and 3.5\(\mu\)m/s, for values of \(|B|^2\) between 0.26\(T^2/m\) and 0.38\(T^2/m\). The measured velocities are on average noticeable lower than predicted. For \(q\) measurement points, the average relative error \(RE\) can be quantified using\(^{[61]}\).
\[
RE = \frac{1}{q} \sum_{i=1}^{q} \left| \frac{v_{ex,i} - v_{th,i}}{v_{th,i}} \right|
\]

Applying equation 4-3 on the presented data points gives an average relative error \( RE \) of 0.33. Furthermore, the measurements show a large spread that can be expressed as a coefficient of variation \( CV \). This is the ratio of the standard deviation to the mean and is calculated as \([61]\):

\[
CV = \sqrt{\frac{1}{q} \sum_{i=1}^{q} \left( \frac{v_{ex,i} - v_{ex,avg}}{v_{ex,avg}} \right)^2}
\]

Using the data of Figure 4.6, a \( CV \) of 0.22 is calculated. The relative error and coefficient of variation can be caused by uncertainties in several parameters from the particles, the experimental setup and the measurement routine itself:

- particle shape: particle (hydrodynamic) radius, sphericity, surface roughness;
- particle magnetic response: mean and variation in magnetic susceptibility;
- surrounding fluid: viscosity, density, non-Newtonian behavior;
- experimental setup: field characteristics, calibration, computational errors.

Light scattering experiments that were carried out on the same particles show a very small distribution in diameter of less than 5\% \([34]\), but could influence the magnetization volume and hydrodynamic drag. According to equation 2-7 the \( CV \) of the experimental velocities could hereby be affected in the order of 20\%. The average magnetic susceptibility per particle has been estimated by a VSM measurement in a concentrated volume of magnetic particles as described in section 2.1.3. Magnetic interactions between particles in the suspension may occur during this measurement. The obtained value may therefore not reflect the single particle magnetic susceptibility \([39]\), which could contribute to the \( RE \). The measurement also conceals a contribution to the \( CV \) that could exist because of a possible but unknown variation in the iron oxide content \([39][62]\). The viscosity of the surrounding fluid has been increased by the density matching process as described in section 4.1.1. Measurements determined the fluid viscosity with an uncertainty of 5\%. However, a small increase of the fluid temperature by heat dissipation of the solenoids and the illumination could lower the viscosity. A temperature shift of 10K is assumed as maximum (measured), to affect the resulting velocities at most with 10\%, which could contribute to the \( RE \) (see Figure 4.2). The estimation of the magnetic field characteristics is
based on simulations \cite{54}. However, deviation could occur by magnetic saturation of the cores and surrounding yoke. The simulations described in section 3.2.1 predicted maximum field intensities of approximately 100mT in the flux guides (applying the same parameter values as in the experiment), which is far below the saturation level of the core and yoke material. The deviation in the experimental velocities because of the field characteristics is determined to be 15% contributing to the \( RE \) and \( CV \). The measurement routine discussed in section 4.1.2 could also be subject of experimental error by image processing and numerical conversions but is assumed to be below 10\% on the experimental velocities, contributing to both the \( RE \) and \( CV \). Considering the above many potential sources of deviation, very high values for the \( RE \) and \( CV \) could be expected. With the experimental determined values of only \( RE = 0.33 \) and \( CV = 0.22 \), the single particle experiments are in close agreement with the established equations of motion.

4.3. DYNAMICS OF PARTICLE CHAINS

The next experiment investigates the utility of chain formation for the acceleration of transport. Because chains will align with the field lines, an axial movement of the chains can be expected, according to the simulations in section 2.3 and 2.4. A higher concentration of 500\( \mu \)g/ml (\( \approx 5 \cdot 10^8 \) particles/ml) forces the particles to aggregate in chains under the application of a magnetic field. Other than this higher concentration, the same experimental settings are used as in the single particle velocity experiments.

4.3.1. CHAIN VELOCITY MEASUREMENTS

To distinguish particle chains with different lengths, neighboring intensity peaks are joined to one area and divided by the actual area of a single particle, giving the number of particles in the chain. The particle chain position is determined by an estimation of the center of mass. To exclude chains that do not move in an axial direction, the relative alignment with the direction of movement is determined, which was not allowed to exceed a difference of 5\(^\circ\). The obtained chain travel paths are shown in Figure 4.7. For all obtained trajectory lines, the resulting velocities as a function of \( \mathcal{PB}^2 \) are calculated as shown in Figure 4.8. It is evident that the chain velocity increases as function of an increasing length of the particle chain. The shape of these curves is roughly linear and comparable with the curve of the single particle experiments.
Figure 4.7  Particle chain trajectories obtained with the tracking routine described in section 4.1.2. Only particles that have a sufficient long track and are axially aligned with their motion direction are taken into calculations. Note that the camera field of view was not aligned with the setup.

Figure 4.8  The velocities of chains are studied by gathering all trajectories of chains that have an equal length (typically around 25 trajectories). For each chain length, the running average is calculated. The experiments show an increase in velocity as a function of the number of particles in the chain.
4.3.2. MAGNETIZATION ENHANCEMENT

Magnetic particles that aggregate in chains require a different analysis due to the large transformation in shape. In a first approximation, one could assume that the total magnetic moment of a chain is given by the summation of all magnetic moments of the particles in a chain. However, dipole interactions between neighboring particles induce a change in the demagnetization fields, represented by the demagnetization factor $N_d$ that is linked to the magnetic susceptibility as already given in equation 2-3. Numerical simulations are performed to study the influence of the chain shape on the demagnetization factor and the resulting magnetization, as shown in Figure 4.9. The chain is modeled as a row of spheres each of 1µm in diameter and initially with the same magnetic susceptibility as the single particles. The spacing of 100 nm represents twice the non-magnetic shell of the particles [34]. The magnetic field lines concentrate in the chain, creating a higher magnetization on the points of contact. The demagnetization factor is decreased by the increasing number of particles in the chain, and the average particle magnetization is therefore increased to a maximum enhancement of 1.2, practically already reached at a chain length of 5 particles.

![Graph](image)

Figure 4.9  A Comsol Multiphysics model is created to investigate the magnetization enhancement by chain formation of particles (inset). A homogenous magnetic field intensity of 15 mT is applied on the particles ($\chi_{\text{eff}}=1.52$) with a diameter of 1µm that are spaced from each other by twice the shell thickness (2-50nm).

We defined a magnetization enhancement as $\alpha_{\text{mag}} = \chi_c / \chi_p$ where $\chi_c$ is the effective susceptibility of a chain. This magnetization enhancement approaches a maximum already...
in the case of 5 particles in a chain. By defining the chain length as \( l_c \) and using the already defined particle radius \( r_p \), the number of particles can be given by \( n = l_c / 2r_p \). The magnetic force on a long chain can now be expressed as:

\[
\vec{F}_m = \frac{\pi l_c r_p^2 \alpha_{mag} \chi_p \vec{v}_B}{3 \mu_0} B^2
\]

4.3.3. HYDRODYNAMIC DRAG

The hydrodynamic resistance on a chain also depends on its shape and orientation. The hydrodynamic drag resistance of elongated bodies is much more complicated to determine than for a simple sphere. The chain of particles moving in axial direction is considered as a long finite cylinder with rounded caps. However, exact solutions have not yet been obtained and therefore approximate methods have been employed for elongated bodies. The hydrodynamic drag mainly depends on the body aspect ratio or, in this case, the number of particles, and can be calculated as follows \(^{[11]}\):

\[
\vec{F}_d = \frac{\frac{1}{2} \pi \eta f l_c \vec{v}_c C_1}{\ln(l_c / r_p) + C_2}
\]

The numerator of equation 4-6 is very similar to Stokes formula for the hydrodynamic drag of a simple sphere in laminar flows, which is a function of the fluid viscosity \( \eta_f \), the body size expressed by its length \( l_c \) and the translational velocity \( v_c \). The denominator is the evident difference adding the body aspect ratio given by \( l_c / 2r_p \). The dimensionless constants \( C_1 \) and \( C_2 \) remain to be determined.

4.3.4. DATA FITTING

If we now combine equation 4-5 and 4-6, the velocity of a chain of particles, traveling in axial direction relative to the medium can be derived as follows:

\[
\vec{v}_c = \left( \frac{\ln(l_c / r_p) + C_2}{\frac{1}{6} C_1} \right) \left( \frac{\alpha_{mag} \chi_{p,eff} \vec{v}_B^2}{9 \mu_0 \eta_f} \right) \left( \frac{\ln(l_c / r_p) + C_2}{\frac{1}{6} C_1} \right) \vec{v}_p
\]
This equation shows that the chain velocity $v_c$ is proportional to the velocity of a single particle $v_p$. The proportionality - in this case enhancement - factor depends only on properties from the particle or chain and is not influenced by external properties such as the magnetic field or the fluid viscosity. The curves obtained from experiments displayed in Figure 4.8 all show roughly linear shape for each chain length, and is proportional to the curve for a single particle, as equation 4-7 also indicates. The experimental data is therefore plotted as the velocity enhancement factor, as a function of the number the chain aspect ratio, shown in Figure 4.10. Equation 4-7 is fitted through the data using a logarithmic function in combination with the magnetization enhancement data given in Figure 4.9. The hydrodynamic constants $C_1$ and $C_2$ are used as fitting parameters. A corresponding fit is found with $C_1 = 9$ and $C_2 = 0.56$, and shows that the experimental data also has the same logarithmic curve shape indicating the model to be valid.

Figure 4.10  The experimental data found in Figure 4.8 is represented as a velocity enhancement factor, normalized to the velocity of a single particle. The obtained curve is fitted with the model in equation 4-7 and shows a similar logarithmic shape, which is a function of only the number of particles in the chain.

Simulations have been performed in Comsol Multiphysics to determine the hydrodynamic drag factor for a chain numerically also (for full model description see Chapter 6, Figure 6.1). The dotted line in Figure 4.10 represents the calculated values with this model, which agrees very well with the obtained fit from the experimental values. If the hydrodynamic values are calculated from the numerical results we obtain $C_1 = 9$ and $C_2 = 0.53$, which is also in very close agreement with the values found in the fitted model. A comparison with hydrodynamic values for an ordinary cylinder dragged in an axial direction through the
fluid \((C_1 = 4 \text{ and } C_2 = 0.72)\) \cite{11}\) indicates that the hydrodynamic drag force of a chain of particles is evidently higher. For example, a chain of 12 particles needs a 40% higher actuation force to reach the same travel velocity as a finite cylinder with the same aspect ratio. The undefined surface roughness and the undulating shape of the chain of particles is most likely the main reason for the higher hydrodynamic drag force.

4.4. ROTATING PARTICLE CHAINS

This section analyzes the behavior or rotating superparamagnetic particle chains using an analytical and mechanistic pin-joint model. The response of chains on a rotating field over time is discussed by governing parameters as the hydrodynamic drag, magnetic forces and chain length. Aspects as different chain shapes and the prediction of chain rupture will be discussed using a numerical model and will be confirmed with experiments.

4.4.1. ROTATING CHAIN EXPERIMENTS

A continuously rotating homogeneous field can be used to actuate the chains that respond by realigning to the field direction \cite{63}. Even in the absence of a field gradient, a torque can act on the particles given that they are assembled in a configuration that has magnetic anisotropy, which in this case arises by the chain shape as already discussed in section 4.3. For the design of a particle-based micro-mixer, it is important to know at which conditions chains of certain length will follow the rotating field or will rupture and reassemble \cite{64}. A key parameter when considering chain rotation is the Mason number \(Mn\) as explained in chapter 1, which can now be adapted to expresses the ratio of hydrodynamic forces and torques to magnetic torques in this case, according to \cite{33}.

\[
Mn = \frac{16\eta f \omega}{\mu_0 \chi_p H^2}
\]  

The rotation frequency of the magnetic field is expressed as \(\omega\). Figure 4.11 shows different states of an initially linear chain of 21 Dynal MyOne particles \cite{34} \(r_p = 0.5\mu m, \chi_p = 1.52\) in water \(\eta_f = 1\text{mPa}\cdot\text{s}\). The chain deforms under the action of the magnetic field rotation \((\omega = 1\text{Hz} = 2\pi\text{rad/s}, B = 5\text{mT})\) to become S-shaped and eventually breaks. The resulting smaller chains rotate with a less pronounced S-shape and when their ends come close enough they reconnect. This process is repeated creating a quasi-steady system.
Figure 4.11  A rotating chain of 21 particles under the action of a clockwise rotating magnetic field with an intensity of $B = 5\, \text{mT}$ and a frequency of $\omega = 1\, \text{Hz}$. The field is exactly tuned in order to show the moment of chain rupture, in this case at $Mn = 3.79 \cdot 10^3$.

4.4.2. PIN-JOINT SIMULATION MODEL

Inspired by the characteristic s-shape and chain rupture, an analytical model was developed that represents a chain of particles as a pin-joint mechanism as shown in Figure 4.12. A pin-joint is a connection that allows rotation but no translation between the connected bars. Hence, the joint can transfer a reaction force but no torque. In fact, the bars between the joints experience a torque by the reaction forces applied on both ends.

Figure 4.12  The pin-joint mechanism that represents a chain of particles that is rotating anti-clockwise under the influence of an applied magnetic field $H$. The particles will magnetize aligned with the field and experience a torque due to the chains phase lag with the field. This torque translates to only forces (and no net moments) on each joint, which induces the s-shape as observed in the experiments.
Next to the magnetic forces, the particles will encounter hydrodynamic drag forces on each particle. Because of the complex and transient S-shape, it is difficult to calculate the exact drag coefficient of the chain. However, to give a first approximation, the drag coefficient in motion direction for every particle is calculated by Stokes law as already given in equation 2-6. As the chain is rotating, also the rotational drag force \( F_{d,\omega} \) for each particle has to be added, which is calculated using \( [11][65] \):

\[
F_{d,\omega} = 8\pi \eta f^3 p \omega
\]

The actual drag coefficients will be different than those calculated with above approximations due to neighboring particles, but will give first approximation values.

4.4.3. Transient Numerical Analysis

In order to study the chain deformation and the point of rupture, the above model is implemented in a transient simulation model written in Matlab \([55]\) that calculates the reaction forces over time. The initial condition assumes the chain to be linear and aligned with the field lines. All displacements and new positions for every particle in the chain are calculated for the next time step, using the calculated reaction forces and drag forces together with a set of kinematic constraints of the chain modeled as a pin-joint mechanism. The tension on each bar is calculated using the reaction forces at the joints. The maximum tension that can be sustained is calculated by using the dipole-approximation in equation 2-9. As soon as the tension exceeds the calculated value, it is assumed that the bar breaks and two chains are formed.

As expected, the transient simulation shows the characteristic development of the s-shape for a particle chain having a phase lag, as observed in the experiments (see Figure 4.11). The end bars are free to rotate and follow the field, however, the reactions at the joints of the constrained bars result in a torque that opposes their rotation causing them to develop a greater phase lag, which results in the s-shaped chain. Furthermore, the phase lag of the chain with respect to the field orientation increases with time and approaches asymptotically a steady state value, if no rupture occurs.

The maximum phase lag and maximum tension are observed in the center bar; hence the chain is expected to break at that position similar to the experimental observations. Figure 4.13 illustrates the critical number of particles at which rupture occurs versus the Mason number, as predicted with the simulation model \([54]\). Varying the fluid viscosity, rotation velocity, magnetic susceptibility or applied magnetic field all give the same curve.
(numerical error of only 0.03%), confirming that the model exactly scales with the Mason number. The computed curve gives the maximum number of particles in a chain as a function of the Mason number, which can still be considered as stable (maximum tension is not reached). As a rule of thumb the maximum number of particles scales as $n_{\text{max}} = Mn^{-0.5}$, which is in agreement with other studies performed on this topic [66].

As already indicated by the experiments in section 4.2, particles are affected by a variation in magnetic susceptibility that could result in a “weak link” in the chain. In order to investigate the influence of this variation, the same transient simulation model is used with. A particle with 33% of its original magnetic susceptibility is placed outside the center: $\chi_p = 0.51$. The simulation results show that the chain still develops within a quasi-symmetric shape, but it becomes unstable at much lower Mason numbers of about 1/3 of that for a regular chain. The calculated maximum tension values are now located next to the particle of lower susceptibility and the closest to the center, which causes the chain to break at that location.
4.5. DISCUSSION

Experiments on single particles showed velocities that can differ with a coefficient of variation (CV) of 0.22, most probably by particle-to-particle variations. The average measured velocity deviates from theoretical predictions with a relative error (RE) of 0.33. Our hypothesis is that this deviation is partially caused by the use of a susceptibility value from bulk VSM measurements, which may not reflect the actual susceptibility of individual particles. Equations for the influence of chain formation on the magnetization and the hydrodynamic drag force have been established and compared to experimental data. We observe a logarithmic dependence of velocity on the chain length. For a given magnetic field, the velocity of chains is proportional to the velocity of single particles with an enhancement factor that depends on the chain aspect ratio and its hydrodynamic properties.

The dynamics of rotating particle chains is described using a pin-joint mechanistic model that is able to predict the characteristic s-shape of the chain, the moment of rupture. It was confirmed by the model that the important parameters that influence chain rotation are the Mason number (representing fluid viscosity, angular velocity, susceptibility and magnetic field settings) and the number of particles in the chain. Even more, the position of rupture in the chain is studied by introducing weak link by a particle having a lower susceptibility. These calculations and predictions can be used as input for the design of applications on system level.

However, this chapter assumed that channel wall boundaries are very far away and could be neglected. Magnetic interactions will not be affected by the presence of any channel walls, but the hydrodynamic interplay between particles, fluid and the wall will be of influence. Therefore, next Chapter 5 and Chapter 6 will focus on related interaction effects induced by close-by channel walls.
In microsystems, magnetic particles are often in close proximity to channel walls, which changes the particle motion in terms of direction and velocity compared to the case of particles in an unbound fluid. The effects of this so-called particle confinement are complex and difficult to predict. This chapter will discuss the experimental studies on the motion and interplay of superparamagnetic particles in a micro channel under constant magnetic driving force conditions. Different particle configurations are discussed on the basis of magnetic and hydrodynamic particle interactions, and analyzed with analytical and numerical models to understand the behavior of particles in highly confined systems.

In condensed form, section 5.1 is published in Microfluidics and Nanofluidics [46], section 5.2 is published in Applied Physics Letters [45], and section 5.3 and 5.4 are submitted for publication.
5.1. PARTICLE CONFIGURATIONS

To investigate possible particle configurations in high surface area systems, the “isodynamic pole-shape” setup described in section 3.3 is used. This system is able to apply a constant actuation force on each of the particles dispersed in the microchannel. However, as a consequence of this property the magnetic field intensity will change as a function of the position within the channel. In the experiment, the Spherotech particles were used \( r_p = 11.2\mu\text{m}, \chi_p = 0.06 \) and analyzed under the application of external magnetic field with \( \mu B^2 = 0.1T^2/m \), in a microchannel of 4mm long and 100µm in width and depth. Figure 5.1 shows the different arrangements of the particles that have been observed as a consequence of the changing magnetic field intensity. In panel a), the particles experience a low field intensity of 10mT \( (y = 1\text{mm, top of the setup}) \). Here, the particles line up on the channel axis owing to a focusing effect induced by the channel walls. In this axially aligned configuration, the particles self organize into a spread poly-twin configuration. Panel b) shows the ensemble of particles that experience a magnetic field of 25mT \( (y = 2\text{mm, halfway the channel}) \). The particles leave their common central motion axis and start to transform in more off-axis configurations. In panel c), the particles are observed in the position of the highest magnetic field setting of 50mT \( (y = 3\text{mm, bottom of the setup}) \), where the particles are fully aggregated into chains and aligned with the field lines that are oriented perpendicular to their motion direction. The chain length appears to be limited by the channel confinement.

Although two stable configurations could be clearly distinguished as shown in panel a) and c), the particles require a transition length before equilibrating in a new configuration. The transformation to a certain configuration is triggered by a set of different forces acting on the particles. Similar to the dynamics in open fluid volumes, the particles are affected by external magnetic driving forces that are assumed to be constant in this case (section 2.2), hydrodynamic interaction forces (section 2.4) and magnetic dipole interaction forces that both vary as a function of particle interspacing (section 2.3). In this special case of the particles and fluid being confined by the channel, also hydrodynamic focusing forces induced by the channel walls have to be considered (see section 5.3). Based on the above findings, the resulting particle configuration can be qualitatively predicted by analyzing the properties of the applied magnetic field, the used particles and the microchannel as shown in Figure 5.2. Panel a) shows the case of formed particle chains in axial direction that is promoted by the alignment of the field lines with the motion direction, which could occur for both highly confined and quasi open systems (similar to the case of chains in open fluid volumes, see section 4.3). In panel b), the case of a magnetic field alignment
perpendicular to the particle motion and low magnetic field intensity is illustrated, where the particles reorder to a spread particle system as already observed in Figure 5.1 panel a).

![Image](https://via.placeholder.com/150)

**Figure 5.1** Spherotech particles traveling with velocities in the order of 100µm/s in a channel of 100µm in width/depth. At the top of the channel ($y = 1\text{mm}$, $B = 10\text{ mT}$), the particles focus towards the channel center and end up into a poly-twin configuration (a). With a higher field amplitude and lower field gradient halfway the channel ($y = 2\text{ mm}$, $B = 25\text{ mT}$), particles re-organize in less ordered configurations (b). At the channel bottom the field intensity is high ($y = 3\text{ mm}$, $B = 50\text{ mT}$), and particles aggregate into chains aligned with the field lines perpendicular to the travel direction (c).

In the case of higher magnetic field intensities, the particles can move off-axis as shown in panel c), where the single particles or small agglomerates get closer to the channel walls than in Figure 5.1 panel b). Panel d) illustrates the observation of Figure 5.1 panel c), where the magnetic field intensity values are much higher and particles will form chains aligned with the field lines, where its length is limited by the channel wall confinement.
However, in less confined systems the chains can be much longer or in the situation the magnetic field values are lower the particles could even deflect its ends by the increased hydrodynamic drag close to the channel walls, as illustrated in panel e). The effects of different multi-particle structures in confined fluid volumes are complex and difficult to predict with analytical methods. The upcoming sections will therefore discuss several notable interaction effects that have not yet been (fully) understood based on the analysis of particles in open fluid volumes of Chapter 4. The special case of poly-twin particle arrangements will therefore be discussed in detail in section 5.2. Section 5.3 will discuss the situation of moving particles close to boundaries, together with an analysis on the observed focusing effects of particles towards the channel center.

![Figure 5.2](image)

**Figure 5.2** A schematic representation of different possible particle configurations as a consequence of the magnetic field settings and chosen geometry in shape and size. This prediction is made by the analysis of the observed experimental particle rearrangements given in Figure 5.1.

### 5.2. The Particle Twinning Effect

As shown in Figure 5.1a, a successive self organization effect was observed for the lined up particles under a low magnetic field condition \((B = 10\text{mT})\). Over time, the two particles in front of the moving row reduce their interspacing, form a twin and travel away with an increased velocity along the channel axis. The new heading particles of the row follow successively the same re-organization processes, through which the row shortens until a full stable poly twin system is formed. Remarkably, the twinned micro particles are close to each other but do not touch. To understand these unforeseen phenomena on the micro-scale, similar experiments have been performed on the macro-scale and a comparison has been made. The mechanisms of successive twinning and spacing regulation are explained by a one-dimensional model based on the axis flow profile and for confirmation compared with full CFD simulations performed in Comsol \[^{54}\] including both magnetic and hydrodynamic particle-particle interactions, as discussed in the following sections.
5.2.1. **Validation with the Macro-Scaled Gravitation Setup**

As thoroughly discussed in Chapter 2, particles are affected by strong but short range magnetic interactions and weaker but longer range hydrodynamic interactions. In order to analyze the twinning phenomena of particles by separating the two different interactions, a second setup has been built for purely gravitational studies excluding the magnetic interactions. Gravitation also enables a constant driving force on each particle, but avoids interference of particle interactions other than hydrodynamics. The decision of using gravitation however impedes the control of the particle motion and therefore the setup has been enlarged to macro-scale. A plastic tube of 1 m in length and 15 mm in diameter was placed in vertical direction aligned with the gravity field, and was closed at the bottom to reflect infinite channel length conditions. Stainless steel particles were used with a diameter of 5 mm and a density of 7860 kg/m³. To meet the low Reynolds number regime as in the magnetic particle experiment, the tube was filled with highly viscous oil (SAE 80W90, Comma, United Kingdom, \( \rho_f = 887 \text{kg/m}^3 \), \( \eta_f = 200 \text{mPa} \cdot \text{s} \) at 293K). The difference in density between the particles and the fluid leads to single particle velocities below 10cm/s. The resulting Reynolds number \( Re \) in the order of 1 indicates a steady laminar flow profile.

![Figure 5.3](image.png)

*Figure 5.3 Steel particles (5 mm) experiment where gravity provides a constant particle force. Only hydrodynamic particle interactions occur that allow twins to fully come in contact, as particles 4 and 5 show. Particles 2 and 3 are still at the onset of twinning.*

In the gravitation experiments, the number of particles and their initial interspacing were varied, and all experiments confirmed the twinning effect as shown in Figure 5.3 for the case of 5 particles. Note that the used particles are perfectly spherical, but seem to be a bit elongated due to the observations through the curved channel wall. We observed fully developed twins with particles in complete contact, in contrast with the particle experiments on the micro-scale where also magnetic interactions could influence the particle motion. As expected, the gravitation driven particles are not subjected to (short range) repelling forces in contrast with the micro particles driven by magnetics, showing that successive twinning is mainly induced by hydrodynamic interactions effects.
5.2.2. 1D ANALYTICAL MODEL

To explain the above statement and understand the observed hydrodynamic interaction phenomena for multiple particles, a purely hydrodynamic laminar 1-D flow model that only considers the channel axis flow profile was developed, allowed by the systems axial symmetry. One or more spherical monodisperse particles with radius \( r_p \) are positioned on the axis of an infinitely long channel. On every single particle an identical initial velocity \( v_p \) is applied in axial direction.

Figure 5.4 panel a) shows the 1-D velocity profile of two separate particles (thin lines) with velocity \( v_p \). If we initially focus on one particle and ignore boundary effects of the channel walls, the velocity of the propelled fluid \( v_f \) surrounding the particle is roughly inversely proportional to the distance \( z \) from the particle center in axial direction, as confirmed analytically by the following calculation\[11\]:

\[
v_{f,z} = v_p - \frac{v_p}{2} \left( \frac{r_p}{z} \right)^3 - 3 \left( \frac{r_p}{z} \right)^2 + 2 \]  

This equation is valid in case \( z > r_p \) in order to only take into account the fluid velocity \( v_f \) where the velocity within the particle \( z < r_p \) is assumed constant at \( v_p \). Because of the purely laminar flow, it is assumed that the channel axis velocity profile induced by two individual particles in motion can be computed by a superposition of both fluid velocity profiles, according to \[11\]: \( v_{f, \text{axis}} = v_{f,p(1)} + v_{f,p(2)} \). Thereby a symmetric curve is obtained as shown in Figure 5.4 (panel a, bold line) where both particles experience an equal velocity increase by their hydrodynamic interactions: the particles will not move with respect to each other.

The velocity enhancement is a function of the particles interspacing and reaches a maximum of 1.29 times the single particle velocity at the point of touch, which is also in close agreement with the 3D numerical simulations performed in Chapter 2, Figure 2.6 that calculated a force enhancement of \( (F_m + F_{d,int}) / F_m = 1.26 \) times the actuation force. In case of a channel wall at distance \( R \), similar curves are computed for single and interacting particles; however the power of the two \( r/z \) ratio terms will both change for different \( R/r_p \) values but result in amplified particle-particle interactions as long the particles are not highly confined, in case of \( R \gtrsim 2r_p \).
Figure 5.4  Calculated velocity profiles of two separate particles (thin lines), both showing that the fluid velocity decrease is inversely proportional to the distance (z) from the particle. The arrow indicates the force direction. The resulting axis fluid velocity profile (bold line) is obtained by superposition of the two velocity curves, which demonstrates an even increase of both particle velocities: a constant spacing over time (a). Hydrodynamic interactions of three particles give a higher velocity enhancement for the center particle by contributions of both neighbors (b). The difference in velocities subsequently leads to formation of a twin that increases velocity and travels away from the left particle (c).

In panel b) a third particle is added. Superposition of the three single particle profiles reveals that the middle particle reaches a higher velocity than the outer particles as a
result of contributions from both neighbors. Over time, the middle particle will therefore approach the heading particle until a stable twin is formed as shown in panel c). As a result of the increased velocity for a twin, it will subsequently travel away from the left particle that stays behind. This mechanism is qualitatively corresponding with the observations on magnetic particles on the micro-scale (Figure 5.1 panel a)) and the particles driven by gravity on the macro-scale (Figure 5.3).

5.2.3. 3D NUMERICAL MODEL

For validation of the 1D analytical model and understanding of the experimental data, a full axi-symmetrical CFD numerical model has been developed in Comsol Multiphysics \cite{54}, similar to the first calculations given in section 2.4. Similar to the magnetic particle experiments, one or more spherical monodisperse particles with radius \( r_p = 11.2 \mu \text{m} \) are positioned on the axis of an infinitely long channel with radius \( R = 5r_p \), surrounded by a fluid with viscosity \( \eta_f = 1 \text{mPa}\cdot\text{s} \). The particles are modeled as individual domains within the fluid having a much higher viscosity (\( \eta_p = 1000\eta_f \)). Every single particle experiences an identical actuation force \( F_m = 1.33 \cdot 10^{-12} \text{N} \) in axial direction that results in single particle velocities in the same order of magnitude as the experiments (\( v_p = 100 \mu \text{m/s} \)) and confirming full laminar flow (\( Re = 10^4 \)). A simulation image of the model at initial position for 15 particles is shown in Figure 5.5.

![Figure 5.5](image)

Figure 5.5 Image of the full axi-symmetrical CFD model for analyzing the twinning behavior of actuated particles. The situation here shows 15 particles in a row that acts as initial position for the simulation performed over time.

In the 3D numerical model the particles are now modeled as full spheres instead of a 1D entity (basically a line segment), which could influence the magnitude of particle to particle interactions. Moreover, the 1D model requires a single particle velocity as initial condition, and the 3D calculates the resulting particle velocities with use of the initial force applied on each particle. In order to compare both models, the two initial conditions have to be fine-tuned to end up with the same average particle velocity. Once done, the axis velocity profile of the above simulation can be compared to the calculations by the 1D model, as shown in Figure 5.6. The 1D analytical model matches within 1% error to the 3D numerical model in terms of the resulting particle velocities. If the particle spacing increases, the error will even become smaller and practically vanish. However the fine-tuning of the initial particle velocity is required for the 1D model, it can be perfectly used
for the qualitative study of hydrodynamic particle interactions and observed particle twinning.

Figure 5.6 Comparison of 1D analytical model (solid thin lines) including resulting superposed axis velocity profile (dotted thin line) and the 3D full numerical model (solid bold line segments). Although the 1D model only considers the spheres as lines, there is less than 1% difference between the resulting axis velocity profile for the 1D and 3D model.

5.2.4. SUCCESSIVE TWINNING

The described twinning mechanism occur also on a longer row of \( n \) particles that is modeled by \( v_{f,\text{axis}} = v_{f,p(1)} + v_{f,p(2)} + ... + v_{f,p(q)} \). Here, a released twin successively creates space for the subsequent particles to twin as observed in the experiments. For this study, the 1D analytical model and the axi-symmetric simulation model are both used with Figure 5.5 and Figure 5.6 as initial starting condition at \( t = 0 \). For a time-dependent analysis, the following condition is applied in both models, known as the Euler integration:

\[
x_{p,t+dt}^{i+1} = x_{p,t}^{i} + v_{p,t}^{i} dt
\]

For each time step \( dt \), the new positions \( x_{p,t+dt}^{i+1} \) for all 15 particles are calculated and the simulation model is ran again to obtain the new particle velocities, and so on. In case two particles would collide, both velocities are equalized to their mean, so that the two particles travel further as a twin. Several time step values \( dt \) have been analyzed to minimize numerical errors. Using \( dt = 1 \) ms, a poly-twin particle configuration is found after approximately 15000 iteration steps (\( t = 15 \) s), as shown in Figure 5.7. Analyzing the simulation in time, the first twin starts to form and increases its velocity to travel away from the row. If the first twin is far away from the row, the next twin starts to form and also gets released. Successively the row of particles ends up in a full poly-twin system. The required time to develop a full twin system and the resulting twin interspacing can be
influenced by the initial particle spacing $s$, the ratio of channel to particle radius $R/r_p$ and the applied particle forces $F_m$. The final poly-twin system is able to regulate and stabilize its interspacing: a twin that approaches a second twin in front will enlarge its intraspancing and thereby reduce velocity. Conversely, the twin in the leading position will reduce its intraspancing (if present) and thereby accelerate to travel away from the following twin. If a twin catches up with a single particle, it almost collides but increases its intraspancing to release the twin rear particle; subsequently the leading particle forms a stable twin again with the initially single particle.

![Figure 5.7](image)

Figure 5.7  A plot of the analytical 1D (graph) and axi-symmetrical simulation (inset) model in transient state after 15000 iteration steps, for 15 particles, initially ordered as a full contact row on the axis of an infinitely long microchannel. The first 3 twins have already formed and, increase their velocity to travel away from the row. Successively the fourth twin starts to form and also travels away from the row. The formed twins are able to regulate and stabilize their interspacing to end up in a full poly-twin system.

5.2.5. **Adding Magnetic Interactions**

The observed twin intraspancing in case of magnetic driving forces is analyzed by adding the magnetic particle-particle interactions as described in section 2.3 to the 3D model. As the field lines are aligned perpendicular to the direction of the particle row, the magnetic dipole interactions end up in a strong but short range repelling forces between the particles. As expected, the simulation model also predicts the particles to end up in a poly-twin configuration including a small remaining intraspancing within the twins, as shown in Figure 5.8. The applied magnetic system parameters in simulation model are identical to the micro-scaled experiment ($B$ = 10mT and $PB^2 = 0.1T^2/m$); therefore the remaining intraspancing within the twins can be compared. In the observations shown Figure 5.1 panel a), the magnetic repelling force ($\propto 1/s^4$) and the hydrodynamic twinning force ($\propto 1/s$) equilibrate at a twin intraspancing $s$ between a particle radius and a particle diameter.
The simulation shown in Figure 5.8 results in a larger remaining intraspacing at $s = 1.92r$, but is simulated for a system with much more particles. Section 2.4 already calculated the point of transition where magnetic and hydrodynamic interaction forces are equal for only two nearby particles (such as a twin), which resulted in an intraspacing value of $s = 1.18r$, which is a bit smaller than the experimental observations. Both calculations are in reasonable agreement, but are highly dependent on the initial particle configuration due to the multi-particle interactions influencing to each other.

![Figure 5.8 Transient simulation of a row of particles in motion that end up in a poly-twin system with a small remaining intraspacing within the twin by magnetic repellence. The presented configuration is in agreement with the experimental observations in Figure 5.1 panel a) and the calculations made in section 2.4.](image)

### 5.3. Reversionary Spin of Off-Axis Particles

In the previous section that analyzed the twinning effect, it was assumed that the actuated particles were aligned along the channel axis. However, the row of particles was considered as an initial condition, while in real systems the particles are required to first focus towards the channel center. This so-called “tubular pinch effect” has already been described in many studies (for instance experimentally by Segré and Silberberg [67] and by Saffman in a numerical way [68]) for the case of passive particles that flow along with a pressure-driven flow. In this section, the focusing mechanism and related rotation effects are compared and analyzed for the specific case of an actuated particle in a quiescent flow (no external pressure), as observed in our experiments shown in Figure 5.1.

#### 5.3.1. Focusing Mechanism of a Passive Particle

Most of the traditional studies on the particle focusing effect, assume a passive particle that flows along with a pressure-driven fluid flow that is described by a parabolic Poiseuille velocity profile or a perfect shear flow between two walls [68][69]. The passive particle is not exposed to any external force except for the viscous forces, and is assumed to be density matched with the surrounding fluid. In the case of a Poiseuille or shear flow, a particle floating near a channel wall will just lag behind the average fluid flow ($v_p / v_{avg} < 1$) and experiences different fluid velocities at its wall-side oriented half sphere (lower
velocity) and at its channel-axis oriented half-sphere surface (higher velocity) as shown in the schematic representation in Figure 5.9 (inset). The lower velocity will induce a higher pressure and vice versa. This mechanism is explained by Bernoulli’s law \((\Delta p + 0.5\rho v^2 = \text{constant})\), but is only applicable for inviscid flows. However, the same mechanism appears to be present in our case of a viscous flow, which drives the particle to levitate from the wall and focus itself towards the channel center. Additionally, the resulting drag forces in opposing direction impose a moment on the particle surface and the particle starts to rotate as if it rolls over the channel wall. This additional rotational degree of freedom amplifies the velocity gradients resulting in even higher pressure differences, further enhancing the focusing effect, which is known as the Magnus effect \([70][71]\).

The resulting focusing trajectory of a single particle is however very difficult to predict and is still under investigation in many recent studies \([69][72][73]\). There are many parameters of influence, such as the axial particle velocity \(v_p\) relative to the average surrounding fluid velocity \(v_f\) and the confinement of the particle by the channel expressed as \(R/r_p\). At the same time, these parameters also affect the rotational velocity of the sphere that could also reduce or enhance the particle focusing. One of the attempts is based on the Kutta-Joukowski lift theorem \([65]\), which calculates the lift or focus force on a spherical object as function of its axial and angular velocity through the fluid according to:

\[
F_{\text{focus}} = 4\pi r_p^2 v_p v_f \omega
\]  

5-3

In this case of a particle being highly confined by the channel, equation 5-3 will not give a very accurate prediction of the focusing trajectory in terms of exact numbers as it is only a two-dimensional approximation (in fact, it models a infinite cylinder). However, as an approximation it can nevertheless be used to qualitatively reconstruct the trajectory shape. The same simulation model described in section 5.2.3 has been used to calculate values for \(\omega\) and \(v_p\) for a passive particle at different radial positions within the channel on the z-axis (see also section 5.3.3), where equation 5-3 was integrated to calculate the focusing force at every position. Besides the transition to a 3D space model as a consequence of the off-axis particles, the same conditions were applied as in the axisymmetric models for describing the twinning effect \((r_p = 11.2 \mu m, R = 5r_p, n_f = 1 \text{mPa-s})\). For this case of a passive particle, the magnetic actuation force \(F_m\) was removed and an external pressure \(\Delta p = 0.25 \text{Pa}\) was applied over the channel \((L = 5 \text{mm})\).

As the simulation results show in Figure 5.9, a passive particle starting from a wall (at \(x = R - r_p\)) and flowing along with (and lagging behind) a pressure-driven flow will levitate from the wall immediately as the radial velocity gradient (in x-direction) is locally very high due
to the Poiseuille profile. While approaching the center, the particle loses its focusing effect very quickly due to the lower radial velocity gradients within the fluid, finally ending up in an “L-shaped” curvature.

![Diagram](image)

**Figure 5.9**  The reconstructed focusing trajectory of a passive particle that flows along with a pressure-driven Poiseuille flow, resulting in an L-shape curve. The inset shows a schematic overview of the driving velocities, pressures and forces on the particle.

### 5.3.2. Observations of an Actuated Particle While Focusing

In experiments carried out under conditions of active magnetic forcing in microchannels related particle focusing effects were observed, but these are different from the case of passive particles. Instead of a continuous focusing effect that was calculated for a passive particle, 4 different stages can be distinguished for the case of an actuated particle focusing towards the channel axis, as shown in Figure 5.10. Very close to the wall, an actuated particle rotates similar to the case of a passive particle as if it would roll over the surface, shown in panel (a). Since the particle is moving faster than the fluid, this rotation obstructs the fluid to reach a high velocity near the particles channel-axis oriented half-sphere and will not result in a focusing force. The particle stays virtually attached to the wall unless any other effect is upsetting this situation. In these experiments the release of the particle from the wall was highly random and it was not clear what mechanism initiated the particle to start focusing. At the macro-scale one could think of a slightest onset of turbulence \[^{[68],[74]}\], but in our experiments the Reynolds number is in the order of $10^4$, indicating a pure laminar flow. In this case, a disturbance may come from roughness
of the wall and/or particle surface, or particle anisotropy in shape or magnetization. Panel (b) shows a particle that has finally come off the wall due to a small disturbance. The particle rotation is reduced and starts to slip due to the reduced wall influence. While going further off the wall, the particle reverses its rotation direction as shown in panel (c). Approaching the channel axis the focusing force slowly disappears together with its rotation and the particle finds its equilibrium at the channel center (d).

Figure 5.10  Several snapshots (top) of an actuated magnetic particle (Spherotech , \( r_p = 11.2 \mu m \)) traveling through a microchannel (50\( \mu m \) diameter, 5mm length), together with simulations showing the fluid flow field with respect to the particle position. The particle starting from the wall rotates as it would roll over the surface and does not get released (a). The particle suddenly gets released due to an external disturbance, and starts to slip over the channel surface (b). The particle starts to counter-rotate and also focuses towards the channel center (c). When the particle finds its equilibrium at the center, the particle has lost its rotation and travels along on the channel axis (d).

Repeated experiments indicated that the particles followed a much more complex focusing trajectory. However the clear transitions shown in Figure 5.10, exact reconstruction of the focusing trajectory on the micro-scale was very difficult. Therefore, macro-scale experiments similar to the ones given in section 5.2.1 have been performed where a particle starting from the channel wall is driven by gravitation. The experiments typically show an s-shaped focusing trajectory, as shown in Figure 5.11.

Figure 5.11  An overlay of different snapshots (\( dt = 0.2s \)) of a particle (\( r_p = 2.5mm \)) focusing in a tube with a diameter of 15mm by gravity, showing a similar s-shaped trajectory that was also observed in the micro-scale experiments.
The same simulation model is used in Comsol \(^{[54]}\) to reconstruct the focusing trajectory of an actuated particle in a confined but quiescent fluid volume, which now experiences an actuation force \(F_m\) in axial direction and where the external pressure component \(\Delta p\) has been removed. As expected, the computed curve for the actuated particle as shown in Figure 5.12 does not even roughly concur with the case of a passive particle, but shows a much more complex “S-shaped” trajectory, similar to the macro-scale experiments.

![Figure 5.12](image)

Figure 5.12: A reconstruction of the focusing trajectory of an actuated particle in a quiescent fluid, confined in a channel. The different stages of focusing that have been observed in the experiment result in a much more complex S-shaped focusing trajectory. The inset shows the different forces and fluid profile affecting the particle while the particle levitates from the channel wall and focuses to the axis of the channel.

The above analysis indicates complete different physics of the focusing mechanism, which results in the much more complex s-shaped focusing trajectory. In contrast with the situation described in 5.3.1, the fluid surrounding the particle only gets into motion by the viscous drag forces induced by the particle motion itself; therefore the particle now moves faster than the fluid with a much higher velocity ratio \((v_p / v_{f,avg} \approx 5-10)\). The local fluid velocity profile around the particle is also completely changed as shown in the bottom simulation pictures in Figure 5.10, where the bulk of the fluid is passing the particle on its channel-axis oriented half-sphere surface. This change in relative fluid velocities at the wall-side oriented half sphere surface (fluid velocity is now lower) and at its channel-axis oriented half-sphere surface (fluid velocity is now higher) results in the pressure difference that forces the particle towards center. Moreover, the induced reversionary rotation leads to an even higher velocity gradient, amplifying the focusing effect.
5.3.3. Actuated Particle Rotation Analysis

Remarkably, only a few publications have been found indicating the counter-rotation phenomenon, but only for actuated particles on the macro-scale and are not yet completely understood [74]. Moreover, our observations that rely on a similar mechanism on the micro-scale have to our knowledge not yet been described. The discussion of the focusing effect of an actuated particle in a microchannel has clearly indicated that the change in fluid to particle velocity and especially the reversionary particle rotation are the driving factors for the focusing effect, which are rather complex compared to the case of a passive particle.

![Diagram of particle rotation](image)

For better understanding, the particle rotation velocities that have been calculated with the 3D CFD model are now plotted as a function of the particles radial position in Figure 5.13, for both a passive particle (dashed line) and an actuated particle (solid line). The particle rotation is normalized to its translation velocity, as the simulation results show that the particle rotation \( \omega \) is proportional to its translation velocity \( v_p \). Negative values for \( (\omega r_p)/v_p \) indicate a co-rotation as if the particle rolls over the channel wall. In this case, the exact value of \( (\omega r_p)/v_p = -1 \) indicates perfect rolling without any slip. Positive values of \( (\omega r_p)/v_p \) indicate counter-rotation of the particle, as observed for the case of an actuated particle (see Figure 5.10). Close to the wall at \( x = R - r_p \), both particles perfectly roll over...
the surface without showing any slip \((\omega r_d)/v_p = -1\). The passive particle slowly decreases its co-rotation; until it experiences no rotation anymore at the position on the channel axis \((\omega r_d)/v_p = 0\). The actuated particle however starts to change its rotation direction once it is released from the channel wall (approximation \(x = R - 1.1r_d\)). The counter rotation of the particle reaches a maximum of \((\omega r_d)/v_p = 0.5\), indicating a shear velocity between the particle and channel wall of nearly 1.5 times its translational velocity. Further away from the channel wall, the counter-rotation velocity vanishes again at the position on the channel axis \((\omega r_d)/v_p = 0\). The computed curves both show the same trend as the calculated curves for the focus trajectories, which indicates that the rotation is one of the main driving effects that induces the focusing.

5.4. PARTICLE OSCILLATION BY MICRO FLUX-GUIDES

The previous sections have shown that the particle motion in confined fluidic systems can be influenced by particle confinement and magnetic and hydrodynamic particle-particle interactions. In fact, the momentum transfer from a particle to the surrounding fluid and potentially back to a nearby particle highly affects the particles motion in velocity and direction, even in a rotational degree. As a next step, this section will study the influence on the particle motion by locally induced oscillating field gradients with much higher values in contrast with the studies performed in section 5.2 and 5.3. For these experiments, the micro flux guide array setup is used that was described in section 3.4. Aspects as maximum crossing velocities of different kinds of particles are measured, and the particle trajectories are analyzed by altering the control scheme of the external applied rotational magnetic field.

5.4.1. PARTICLE VELOCITY MEASUREMENT

In order to analyze the maximum performance of the micro-flux-guides array in terms of particle actuation, a first set of experiments was carried out by measuring the maximum single particle velocities in a steady and quiescent flow. The flux guide array on the chip is magnetized by applying an external rotating magnetic field as already explained in section 3.4. For ease of visibility, the larger Spherotech particles were used \((r_p = 11.2\mu m)\). As the travel distances of the particles was very small and comparable to the size of the channel diameter \((2R = 75\mu m)\), it appeared to be difficult to accurately measure the actual velocity of a particle while crossing the channel. Instead, the particle travel was tracked over time while applying an oscillating external field that instantly switches the direction of the
magnetic force. The switching frequency was gradually increased until the particle was not able to fully reach and touch the channel walls anymore. The maximum switching frequency in this situation was determined to be 3.0Hz. In other words, at this setting the particle was able to cross a distance of \( x = 4R - 4r_p = 105 \mu m \) within \( 1/3 \) seconds, which results in an average crossing velocity of \( 320 \mu m/s \). Assuming a parabolic velocity distribution over its trajectory, the maximum particle velocity is calculated to be \( v_{p,max} = 450 \mu m/s \).

The same experiment has been performed for the smaller Dynal MyOne particles \((r_p = 0.5 \mu m)\). The maximum switching frequency was determined at the same value of 3.0Hz, but the crossing distance is in this case increased to \( x = 4R - 4r_p = 148 \mu m \) giving an average velocity of \( 440 \mu m/s \) and a maximum particle velocity of \( 630 \mu m/s \). The smaller radius of these particles would expect to result in much lower velocities; however the magnetic susceptibility is much higher for these particles as can be seen in section 2.1. In this case, these two variations appear to compensate and result in velocities of the same order of magnitude, but are both very high compared to the velocities that were measured with the other experimental setups.

5.4.2. **Shape Control of Particle Trajectory**

Next to the amplitude and frequency of the applied magnetic field, also the shape of the control signal can be varied. For an instant switching between the two preferred magnetization directions of the flux guides, a square-shaped control signal can be applied. If a sinus-shaped control signal is applied, the transition between the two preferred magnetization directions will be more gradual and smoother. As already confirmed in the previous section, the square-shaped control signal simply results in an almost purely radial motion between two opposite pole tips. A second set of experiments was performed in order to analyze the influence of the control signal on the shape of the particle trajectory. If the control signal is gradually changed from square-shaped towards a sinus-shape, the particle trajectory widens in axial direction until the particle practically describes a circular trajectory as shown in Figure 5.14 for the case of the large Spherotech particles. A maximum field frequency in the order of 1Hz was determined to allow the particle to follow the complete trajectory that exactly fits between the pole tips.

The same experiments have been performed with the Dynal MyOne particles. Instead of using a dilute sample and tracking the motion of only one particle, here small particle chains were tracked that formed as a consequence of a concentrated sample \((= 5\cdot10^8 \) particles/ml). The assembled structures showed a similar trajectory shape as found for the larger particles. However, the influence of the chain formation was observed by a change
in chain orientation as function of the angle of the local field lines between two constituent magnetized flux guides, as shown in Figure 5.15. In this case, a frequency of only 0.5Hz was used as higher frequencies obstructed the ability to visualize the particles and chains of particles in motion. Nevertheless, from the maximum velocity experiments in section 5.4.1 that showed similar values, the maximum frequency that could be applied here should be in the same order as for the larger Spherotech particles, hence 1Hz.

Figure 5.14 An overlay of snapshots at different moments in time (1 = 0.0s, 2 = 0.2s, 3 = 0.6s, 4 = 0.8s, 5 = 1.0s, 6 = 1.2s) to illustrate the particle trajectory while applying a sinus-shaped control signal. The particle will travel in a rotational trajectory that meets with the pole tips (not shown on the picture), at a maximum frequency of about 1Hz.

Figure 5.15 A similar experiment performed with the smaller Dynal MyOne particles to illustrate the particle trajectory and the chain alignment in a sinus-shaped rotational field (0.5Hz). The different positions of particle chains are emphasized with the ellipse shaped markers, as the particle (and chains) were very difficult to visualize in motion.
5.5. DISCUSSION

Within spatial confinements of a microsystem, the interactions between particles, fluid, and nearby walls were studied. Different particle configurations were observed. The configurations appeared to be influenced by the strong short-range magnetic interactions and the weaker but longer ranged hydrodynamic interactions. At high fields (50 mT in our case) the particles aggregate in chains oriented perpendicular to their motion direction. At low fields (10 mT in our case), the hydrodynamic interactions appeared to generate unforeseen self-organization phenomena.

For instance, superparamagnetic particles aligned on the channel axis successively organize towards a stable poly-twin system, which could be explained by a 1-dimensional model based on the axis flow profile. This behavior was further validated with 3D CFD models. In this case, calculations for the influence of magnetic repelling interactions resulted in a small remaining intraspaceing in the order of a particle radius to a particle diameter, which is in agreement with the experimental observations. In addition, particles traveling close to a channel wall show complex reversionary rotation behavior. Four different stages of focusing could be observed, where the rotation shift from co-rotation to counter-rotation appears to be the driving factor for the s-shaped focusing trajectories towards the channel center. Using micro-scaled flux guides on chip that generate high magnetic field gradients, the particles reached amplified velocities and could be controlled in their circular pathways within the channels.

This chapter made the first step to visualize the particle behavior under the effect of adjacent boundaries. The discussed hydrodynamic momentum transfer between the particles already indicates that local fluid velocity profiles are heavily influenced by the presence of the particles. Therefore, the next Chapter 6 will study these effects numerically, for the application of particles acting as fluid drivers in high-surface-area microsystems.
Chapter 6

SUPERPARAMAGNETIC PARTICLES AS FLUID DRIVERS

In the previous chapters the effects of magnetic and hydrodynamic particle-particle interactions were analyzed in detail. It was shown that the hydrodynamic momentum transfer from particle to its surrounding fluid (and back to neighboring particles) can dominate over magnetic particle interactions. The same hydrodynamic momentum transfer between the particles also influences the motion in velocity and direction of the surrounding fluid. This effect allows using superparamagnetic particles as integrated fluid drivers in high surface area microsystems, which is studied in this chapter. Several particle configurations that were observed in the previous experiments in confined microchannel systems (see Chapter 5) will be analyzed on the basis of their fluid driving performance and efficiency for microfluidic pumping and local mixing purposes.

In condensed form, sections 6.1 and 6.2 are published in Microfluidics and Nanofluidics \cite{46} and section 6.3 is submitted for publication.
6.1. CFD SIMULATION MODELS

To investigate the fluid driving effects of the particles in the experimentally observed configurations, two numerical simulation models have been developed using Comsol Multiphysics\[^{[54]}\]. In the first model, particles or chains aligned and traveling along the channel axis (similar to the observation in Figure 5.1a) are studied by a two-dimensional axi-symmetric CFD model. The second and more complicated configuration of particles off-axis or chains centered but oriented perpendicular to the channel axis and their motion direction (as the case of Figure 5.1b and Figure 5.1c) is studied by a full three-dimensional CFD model. In both models, a micro channel with no-slip boundary walls is assumed with radius \( R \) and length \( L = 100r_p \), which is filled with fluid with a density \( \rho_f = 1000\text{kg/m}^3 \) and a viscosity \( \eta_f = 1\text{mPa-s} \).

The actuated particles that are used in this model have the same properties as the used Spherotech particles \[^{[35]}\] in the confined channel system experiments (\( r_p = 11.2\mu\text{m} \)). On each particle a magnetic force of \( F_m = 1.33 \times 10^{-11} \text{N} \) is applied, as a consequence of an external applied magnetic field with \( B = 10\text{mT} \) and \( \mu B^2 = 0.1\text{T}^2/\text{m} \). The particles are modeled as individual domains within the channel by setting a several orders of magnitude larger viscosity: \( \eta_l = 1\text{Pa-s} \). To avoid influences from possible entrance and exit effects, particles are positioned at least 10 times its diameter away from the inlet and outlet \[^{[75]}\]. As in the experiments, the fluid flow is laminar (\( \text{Re}<<1 \)) and Brownian motion can be neglected. In this regime, the models are fully scalable and results are therefore normalized to the particle radius \( r_p \) or the calculated single particle velocity \( v_{p_r} \), where possible.

6.2. AXI-SYMMETRIC ALIGNMENTS FOR MICROFLUIDIC PUMPING

Several papers have addressed the use of magnetic particles for fluidic pumping on the micro-scale \[^{[76]}\][^{[77]}\]. However, most examples use an oil-based solution with irreversibly aggregated plugs of enormous numbers of ferromagnetic nano-particles that drive the fluid as a whole. The proposed systems are hard to match to micro channel dimensions, and harmonization of channel-to-particle dimensions is not considered. To understand the influence of local magnetic and hydrodynamic particle interactions on the application of integrated microfluidic pumping, the following section will study the particle pumping performance in the observed particle configurations.
6.2.1. **CONFINED PARTICLE OR CHAIN VELOCITY IN A MICROCHANNEL**

The axi-symmetric model is used to study the influence of the channel confinement on the velocity of a single particle or a number of particles lined up along the channel axis (as seen in the experiments, Figure 5.1a). In this simulation the channel-to-particle radius ratio $R/r_p$ is being varied ($R$ is varied where the $r_p$ is kept constant) and the particle velocity $v_p$ is calculated. In the case of more particles the interspacing is kept small to $s = 0.1r_p$, where the average of all particle velocities is calculated and presented as a single data point. In Figure 6.1 the particle or chain velocity in the confined state $v_{\text{channel}}$ is compared to the velocity of a single particle in an open fluid volume $v_{\text{free}}$ as calculated with equation 2-7.

![Diagram showing particle or chain velocity in a microchannel](image)

Figure 6.1  Simulation results to study the particle or chain velocity as function of the channel-to-particle radius ratio. Similar to the case of particles in an open fluid volume, longer chains or rows of particles move faster. On the other hand, the channel wall confinement slows down the particles or chains.

The simulations show that hydrodynamic interactions of the no-slip channel walls force the particles to slow down while getting more confined. In the case of more particles in a row, the average particle velocity is increased, as was also predicted by the 1D simulation model that explained the particle twinning. Moreover, the shape of the curves shows a behavior similar to the case of chains in open fluid volumes (section 4.3). Therefore, a first order approximation of the velocity of a confined particle or particle chain is fitted using equation 2-7 as the starting condition for the particle or chain velocity in case of very high
values of $R/r_p$, as this situation is practically similar to an open fluid volume. Fitting the simulation results for different values of the number of particles in the chain results in the following equation applicable for single particles or particle chains that takes into account the channel confinement effect ($R$-squared-value = 99.95 and in consistency with literature for a single confined particle [78]):

$$\vec{v}_{\text{channel}} = \frac{R - r_p}{R + r_p} \vec{v}_{\text{free}}$$  \hspace{1cm} 6-1

6.2.2.  **INDUCED CHANNEL OUTFLOW BY PARTICLES AS FLUID DRIVERS**

The channel to particle confinement also influences the particles capability to actuate the fluid within the channel. The average fluid channel outflow is the most important parameter to describe the pumping performance of the magnetic particles acting as fluid drivers. The next simulation therefore calculates the obtained average fluid velocity $v_f$ at the outlet as function of the particle confinement given by the $R/r_p$ ratio. The volume of the particles present in the channel is subtracted from the calculated outflow to obtain the fluid flow. The simulation results are based on the axi-symmetric model where only one channel is considered. To reflect the case of a multi-channel system the obtained volumetric flow rate is divided by the channel cross-sectional area to obtain the average fluid velocity, as smaller channel diameters allows for more channels on the available system surface. A high fluid flow is reached if particles reach a reasonable velocity itself, but should on the other hand create sufficient drag on the surrounding fluid. As shown in Figure 6.2, the highest average fluid velocity is obtained at a channel-to-particle radius ratio $R/r_p$ between 5 and 10, and is proportional to the number of particles in the system.

Next to the variation in particle confinement, the influence of different particle configurations is studied for the case of axial aligned particles on the channel axis. The radius ratio in this simulation is now fixed at $R/r_p = 5$. Similar to the experimental observations, the average interspacing between particles is being varied. Spreading the particles reduces the exchange of momentum between particles leading to lower particle velocities, but increases the effective fluid drag per particle. These effects appear to compensate each other beyond an average interspacing of $s > 5r_p$, where particles are less affected by local disturbances in the fluid flow profile induced by a neighboring particle. Moreover, the resulting average fluid outflow that was analyzed in Figure 6.2 is not affected by the spreading of the particles, as spreading only influences the particle residence time in the channel. This effect is described as the pump efficiency per particle, calculated by the ratio between the induced fluid velocity and the particle velocity $v_f/v_p$ as
presented in Figure 6.3. If more particles are added to the system, this pump efficiency increases proportionally to the number of particles, similar to the case of the pump performance. The fluid velocity can then exceed 10% of the average particle velocity.

Figure 6.2  Numerical simulation results of the induced fluid flow by particles as fluid drivers, for the case of \( s = r_p \) and \( L = 100r_p \). The highest fluid flow rate is reached at \( R/r_p = 5\text{-}10 \).

Figure 6.3  Analysis of the particle pump efficiency for the case of \( R = 5r_p \) and \( L = 100r_p \). Equidistant spreading of the particles enhances the particle pump efficiency defined as \( v_f/v_p \). The pump efficiency and performance increase proportionally to the number of particles in the system.
6.2.3. **Reduction in Channel Pressure Drop**

As was discussed in Chapter 1, one of the main problems to challenge in microfluidic systems is the enormous pressure drop required to reach reasonable fluid velocities. Equation 1-3 showed that for a pressure-driven system described by the law of Poiseuille, linearly downsizing the channel diameter results in a quadratic increase of the required pressure over the channel to maintain the same average fluid velocity. Figure 6.4 represents the maximum values of the particles-induced pressure drop in the channel obtained from the axi-symmetric model. The results are normalized to the pressure drop required in a pressure-driven system for the same fluid outflow.

In the case of spread particles in a channel being used as fluid drivers, the pressure drop over the whole channel is distributed into multiple smaller pressure drops over each particle. The pressure drops are reduced further by the spreading of particles. The pressure reduction is proportional to the number of particles added to the system. In the case of a channel filled with evenly spaced particles, the required pressure can decrease to only 10% of the pressure required if using a pressure-driven pump mechanism (not shown in the graph).

![Equidistant spreading of the particles reduces the internal pressure drops within the micro channel considerably. In case of a fully loaded channel with particles on the axis (in this case $R = 5r_p$ and $L = 100r_p$, $n = 30$) having an interspacing of $s = r_p$, the required pressure reduces to only 10% of the value that was calculated for a pressure-driven system to obtain the same fluid outflow (line falls beyond the boundaries of the graph).](image-url)
6.2.4. **Influence of Formed Chains in Perpendicular Orientation**

As seen in the experiments, at high fields the initially axially aligned particles leave their common center axis of motion and possibly form chains perpendicular to their motion direction. In order to study the effects of this configuration transition on the particle pumping performance, the 3D CFD model has been used to calculate the actual fluid channel outflow as function of the chain length expressed as the number of particles \( n = l_c/2r_p \). The channel radius is again fixed at \( R = 5r_p \) and therefore the size of the longest chain is set to be \( n = 4 \), which is just fitting in the channel without physically touching the channel walls. The velocity of a chain in this perpendicular orientation increases as a function of its length (in the simulation valid up to \( n = 3 \)). However if the chain length is further increased, the ends of the chain approach the channel walls and slow down the entire chain (in the simulation for \( n = 4 \)), which can result in curved chains or break-ups.

If the induced fluid outflow by chains in this configuration is calculated, the simulation shows that longer chains result in a higher fluid outflow as shown in Figure 6.5. However, as already concluded from the chain velocity analysis, particles within the chain that are located away from the channel axis experience more drag by the channel walls and therefore lower the pump efficiency. The increase in fluid outflow with the number of particles within the chain is therefore less than proportional, as was the case of particle chains aligned along the channel axis (section 6.2.2). The contributions of multiple chains can still be linearly superposed and these do not depend on the interspacing.

![Figure 6.5](image)

**Figure 6.5** Simulations results of the average fluid outflow induced by particle chains oriented perpendicular to their motion direction, for \( R = 5r_p \) and \( L = 100r_p \). Longer chains result in higher fluid velocities, as long chain-end particles are not nearby the channel walls.
6.3. **Mixing Effects by a Single Actuated Particle**

In addition to the previous analysis of fluid outflow parameters on system level, superparamagnetic particles acting as fluid drivers will also affect the local fluid flow profile. This effect could potentially enhance mixing. In order to visualize the effect of a moving particle on the fluid, the 3D simulation model has been used again \(^{[54]}\). A collection of fluid elements is tracked while a particle is passing by. The fluid elements are initially distributed on a line element from \(x = -R\) to \(x = R\), at the radial position \(z = 0\). The travel of the actuated particle starts before this line at \(z = -10r_p\) and continues in axial direction until no effect is induced anymore on the fluid elements. In the following examples, the simulation is stopped as the particle is positioned at \(z = 20r_p\). A channel radius of \(R = 5r_p\) is again chosen, together with a channel length \(L = 100r_p\), which is the same as in the previous simulations.

6.3.1. **Fluid Motion Induced by a Particle Traveling On-Axis**

In Figure 6.6, an axially symmetric collection of fluid trajectory lines is calculated for an actuated particle that travels exactly through the center of the channel as found in the experiments (see Figure 5.1a). As a consequence of the axially symmetric position, the particle will not experience any rotation. The particle travel is indicated with the gray area, and the fluid trajectory lines are plotted as solid lines. Near the channel axis, most of the fluid is driven in the same axial direction as the particle motion, which is considered as the main cause for the net fluid outflow that was calculated in section 6.2.2. However, the fluid trajectory lines show that the particle motion locally disturbs the fluid in different directions.

![Figure 6.6](image_url)  
Simulation of the induced fluid motion by an actuated particle in the center of a channel \((R = 5r_p\) and \(L = 100r_p)\). The shaded area indicates the travel of the particle and the solid lines the travel of fluid elements that were initially distributed on the line \(z = 0\). If a particle travels in the center of a channel and has no rotation, the fluid is mainly disturbed in the center in axial direction.
Focusing to the fluid elements near the channel wall, the simulation reveals that the particle confinement (in this case \( R = 5r_p \)) results in local backflow effects. Moreover, the spherical shape of the particle also induces fluid actuation in a radial direction, especially near both sides of the particle at \( x = \pm r_p \). As a consequence of the particle moving in the center of the channel, the main fluid motion and intermixing is observed in the path of the particle (shaded area). Close to the channel walls hardly any fluid motion is found.

### 6.3.2. Fluid Motion Induced by a Particle Traveling Off-axis

Next to centered particles that show no rotation, experiments also have shown rotating particles that travel off-axis (see section 5.3.2). The rotation transitions of an actuated particle while focusing was one of the most notable phenomena that was analyzed in detail. Simulations on the particle rotation revealed that in the case of \( R = 5r_p \), the particle rotation could reach \( \omega = (0.5v_p)/r_p \). In other words, the location on the particle that is the closest to the axis will only experience an axial velocity of \( 0.5v_p \), where the point on the particle that is the closest to the wall will experience a much higher axial velocity of \( 1.5v_p \).

To illustrate the effects on the fluid motion, Figure 6.7 shows the calculated fluid trajectory lines in case of a traveling off-axis rotating particle at a constant radial position \( x = 0.5R \). In this simulation, the main axial fluid motion is again observed in the path of the actuated particle (grey area). On average, the fluid trajectory lines are much longer (up to 2 times as long) than in the case of a centered actuated particle. This effect is clearly visible between the channel wall and the particle, as a consequence of the locally high shear velocity that was mainly induced by the counter-rotation of the particle. A comparison of both figures indicates that an off-axis particle creates a much higher fluidic exchange in both axial and radial direction, especially in the low velocity areas near the channel walls.

![Figure 6.7](image.png) Simulation results of an actuated particle that travels halfway between the channel center and wall \( (x = 0.5R) \), which induces a high fluidic exchange especially in the low-velocity regions near the channel walls.
6.3.3. **Mixing Rate Calculations**

The most straightforward way to determine the mixing rate in laminar systems is to analyze the rate of stacking and folding of fluid layers, which is known as the Bakers transformation \(^{[17]}\). The above illustrations already show that fluidic mixing is performed by a traveling particle in a centered position and especially in off-axis direction, indicated by the disturbances and intersecting fluid trajectory lines. To give a more quantitative measure for the mixing performance, the rate of stretch of the presented lines of fluid elements at \(z = 0\) is calculated for both situations described in sections 6.3.1 and 6.3.2. The rate of stretch \(\lambda\) for both axial (\(z\)) and radial (\(x\)) directions is normalized to the axial distance covered by the actuated particle \(\Delta z_p\), according to:

\[
\lambda_z = \frac{1}{q} \sum_{i=1}^{q} \left| \frac{z_i^{f,\text{max}} - z_i^{f,\text{min}}}{\Delta z_p} \right| \quad \text{and} \quad \lambda_x = \frac{1}{q} \sum_{i=1}^{q} \left| \frac{x_i^{f,\text{max}} - x_i^{f,\text{min}}}{\Delta z_p} \right|
\]

Applying the set of equations 5-3 to the case of an actuated centered particle, average rates of stretch are calculated for the axial direction \(\lambda_z = 7.08\%\) and radial direction \(\lambda_x = 4.42\%\). The same calculations for the case of a rotating particle that is traveling off-axis at \(x = 0.5R\) gives average rate of stretch values for axial direction \(\lambda_z = 11.93\%\) and radial direction \(\lambda_x = 8.21\%\). The calculated values again show that an off-axis particle is much more effective to create local fluidic mixing as opposed to a centered particle. Moreover, if the position of maximum rate of stretch is calculated, the centered particle example calculates maximum values for \(\lambda_z\) at \(x = 0\) and for \(\lambda_x\) at \(x = \pm r_p\). In case of the off-axis particle the maximum rates of stretch are calculated at \(x = 0.5R + r_p\) for both \(\lambda_z\) and \(\lambda_x\), which is the particle area located at the closest distance to the channel wall.

In order to compare the calculated fluid velocity to the situation of molecular diffusion limited transport, the Péclet is the next parameter to be considered (see section 1.2). For the calculations, the real values from the experiments in section 5.1 are used: particle radius \(r_p = 11.2\mu m\), particle velocity \(v_p = 100\mu m/s\), channel radius \(R = 5r_p = 56\mu m\). The absolute fluid velocity is calculated from the plots shown in Figure 6.6 and Figure 6.7. The length unit in the Péclet number is represented by the channel radius. Figure 6.8 shows calculations for the Péclet number as function of different diffusion constants. Values giving \(Pe > 1\) indicate convection dominated mixing, indicated in the white area. Both situations show that the fluid mixing is convection dominated for diffusion constants below \(10^{-10} m^2/s\). In fact, the particle velocity could even be increased to \(500\mu m/s\) (see section 5.4) which induces convection dominated mixing already for \(D \leq 10^{-9} m^2/s\).
Figure 6.8 Calculations for the Péclet number for the rate of convection induced by an actuated particle. Both situations (particles actuated on-axis and off-axis) induce mixing that dominates diffusion for $D$ below $10^{-10}$ m$^2$/s.

Figure 6.9 Calculations for the Péclet number as function of the radial channel position for $D = 10^{-11}$ m$^2$/s. The maximum rate of convection is amplified and shifted towards the channel wall surface for the case of a particle traveling off-axis.

Considering diffusion constant values for proteins or DNA molecules ($D = 10^{-11}$ m$^2$/s), actuated particles could therefore be supportive for mixing of biological material such as DNA or proteins. For most applications mixing is especially required near channel surfaces; therefore the Péclet numbers are also calculated as function of the radial position within the channel for $D = 10^{-11}$ m$^2$/s, as shown in Figure 6.9. As was already expected from out the fluid trajectory calculations in Figure 6.6, the actuated particle traveling on-axis induces advection dominated mixing especially in the center of the channel. The actuated particle traveling off-axis at $x = 0.5R$, induces advection dominated mixing more close to the channel wall surface (also see Figure 6.7).
6.4. **DISCUSSION**

This chapter has studied the application of magnetic particles as integrated fluid drivers in high surface area Microsystems, by analyzing the effect on the fluid motion by the particle configurations that were observed in the experiments shown in Chapter 5. In case of the application for microfluidic pumping, simulations have shown that the highest fluid outflow is achieved with particles lined up on the channel axis, at a channel-to-particle radius ratio $R/r_p$ ranging from 5 to 10. If the particles are spread out along the channel, the highest particle pump efficiency can be reached, where the average fluid outflow velocity can exceed 10% of the average particle velocity. The spreading of particles considerably lowers the required pressure drop in the channel to only 10% of what is required in a pressure-driven system.

Particle chains in a perpendicular orientation increase the average fluid outflow, but the pump performance and efficiency per particle is lower compared to the case of axial configurations. On a more local scale, actuated particles also amplify fluidic mixing within the channel. Moreover, off-axis particles that counter-rotate can induce high rates of fluid stretch in both axial and radial direction, especially between the particle wall-side surface and the channel wall itself, where fluidic exchange is usually very low.

Next steps would involve the experimental validation of actual fluid outflow velocities, reductions of the required pressure drops and the local mixing efficiency induced by particles in motion. However, the experiments presented in Chapter 5 have shown that particles continuously reorganize in different configurations. The channel confinement on the particles even cause amplified particle-particle interactions, which obstruct accurate measurement of the mentioned performance parameters.

Nevertheless, the shown mechanisms of fluid actuation by magnetic particles can be fully integrated in a porous system, without generating dead fluid volumes. The local particle actuation could be carried out using miniaturized current wires or soft magnetic field concentrators as already shown in section 5.4. The investigated situations that up to now only considered the effects of a single particle should be extended to more particles, which would enhance chaotic advection within a microsystem. Moreover, integrated fluid actuation by magnetic particles can also be used in dead-end micro pore systems, where pressure-driven systems are completely ineffective for the exchange of fluids.
Particle dynamics feels like music: Interplay and interactions are the integral parts, which are as important as the music notes or individual particles. — Adopted from a quote of John Mc Laughlin, English guitarist / composer.
7.1. **CONCLUSIONS**

Devices for biosensing often contain high-surface-area elements for efficient reaction kinetics. Within microfluidic applications it is a challenge to find an integrated fluid actuation technique that facilitates pumping with reasonable flow rates, while having a robust control on local fluid replenishment and mixing near no-slip surfaces. Pressure-driven systems are not favorable on the micro-scale due to scaling effects by the high surface-to-volume ratio. Therefore, there is an interest in the use of superparamagnetic particles in lab-on-a-chip systems for fluidic actuation, supported by their multifunctional purposes and flexible motion control. The fundamental dynamics and interactions of particles within a microfluidic system were studied in this thesis. In literature the magnetic interaction forces are often taken into account by a point-dipole approximation, which we found can deviate 64% from numerical simulations if particles are in contact. Furthermore, hydrodynamic interactions are often not considered, while our simulations revealed that these interactions can dominate over magnetic interactions at a distance of only a few particle radii away ($s = 2r_p$). This is especially of concern at system level for a particle-loaded fluid, where the longer ranging hydrodynamic interaction forces ($\sim 1/s$) dominate over the magnetic interaction forces ($\sim 1/s^4$).

For experimental studies, three different setups were designed. First, a “4 orthogonal solenoid” setup was created for our particle studies in open fluid volumes of about 1µl. This setup is able to apply particle forces proportional to $DB^2 = 1T^2/m$ where the magnetic field shape is highly configurable in strength and direction. Second, an “isodynamic pole-shape” setup was created in order to apply constant actuation forces on individual particles traveling in a microchannel. Magnetic field measurements revealed that the final design could achieve a constant value for $DB_{\text{max}}^2 = 0.22\pm10\%T^2/m$, over a microchannel of 4mm. Third, a “micro-flux-guide array” setup was created on the basis of shape anisotropy of embedded magnetic micro structures to locally amplify magnetic forces proportional to $DB_{\text{max}}^2 = 10T^2/m$.

Using the “4 orthogonal solenoid” setup, the motion of single superparamagnetic particles was measured. The experimental results deviate from the theoretical predictions by a relative error $RE = 0.33$. The measurements also showed a high variation in velocities, quantified by a coefficient of variation $CV = 0.22$. Most probably the offset and spread in velocities is caused by the variation and distribution of magnetic material within different particles. If concentrations above $5\cdot10^8$ particles/ml are used, magnetic interactions appear to support the formation of particle chains. Chain lengths up to 26 particles were observed and velocity measurements revealed that longer chains move faster. The velocity enhancement was modeled as a function of the number of particles in the chain.
and shows a logarithmic behavior owing to a magnetization enhancement (calculated to be 1.2 for chains having more than 5 particles) and a varying hydrodynamic drag by the shape elongation. Particle chains in rotating fields were modeled as a mechanistic pin-joint model, which revealed that the chain rupture is only a function of the Mason number (ratio between viscous and magnetic forces). In fact, the maximum number of particles within a chain in rotation that does not rupture was calculated to scale as $n_{\text{max}} \propto Mn^{-0.5}$.

The dynamics of superparamagnetic particles within microfluidic channels were studied using the “isodynamic pole-shape” setup. Experiments revealed that at low fields of $B = 10\, \text{mT}$ applied perpendicular to the axis of motion, particles line up on the channel axis and form a stable poly-twin formation. Within a twin the remaining intraspacing results from a balance between magnetic repelling and hydrodynamic attraction. The intraspacing $s$ was experimentally found as $s = r_p$, which matches with our calculations that gave $s = 1.18r_p$. At high fields of $B = 50\, \text{mT}$ the magnetic interactions forces drive the particles to go off-axis and form chains perpendicular to their motion direction. Individual particles traveling close to a channel wall show a complex rotation behavior. In contrast with passive particles flowing along with a flow, actuated particles start to counter-rotate observed as an anti-rolling close to the surface. The particle rotation results in shear velocities between the particle and channel wall of 1.5 its translation velocity. Using the “micro-flux-guide array” setup we found the particles could reach amplified velocities between 320 $\mu\text{m/s}$ and 630$\mu\text{m/s}$ due to the high forces that where induced locally by the miniaturized flux guides. The particle trajectory within the microchannel could be controlled from a 1-D translational path towards a full circular motion by tuning the control signal shape from a block shape to a sinus shape. In the case of formed particle chains, their alignment could be shifted in different angles varying up to $90^\circ$ with respect to their motion direction.

The particles have also been studied as fluid drivers in microfluidic systems by numerical simulation models. For microfluidic pumping, axial particle configurations induce an average fluid velocity that can go up to 10% of the average particle velocity, at a channel-to-particle radius ratio ranging $R/r_p$ from 5 to 10. Spreading of the particles reduces the induced pressure drops to only 10% of what is needed if a pressure-driven system was used to achieve the same fluid outflow. Regarding microfluidic mixing, actuated particles within a microchannel can induce fluid disturbances in axial and radial direction. Especially particles traveling off-axis are very effective mixing elements for near surface mixing by their counter rotating behavior ($Pe = 1$-$10$). The presented experimental proof and theoretical understanding paves the way for studying actuated particles as well controlled integrated fluid drivers, particularly in miniaturized, high surface area, multi-particle / multi-channel systems.
7.2. **Outlook**

The investigations on the particle dynamics in open and confined fluid volumes revealed interesting phenomena that can in principle serve several functions in lab-on-a-chip systems. However, the application of particles in real magneto-fluidic systems requires further studies on aspects such as the variation in magnetic particle properties, different particle functionalities, up-scaling effects and system integration. In this section we will formulate new research questions that should be addressed to pave the way for technological applications and system implementation.

7.2.1. **Magnetic particle properties**

Our measurements in open fluid volumes revealed a large spread in single particle velocities. Recently published research on this matter supports the indications we found for the polydisperse nature of superparamagnetic particles, and shows that particles can differ a lot in susceptibility \(^{79}\) and even show a remanent magnetic moment \(^{40}\). The particle dynamics and interaction effects we have analyzed will be affected by a spread in particle properties. For instance, magnetic interaction effects depend on the particle volume or material composition. Another example was shown in our studies on rotating particle chains in open fluid volumes, where a single particle of lower susceptibility completely changed the chain dynamics in terms of moment of rupture. The variation in properties of the magnetic particles has to be under control. For functions such as selective separation or sensing, monodisperse magnetic properties are preferred to offer a well defined magnetic moment. Polydisperse magnetic properties could on the other hand be beneficial for inducing chaotic motion in confined systems. Next to the application as fluidic manipulation vehicles, the particle properties such as magnetic content, density and size may not yet be at optimum for the combination with other microfluidic lab-on-a-chip functionalities such as labeling and detection. An interesting step for further analysis is to investigate particle dynamics and interactions as a function of a controlled distribution in for instance particle size or magnetic susceptibility.

7.2.2. **Large ensembles at system level**

We have gained knowledge on the dynamics and interplay at the scale of a few particles, while real applications will require the use of large ensembles of particles \(^{25}\). The studied particle interaction effects could cancel out and vanish for large particle systems in a random orientation, but could also amplify each other as shown in our studies on confined particles in the application of fluid drivers. The experimental setups were designed for
optimal control on particle forces in amplitude and directions. As a result of both, different particle dynamics regimes can exist within a single chip as we have already shown in our confined particle studies. Further analysis is needed in order to quantify the contributions of different particle dynamics regimes on a larger scale. Our presented few-particle descriptions should be integrated into a more statistical approach to account for effects in large ensembles of particles present in real systems.

The design of a magneto-fluidic microsystem mainly depends on the described function requiring a specific degree of particle motion control. This thesis has given several examples at different scales and particle behavior. Our studies showed that the integration and fabrication of passive magnetic field guiding structures on chip appears to be a very promising approach for the integration of particle manipulation control. Solenoids or permanent magnets could be placed just outside the chip for the generation of the required external magnetic fields. However, a cost-effective and functional design for different magnetic field shapes is still an aspect for improvement. Practical issues such as how particles will enter microfluidic pores, how to avoid particle sticking and potential clogging still need to be studied. Furthermore, the motion of particles and particle chains should be confirmed in complex biological samples.

7.2.3. **FUNCTIONALITIES OF ACTUATED PARTICLES**

Our experiments have shown that superparamagnetic particles can in principle be used for accelerated transport in microfluidic systems. For example, amplified particle velocities were reached in our experiments with the help of chain formation. Target molecules can be specifically bound on the surface of the particle, for the particles to act as analyte carriers in a microfluidic system or to perform up-concentration steps in a well controlled way. Particle chains can also be used in external applied rotational magnetic fields as miniaturized mixing elements\[^{64,80,81}\]. Implementation could be possible in larger fluid volumes and in arrays of small and shallow mixing chambers that are a few to tens of a particle diameter in size. Different lengths of chains support chaotic break-up and re-formation processes. Therefore, the mixing efficiency on the fluid itself needs to be investigated experimentally with for instance micro-PIV measurements.

The hydrodynamic momentum transfer of actuated particles shows possibilities for using particles as fluid drivers in microfluidic systems. Superparamagnetic particles can be applied in large as well as small sample volumes, without generating dead fluid volumes. The balance of magnetic and hydrodynamic interactions between particles, fluid and nearby boundaries can be optimized for specific purposes. For example, particles in highly confined systems can be controlled by means of their configuration and interspacing to
support their application as fluid drivers, as schematically shown in Figure 7.1. In addition, single particles that travel off-axis amplify near-surface mixing. The presence of solid-body particles in the confined channel systems disturbs the originally continuous fluid flow profile, which could even result in an irreversible system that supports chaotic motion of the particles in confined systems [82]. Complex off-axis particle configurations shall be further investigated with their influence on system level performance. Pulsed magnetic particle triggering could support zigzag arrangements, in order to optimize fluid driving and mixing at the same time. Our numerical simulations on the fluid driving capabilities need to be confirmed experimentally with for instance micro PIV experiments. In addition to open-ended channels, we foresee that integrated fluid actuation by magnetic particles can be used even in dead-end micro pore systems, where pressure-driven systems are ineffective for the exchange of fluids.

Figure 7.1  A sketch of the fluid driving concept in a micro-pore structure. The sample with analyte experiences difficulties entering the pores and gets trapped. Magnetic particles as integrated fluid drivers (force direction indicated with bold arrows) generate transport of fluid and analyte in and through the pores (indicated by the dashed streamlines).
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LIST OF PUBLICATIONS

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Thanks a lot!

Roy.
Roy Derks was born on the 23th of August 1981 in Nijmegen, The Netherlands. After finishing high-school in June 1998 (HAVO, Scholengemeenschap Stevensbeek, The Netherlands), he started his studies in Mechanical Engineering. In June 2002, he received his Bachelor’s degree in Mechanical Engineering at the Fontys HTS Eindhoven, The Netherlands.

Afterwards, Roy shifted to the Technische Universiteit Eindhoven (TU/e) in The Netherlands, where he specialized in the fields of magnetics, microfluidics and laser-based micro-fabrication. His final internship on magnetic particle manipulation was carried out at Philips Research (Eindhoven, The Netherlands) under supervision of prof.dr.ir. M.W.J. Prins and prof.dr. A. Dietzel. With this work, Roy received his Master’s degree in Mechanical Engineering in September 2005.

In March 2006, Roy started as a PhD candidate at the Technische Universiteit Eindhoven in the group of Micro- and Nano-Scale Engineering. Under supervision of dr.ir. A.J.H. Frijns (Mechanical Engineering, TU/e), prof.dr.ir. M.W.J. Prins (Applied Physics, TU/e) and prof.dr. A. Dietzel (Mechanical Engineering, TU/e), he performed different studies on “particle dynamics in magneto-fluidic microsystems”, which are described in this thesis.

Next to his professional interests described above, Roy has a great interest in working within the interdisciplinary fields of bio-medical technologies and mechanical engineering on the micro-scale. During his free-time, Roy enjoys to practice various sports: volleyball, mountain biking and skiing.