Separation of Mixtures in Microfluidic Devices: A Macroscale Model Using Magnets

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Abstract

The goal of this research was to separate particles in microfluidic devices using magnets. Microfluidics research involves working with liquids on extremely small scales, which makes observing what happens in these devices difficult. Experiments can be performed on the macroscopic scale using the principles of dimensional analysis to translate the findings back to microfluidic devices. Here, magnets were attached to acrylic boards in various patterns, and steel balls of varying sizes were then rolled down the board at a 4° angle or propelled across the board using a flow of water in a sealed tank. In two of the three gravity-based trials, the balls were effectively separated based on size by varying the magnetic field. Through these setups, it was discovered that using varying strengths of magnets was the most effective method of separating magnetically charged particles, and that other methods, such as varying the spacing of same strength magnets, were not as effective.

I. Introduction

In recent years, the growth of microfluidic technology has led to its increased use in various disciplines, from commercial printers to DNA chips. The small amounts of liquid present in microfluidic devices have their own unique properties of flow and reaction rates, and many macroscale properties of liquids do not apply. Fluids are able to mix and react quickly because of these changed properties and small volumes, and their popularity, growth, and success is largely due to these fast reaction speeds. However, separating mixtures in microfluidic devices involves extensive control over factors irrelevant on the macroscale, resulting in an abundance of separation devices that address different concerns and none that are effective for every situation and type of particle.

The primary goal of this research is to fabricate a macroscale model of a magnetic microfluidic separation device by building off of current research in magnetic tagging and microscale technology. While there is an extensive array of microfluidic separation devices, each has its drawbacks. Thus, finding the most effective separation device for all situations is important to the future application of microfluidic devices. Deterministic lateral displacement (DLD) is a method in which differently sized particles are separated using a set of physical barriers. Since this process is based on the collision of the particles with these barriers, the particles may be damaged in certain situations, such as when cells are separated in biological experiments. In this experiment, previous research in microfluidic separation has been expanded through the use of magnets. By using magnets alongside the already established method of DLD, there is promise that future microfluidic devices will be able to separate particles by magnetic strength, charge, and size while minimizing collision and damage.

II. Background

Research into the development of microfluidic devices is full of potential to improve the way scientists work with chemical and biological samples, promising
to make the mixture and separation of fluids on the micro-scale more efficient and cost-effective. Many researchers predict a wave of technological innovations mirroring that of computers; processes will be made more efficient by translating the technology to function on a smaller scale.¹

II.i. Benefits of Microfluidic Devices

A significant benefit of microfluidic devices is their relatively low cost in comparison to traditional lab setups. Because of their extremely small size, microfluidic devices require only very small amounts of fluids to function, which can greatly reduce the costs of expensive chemicals and reagents. Additionally, reactions in microfluidic devices often occur faster because of their high surface to volume ratios, faster heating, and short diffusion distances. Several microfluidic processes can often be combined into one device in what is known as a lab-on-a-chip, named so for its integration of multiple laboratory functions onto a millimeters-long chip. This lab-on-a-chip technology is an extremely significant development, as it is more productive and inexpensive than devices found on larger scales. Overall, microfluidic devices have low cost and fast turnaround, as well as never-before-seen portability, making them important new research tools with myriad uses.²

II.ii. Methods of Microfluidic Separation

There are currently many methods of separating fluid components on the microscale, all of which have their own advantages and disadvantages. One common method, centrifugal separation, works by spinning a container so that particles of different densities settle on higher or lower sections of the container. This process can be very time-consuming and frequently involves other forms of separation in order to be efficient.³

Another separation device is a deterministic lateral displacement (DLD) device, which uses the patterns that particles of different shapes and sizes make through a grid of obstacles in order to predict where different particles will end up.⁴ One of the drawbacks of this system is that the particles must physically collide with obstacles in order to separate, which in some applications would damage particles that must be kept intact, e.g. biological particles.

A more traditional method of separation is filtration, in which solutions are sent through a series of sponge-like structures with holes that only some particles can fit through. Eventually particles are separated by their different sizes or shapes. One important filtration-based separation method often used in biomedical engineering is gel electrophoresis, in which different fragments of negatively-charged DNA are separated according to their size and charge strength. This process takes place in a porous gel. The DNA fragments are loaded into wells and a positive charge is placed at the other end of the gel. The smaller particles are more attracted to the positive charge than the larger particles; therefore the smaller particles move faster and end up closer to the positive end than the larger particles do.⁵

The concept of using magnetism in separation devices has been expanded further in a process called magnetic tagging. Magnetic tagging of cells is an emerging method of drug targeting and bioseparation, important research areas in the medical field. It is used in magnetic resonance imaging (MRI) tests and cancer treatments. Magnetite cationic liposomes (MCLs), positively charged magnetic particles, are used to transport particles to negatively charged cells. MCLs have been useful in creating layers of cells in culture and in
tissue engineering. This concept has been translated into separation techniques to target tumor cells and separate blood cells. An additional method of microfluidic separation utilizes microscopic speed bumps. In a lab-on-a-chip microfluidic device, the aforementioned speed bumps are diagonally slanted ramps, each 1 micron high. Using this device a liquid, such as blood, is poured past this series of ramps, and the ramps cause the particles of the liquid to separate based on discrete factors, including weight and size. As the liquid continues to flow along the ramps, the heavier, larger particles often have a more difficult time crossing the ramps, which causes them to instead travel diagonally along the length of the obstacle. Eventually, the particles end up separated completely; the larger particles travel down one path and the smaller ones on another, allowing for continuous separation.

II.iii. Translating Microfluidics to the Macroscale

Before any of these devices are created on the microscale, they are first modeled on the macroscale. Most research models utilize the concept of dimensional analysis, in which a process is studied at a different size and time scale while keeping the governing principles of physics the same. The most relevant example of a macroscale model to this research utilizes deterministic hydrodynamics. Experiments involving deterministic hydrodynamics recreate a microfluidic array in order to perform a controlled experiment that can then be translated into the microscale. In this model, a lattice was created on a LEGO grid using double-stacked LEGO pegs. This grid was then placed vertically against the wall of an aquarium filled with glycerol, and plastic and steel balls of various sizes were dropped down the lattice to replicate the particles on the microscale. In this model, the larger balls did not move throughout the array or diffuse, and their trajectories could be predicted precisely. However, the smaller balls bounced randomly along the lattice, and no pattern could be predicted. The balls continue to move in these ways no matter the angle at which the board is rotated, an occurrence known as phase locking. Although this research was performed on the macroscale, these results can be translated onto the microscale through dimensional analysis.

Every design and manufacturing process related to microfluidic separation is modeled using an alternative physics explaining microfluidic motion. This other physics of particles on the nanoscale actually refers to the drastically increased importance of three phenomena: Brownian motion, surface tension, and the surface-to-volume ratio. While movement of fluids on the macroscale is directed primarily by pressure and gravity, on the microscale it is controlled more by the bonding of molecules (surface tension) and the kinetic energy of all molecules above absolute zero (Brownian motion). The surface-to-volume ratio is a measure of the influence that molecules on the surface of the fluid have on the movement of the fluid itself; both values are drastically higher on the microscale. Macroscale models of microfluidic devices must therefore attempt to account for factors that do not actually influence them. The Brownian motion issue has been successfully dealt with in certain microfluidic models, including DLD devices. Skepticism that Brownian motion would render the motion of fluids in the microscale device unpredictable was invalidated when tests showed the fluids moved just as predicted in the macroscale model.
All of this research is crucial to understanding the implications of microfluidic separation in regards to the following project, which explores the use of magnets in the fabrication of a microfluidic device.

III. Creating Macroscale Models with Magnets

III.i. Materials and Devices

Each setup used an acrylic board of either 0.15875 cm or 0.3175 cm thickness as the base. Three different sizes of steel beads were used to imitate the particles in the separation device. The smallest beads were 2.0 mm in diameter, the medium-sized beads were 3.5 mm in diameter, and the largest beads were 5.0 mm in diameter. Round disk magnets, strip magnets, and strong bar magnets were used to attract the variously sized beads. Double stick tape was used to attach the magnets to the boards. Additionally, a protractor was used to measure the angle of the incline of setups in which gravity was the driving force.

In all three gravity-based setups, the steel beads were dropped randomly from one of seven starting points at the top of the magnetic patterned board. To ensure that there was a degree of consistency as the beads were randomly dropped, a piece was printed on The Replicator, a dual-extruding fused deposition modeling (FDM) 3D printer. The piece is 19.3675 cm long, 5.55625 cm wide, and 1.27 cm tall with pathways carved out every 1.08 cm for the beads to roll down. The piece was also angled slightly to ensure that all beads would have the same velocity as they rolled down the 3D printed origin piece and onto the magnetic pattern.

III.ii. Gravity-Based Magnetic Separation

Three different setups were fabricated for use with gravity-based separation, each exploring a different aspect of the relationship between magnets and gravity.

![Diagram of Setup 1](image)

Figure 1: Diagram of Setup 1

The first setup (Figure 1) is meant to separate the variously sized beads based on their relative momentum and their distance from the magnets. The model is a series of two or three steps, depending on the trial, on top of a level magnetic surface. The beads are dropped from the slightly angled 3D-printed dispenser so that they roll down onto the highest step. Their momentum and size determine if they will be trapped at the highest step or if they will roll onto the other steps that are closer to the magnetic surface.
The second setup (Figure 2) was based off of the first setup, but instead of changing the distance between the magnets and the beads, the strength of the magnets was altered. The setup consisted of 2.54 cm wide weak strip magnets, strong disk magnets spaced 2.54 cm apart and a 48 mm wide powerful bar magnet in three separate sections on an acrylic board. The board was placed at a 4º angle. The beads were first rolled across the weak magnets and continued to traverse the disk magnets and then over the bar magnets. The beads were expected to be trapped at different locations based on their size.

For the third setup (Figure 3), a diagonal lattice with varied spacing was created. The first two rows, with the widest spacing, had magnets each spaced 5.08 cm apart horizontally and vertically and 7.18 cm apart diagonally. The next set of four rows had magnets spaced 2.54 cm apart horizontally and vertically, which was the standard spacing for this project, and 3.59 cm apart diagonally. The last four rows were the most closely spaced and were 1.27 cm apart horizontally and vertically and 1.79 cm apart diagonally. For the trials, the acrylic board was placed at a 4º angle, and the 3D printed piece was placed at the top of the board.

III.iii. Water-Based Magnetic Separation

For the next three trials, the acrylic board with the magnets attached to it was placed into a shallow tank. This shallow tank was connected via tubes to a water container that dispensed water into the tank and then connected to a second container at the other end of the tank to collect the water. The tank is tightly closed with a plastic sheet lid that is 60 cm long, 30 cm wide, and 1.4 cm thick. This sheet had a built-in tube through which the beads were added. The rate of flow was controlled by the height of the container that held the water. The incline of the board was controlled by the height of rubber strips under the magnetic surface; the same number of rubber strips was added on top of the lower end of the magnetic board so that the second, flat surface could be placed exactly level above the magnets. The magnetic board used was still the grid of magnets spaced 2.54 cm wide.

Setup 4, a water-based setup, was a similar model to Setup 1, which still attempted to separate the beads based on their distance from the magnetic surface but without using gravity as the driving force. This was necessary because on the
microscopic scale, gravity will likely not be as effective a force to control. This setup used a shallow tank that had water pushed through it at a constant flow rate. The surface the beads would travel on was kept level, while the magnetic surface was tilted under it so that the distance between the beads and the board was the farthest at the entrance of the flow and the closest at the exit. This tilt created a distance between the magnets and the level of the beads which decreased the force of the magnetic attraction.

Setup 5 used magnets with different strengths to separate the differently sized particles in water. The first portion was made up of three rows of weak strip magnets, followed by four rows of disk magnets and ending with two powerful bar magnets at the bottom. All the magnets were placed on a flat acrylic board with no incline measured. There was no incline in this setup as this experiment tests the effectiveness of the device and placement of magnets in separating the beads when in a liquid medium. To create a flow of water in this setup, four different mechanisms were designed. First, a water jug was attached to a tube that directly transported water into the tank through a set of ten other tubes. This jug was placed at a higher altitude than the tank in order to ensure that the flow traveled down towards the tank. The next trial was designed with the water jug at the top of a flight of stairs, 5m above the tank. The tubes connected the water to the tank at the bottom of the stairwell. In a new trial, a pump was used to regulate the flow rate. Lastly, a direct connection was created from the sink to the tank. This design allowed for control of the flow rate with the faucet.

### IV. Results & Discussion

#### IV.i Results of Setup 1

<table>
<thead>
<tr>
<th>Size of Bead</th>
<th>.64 cm displacement</th>
<th>.48 cm displacement</th>
<th>.16 cm displacement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small</td>
<td>2</td>
<td>23</td>
<td>5</td>
</tr>
<tr>
<td>Large</td>
<td>0</td>
<td>1</td>
<td>29</td>
</tr>
</tbody>
</table>

**Table 1a: Vertical Displacement Setup 1a Trials**

<table>
<thead>
<tr>
<th>Size of Bead</th>
<th>.48 cm displacement</th>
<th>.16 cm displacement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small</td>
<td>27</td>
<td>3</td>
</tr>
<tr>
<td>Large</td>
<td>4</td>
<td>26</td>
</tr>
</tbody>
</table>

**Table 1b: Vertical Displacement Setup 1b Trials**

This setup is based on the rule that the force of attraction is proportional to inverse of the distance squared, and on the definition of momentum: the product of mass and velocity. The smaller beads had little momentum that was overcome by the magnetic attraction, so they stopped on the step farthest away from the magnetic surface. The larger beads’ momentum was not overcome until they were closer to the source of magnetism, so they stopped on the lowest step. This setup would physically stop the beads in different places, after which the steps would be cleared off and the process repeated in intervals.

Table 1a presents the results of the first setup, which show that regulating the distance from the source of magnetism is an effective method of separating beads of different sizes. The first trial was used simply to determine what heights would effectively discriminate which beads would stop on which step. They showed that the .64 cm step was unnecessary (as only 2 beads stopped there) and that the .48 cm step...
effectively stopped the small beads but not the large. The large beads were captured by the .16 cm step, which was closest to the magnets. The second trial (Table 1b), based on this information, had just two levels, the .48 cm and the .16 cm heights, and effectively separated the beads correctly the large majority of the time. The farthest step captured 27 out of 30 small beads, while the largest step captured 26 out of 30 large beads.

**IV.ii Results of Setup 2**

<table>
<thead>
<tr>
<th>Bead Size</th>
<th>Weak Strip Magnets</th>
<th>Medium- Strength Disk magnets</th>
<th>Strong Bar Magnet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small</td>
<td>30</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Medium</td>
<td>8</td>
<td>21</td>
<td>1</td>
</tr>
<tr>
<td>Large</td>
<td>2</td>
<td>8</td>
<td>20</td>
</tr>
</tbody>
</table>

Table 2: Relative Magnet Strength Setup (Totals after 6 Trials of 15 beads/trial)

Table 2 shows six trials of fifteen beads each (five of each size) that were tested for setup 2. This apparatus, involving various strengths of magnets, proved effective in separating the differently sized beads. The hypothesis being tested was that the smallest beads would stop over the weakest magnets and the largest would stop over the most powerful magnet. The hypothesis was supported with the results of the trial in which all 30 of the small beads stopped at the first level on the strip magnets. The majority of the medium sized beads (21/30) settled in the middle portion where the disk magnets were. Additionally, the majority of the largest beads (20/30) ended up in the final area with the strongest magnet. However, nine of the thirty medium sized beads and ten of the thirty large beads settled in the other two areas containing weaker magnets. This error may be attributed to the clumping that occurred when beads were attracted to the magnets and transferred this charge to other beads traversing the setup.

**IV.iii Results of Setup 3**

<table>
<thead>
<tr>
<th>Bead Size</th>
<th>Wide Spacing</th>
<th>Standard Spacing</th>
<th>Close Spacing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small</td>
<td>11</td>
<td>17</td>
<td>2</td>
</tr>
<tr>
<td>Medium</td>
<td>8</td>
<td>19</td>
<td>3</td>
</tr>
<tr>
<td>Large</td>
<td>4</td>
<td>13</td>
<td>13</td>
</tr>
</tbody>
</table>

Table 3: Varied Magnet Spacing Setup (Totals after 6 Trials of 15 beads/trial)

The results of setup 3, as shown in Table 3, were disappointing because the beads did not separate as hypothesized. When designing this setup, it was believed that the smallest beads would be attracted to the first set of magnets; despite the small size of the beads and the large spacing of the magnets, the small beads would be more likely to settle on a magnet and less likely to overcome the magnetic force with their own momentum, as their momentum was fairly low. It was also believed that the largest beads would not stop until the very last set of magnets, which were closely spaced together, as the largest beads had far more momentum than any other beads and were thus less likely to succumb to magnetic force. It was believed that the medium-sized beads would fall somewhere in between the largest and the smallest beads, and would thus settle in the standardly spaced magnets.

Although 19 of the 30 medium-sized beads did end up as expected in the standard-spacing section, they were the only beads that ended up where predicted. The small beads ended up mostly in the standard-spacing section as well (17/30) instead of the top section (11/30). With the
large beads, very few ended up in the section with the widest spacing (4/30), but for every bead that ended up as predicted at the bottom in the closest-spaced section (13/30), there was another bead that stopped in the standard section (13/30). The most likely explanation for these results is simply the ineffectiveness of the setup: if a bead was randomly dropped from the most central spot, no matter its size, it would settle on one of the very first magnets, which were in the wide-spaced section. The varied spacing of the magnets also did not actually decrease or increase the likelihood of the magnet stopping, but instead affected the chance of a magnet appearing in the exact spot needed for the bead to stop. Ultimately, the results of the trials conducted on Setup 3 lead to the conclusion that varying the spacing of magnets with the same strength is not an effective method of separating particles.

IV.iv Results of Setup 4

The attempt at translating the first of our gravity-driven setups to a fluid-based setup was less successful than expected, due entirely to resource restrictions. The shallow water tank used was only 2.0 centimeters high, and was unable to accommodate an angle sufficient for the beads to be attracted at the right locations and yet not get stuck on the lid. The setup, as determined by the dry trials, required the initial distance between the beads and the magnetic surface to be around 0.5 cm. Once the widths of the magnetic and level surfaces and the rubber lining were added to this, it became clear that the tank was not deep enough for the largest beads to flow unimpeded. However, it is highly probable from the results of the gravity-driven trials that this setup would have functioned at least adequately had the essential resources been available during experimentation. Other technical issues besides the height of the tank interfered as well, including regulating the height of the level plane properly with a limited supply of rubber lining. It was also a challenge having to use a setup with one narrow tube feeding a wide tank, as it necessitated having a chamber in the beginning of the tank where the water could circulate and provide a uniform flow throughout the width of the tank. This chamber refers to an empty space for a short span in the tank, and this need had to be reconciled with the concern that the beads would fall off the side of the level surface into this chamber instead of flowing forward. In total, we were forced to accept that Setup 4 would not be the optimal model for microfluidic separation, as our materials were simply not adequate for experimentation of this setup.

IV.v Results of Setup 5

It was predicted that this design was the most promising; however, there were a few issues that inhibited the flow from properly moving the particles. When first tested, the flow rate was fairly slow and therefore was not able to push the particles forward. In order to fix this, the setup was transferred and altered so that the water from the tank trickled down through the plastic tubing down the height of a flight of stairs (5 meters) to increase the flow rate of the water as it entered the tank. Once in the tank however, the water could not push the particles forward as the beads were inhibited by the boards and tape on the acrylic board. Another issue was that the tank of water was too shallow for the flow to move the beads effectively as the beads continued to get trapped between the board and the top of the tank. Additionally, the various sections of tubing were not connected exactly and allowed air bubbles to enter the setup. The air bubbles inhibited the flow of water.
After having issues with the plastic tubing, the setup was once again changed to use a pump for the water which would regulate the flow in a controlled and forceful manner. While this method was ideal in theory, there were difficulties in priming the pump and keeping the tubes free of air pockets, primarily due to faulty tube connectors. In order to minimize the number of connectors needed in the setup, the tank was then connected directly to the sink; the flow of water could then be controlled with the faucet. This source of water flow had the most potential, as it was capable of providing a large and easily controlled flow of water. However, the setup itself was unable to handle the pressure of the flow necessary to move the beads and leaked excessively.

V. Conclusion

Ultimately in this research, it was discovered that effective separation of mixtures in microfluidic devices using magnets could be achieved by using magnets of varying strengths. In Setup 1, the variable was the distance between the magnets and the steel beads as they rolled down the setup. The further the distance between the magnets and the beads, the weaker the magnetic force. In Setup 2, the variable was the different strengths of magnets used. Both setups showed success in separating the steel beads based on their size and momentum. Setup 3 was the only gravity-based model where some form of magnet strength was not a factor; instead, all of the magnets used had the same strength. Setup 3 was also the least successful setup, and the amount of beads that separated successfully in Setup 3 was much lower than that of Setups 1 and 2. In the water-based Setups 4 and 5, which most closely simulated a microfluidic environment, similar results were found. The flow of water moved the beads along the board until the magnetic force overcame the force of the flow. In the end, the experiments showed that the most effective method to separate variously sized particles in microfluidic devices is controlling the strength of the magnets used.

To translate these findings onto the microscale, dimensional analysis must be utilized in order to convert this data from macroscale results to microscale applications. On the microscale, many of the properties of a liquid do not apply. However, one of the greatest differences between the macroscale research and the microscale application is the nature of the particles. In a microfluidic device, the particles would not be solid steel beads, but instead they would most likely be magnetized particles. The particles will also not be separate from the rest of the liquid like they were in Setups 4 and 5. In Setups 4 and 5, only a small number of beads were used, even though in a real world application the number of particles would be far greater. To regulate this potentially problematic crowding of particles, a microfluidic device would need to release the particles in short intervals. Despite what must be considered and perhaps altered on the microscale, previous research shows that magnetic separation in microfluidic devices is a promising method of separating microfluidic mixtures. Combining the results of this experiment with the concept of magnetic tagging could potentially result in more effective separation techniques, specifically in sensitive biological experiments that would benefit from less invasive methods of separation.

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VII. References


