A Novel Device for the Characterization of Viscosity via Magnetic Particle Translation

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Abstract

Synovial fluid viscosity has been shown to be useful as a biomarker for the disease progression of osteoarthritis, which is a common in both humans and large mammals. Particularly in veterinary medicine, clinical practices for synovial fluid viscosity measurement are limited at best in their precision. In this paper, a new concept called magnetic deflection is proposed and the developments of a device to validate it are detailed. This device is in the form of a flow chamber that creates a stream of superparamagnetic microparticles within a solution to be measured. The particle stream flows past a series of fixed, permanent magnets which attract the particles, while a drag force opposes the magnetic force and is scaled proportionally by the liquid's viscosity. This leads to a deflection of the stream that is dependent on the fluid's viscosity. After the stream has passed the magnet and been deflected, it is imaged for measurement. The device developed was used to empirically validate the concept using a series of glycerol/water standard viscosity solutions. A relationship between viscosity and the stream's magnetic deflection was found to be linearly dependent on the reciprocal of the solution's viscosity.

Introduction

Osteoarthritis (OA) is a maladaptive disease of articular joints affecting 10% of men and 13% of women above the age of 60 [1]. In addition to cartilage, it effects ligaments, bone, and the synovium [2]. As early as the 1920's, the viscosity of synovial fluid (SF) has been studied for its relevance to disease progression and has been shown to decrease in correlation with the disease's severity [3], [4]. For this reason, our laboratory has considered SF viscosity a potential biomarker of interest to characterize OA progression and is interested in developing new techniques for its characterization.

Particularly in equine veterinary medicine, OA is a widespread problem where an estimated 60% of all cases of lameness can be attributed to OA [5]. For clinicians, SF viscosity is used as a measure of the degree of hyaluronic acid polymerization, where a reduction would indicate inflammation [6],[4]. This is useful in characterizing OA and other inflammatory diseases of the joint. Presently, clinicians attempt to quantify SF viscosity by its 'stringiness' either between the thumb and index finger or at the tip of the needle used to aspirate it [6]. While these practices have been effective, it is the view of our group that an alternative which could more precisely characterize viscosity would raise the standard of care and be welcomed by veterinarians.

In a study by Garraud et al [7] investigating the feasibility of collecting magnetic particles from a high viscosity solution, our laboratory investigated the translational properties of magnetic particles through highly viscous Newtonian fluids. Analytically, it can be demonstrated that particle translation is governed by two forces, those of drag and magnetism [8], [9]. While the magnetic force acts as a function of the field gradient, the drag force opposes it and is scaled proportionally by the viscosity of the medium. This fundamental understanding formed the basis of a subsequent empirical study by Shah et al to characterize the effect of viscosity on particle collection in vitro over a finite period [10]. They demonstrated a strong correlation between the fraction of particles collected and the viscosity of the fluid through which they translated. These findings will be used to support the premise for the device to be discussed here.

While a novel technique, particularly because it required such small sample volumes, the methodology employed by Shah et al has little practical use in veterinary practice due to its

reliance on laboratory equipment for measurement. Aware of these limitations, Dr. Jon Dobson proposed a microfluidic device that could measure viscosity by deflecting in steady state a stream of magnetic particles while visually measuring the stream's displacement. This measure would be a surrogate to quantify the balance of magnetic and drag forces and thus the fluid's viscosity. This concept, if possible, could offer a practical and more quantitative method of measuring SF viscosity, particularly for veterinary medicine. In the subsequent sections, the development of such a device to demonstrate the practicality of this concept will be detailed.

Methods

Prototype for a Qualitative Proof of Concept

In developing the first prototype, the objective was to qualitatively demonstrate that a stream of particles could first be formed uniformly, and then be deflected by a magnet. The first priority was to combine two separate flows, one from the fluid to be measured, and another for the stream of particles without inducing excessive turbulence. After establishing a uniform flow of particles its deflection could be attempted.

With respect to deflecting the stream, the approach I elected to follow was to maximize deflection in the minimum viscosity boundary condition, that of water, assuming that if a design could maximize deflection in water, its efficacy should translate to the other boundary condition, that of high viscosity, thus achieving the broadest possible measurable range. Thanks to a suggestion from Dr. Z. Hugh Fan, the first flow chamber would be prototyped using two glass microscope slides and other materials scavenged from around the laboratory.

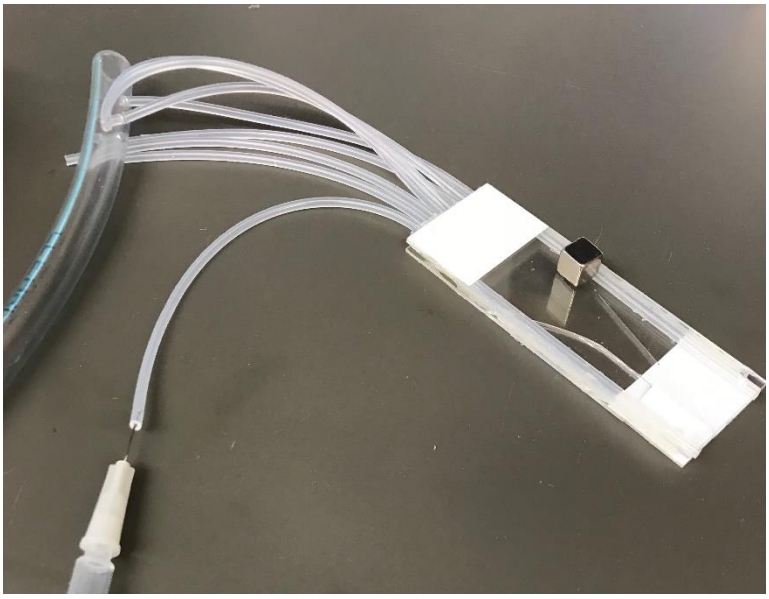
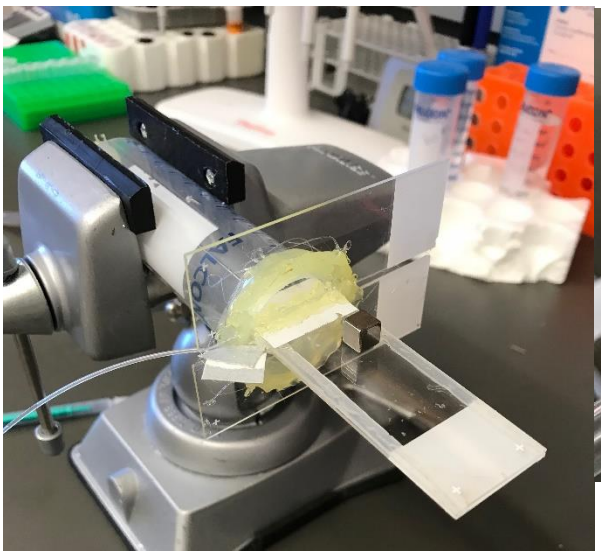


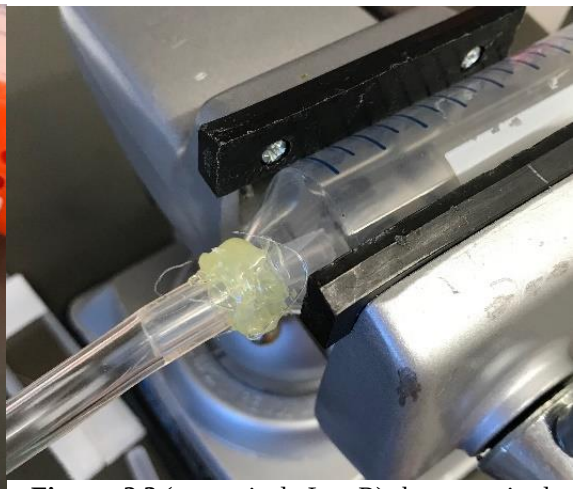
Figure 1: The first flow chamber prototype. The syringe and connected tube are used to inject a stream of particles, while the other tubes inlet the fluid of interest through the flow chamber.

In *figure 1*, the first prototype built can be seen. The same silicone tubing (Cole Parmer 1/50" ID) is used as a gasket to seal either side of the chamber as is used for the particle and fluid inlet streams. Before the fluid inlets were placed, a line of silicone sealant (GE5000 Clear Silicone Sealant) was laid down to seal their underside. Then, the tubes were lined up and delicately pinned into place. Then, the 'gasket' tubes were laid along each edge of the bottom slide and fixed with pins. Before the top slide could be placed, another line of silicone was placed along the top of the tubes. After placing the covering slide, the two slides were clamped together then the pins were removed. Along each slide of the chamber, a line of silicone was placed to lock the gasket into place and ensure its seal. Using a 2mm biopsy punch, interference fittings were created in the end of a ¼" ID PVC tube. Finally, the particles were injected into the chamber using an insulin syringe and the target fluid was propelled via a syphon with the PVC tubing. A clamp throttled the tubing to regulate its flow rate.

While a resourceful arrangement, this prototype had a variety of issues, but the most significant was the fluid entry. The parallel arrangement of tubes was intended to form a tight seal with the benefit of resembling a crude diffuser. Unfortunately, the substantial wall thickness of the silicone tubing led to a large disparity between the height of the chamber and the ID of the silicone tubing feeding it. This created regions on the top and bottom plates where bubbles congregated, thus inducing substantial turbulence through the chamber which prevented a uniform stream of particles from forming.

The first prototype was unable to deflect a stream because the induced turbulence made the requisite uniform particle stream impossible to achieve. In addition, a lesser problem existed, and that was the large fluid volume required. Moving forward, an improved prototype should firstly be free of turbulent flow, and secondly reduce the volumetric requirements.





Figures 2,3 (respectively L to R) show a revised prototype. *Figure 2* shows how the chamber is attached to the fluid inlet without the use of the parallel tubing arrangement. *Figure 3* shows the attachment between tubing and a 50ml tube.

Figures two and *three* show the second prototype which was designed to resolve the turbulence associated with the inlet/chamber junction by removing the diffuser. Additionally, a new approach to the gasket was devised to move beyond the outer diameter constraint imposed by using tubing. More specifically, two slides were stacked and staggered, then a line of silicone was placed along the 'step' at the edge of the slide. It was formed with the pass of a finger. After the silicone cured, a scalpel was run along the edge of each slide (touching both staggered edges) before separating the slides. This trimmed down the excess material and left a resulting molded edge with the height of the slide (1mm) that would constitute the gasket.

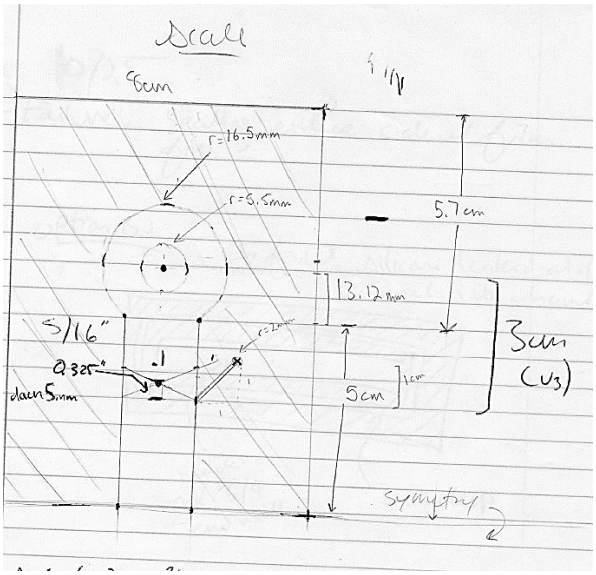
To add the particle inlet, an ~45º by 1mm wide groove was cut into one of the gaskets and a drop of silicone was placed in the notch. Then, a short length of 1mm OD tubing (BD Intramedic PE tubing) was laid through and time was allotted for the silicone to dry. Finally, the excess tubing (laying on the inside of the slide which will become the flow chamber) was cut along the edge of the gasket. At this point the two formed slides were clamped together and silicone was used to seal either edge from the outside.

After sealing off the sides, a slide was hot glued onto the bottom of a 50ml tube as can be seen in *figure 2*. The chamber was laid on top and another slide placed above to cover the opening. Hot glue was applied liberally to seal the joint, but with great care to avoid melting the PE particle feed line (this was learnt the hard way at a great expense of time).

This design met the objectives set to improve the first version. Firstly, the bubble induced turbulence was overcome with a new junction, thus the flow characteristics became far closer to optimal. Secondly, the new gasket allowed for the chamber height to be reduced by half (to 1mm), thus requiring a reduced volume of fluid and magnetic particles. Because of this, the second prototype provided characteristics more conducive to creating and deflecting a particle stream, and indeed, it could demonstrate a noticeable deflection depending on the permanent magnet configuration and flow rates. Unfortunately, several problems arose. Firstly, uniformity was difficult to achieve in gasket thickness when the slides were clamped, thereby producing an inconsistent chamber cross section and thus invalidating the requisite assumption of a constant linear flow rate through the chamber. Additionally, the methodology and materials employed to seal the chamber/inlet junction were ineffective, causing the device to leak, thereby preventing the precise regulation of the flow rate which will eventually be required. Ultimately, this device served its purpose in offering qualitative verification; however, its flaws made collecting repeatable and valid data impossible.

Prototype for the Collection of Quantitative Data

Having established that a stream could in fact be deflected, the next objective was to achieve that deflection in a controlled manner by sealing the device and forming a geometrically uniform chamber. From this point, electronic pumps were adopted for both inlets to regulate flow rates, and the new device was intended to be conducive toward imaging.



For its availability and ability to be machined in our lab, this next series of prototypes would be built using acrylic sheets. With these, the chamber itself could be created in two ways: either additively, with a gasket acting as a spacer to separate and seal the sheets, or subtractively, with the plates fixed together and the chamber machined into one of them.

Figure 5 shows a rough sketch for the sizing of the plates and chamber. The chamber is region in the center without crossing lines and the center hole represents the location for the elbow connector (inlet). Magnet placement is noted in the center of the chamber, and the particle inlet to the right of the chamber was never realized due to the difficulty in sealing and aligning the gasket with such a cut in it.

For the first attempt, I chose the additive method. *Figure 5* shows the dimensions and a sketch of the plates/gasket that would be used. Unfortunately, I did not photograph this failed attempt, and the prototype would be modified in subsequent versions. It involved two 8 x 21.4 cm sheets of 6mm thick acrylic separated by a 0.5 mm silicone sheet (gasket). The top plate would have another piece of acrylic (scraps used) that were glued on top of either end. This served to provide sufficient thickness to thread ¼" hose barb elbow connectors (0.125" x 27 NPT threads, US Plastics) into either end of the chamber for the flow inlet and

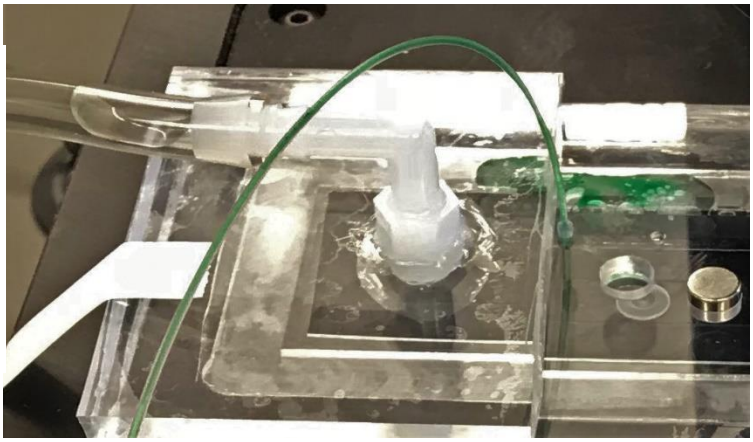
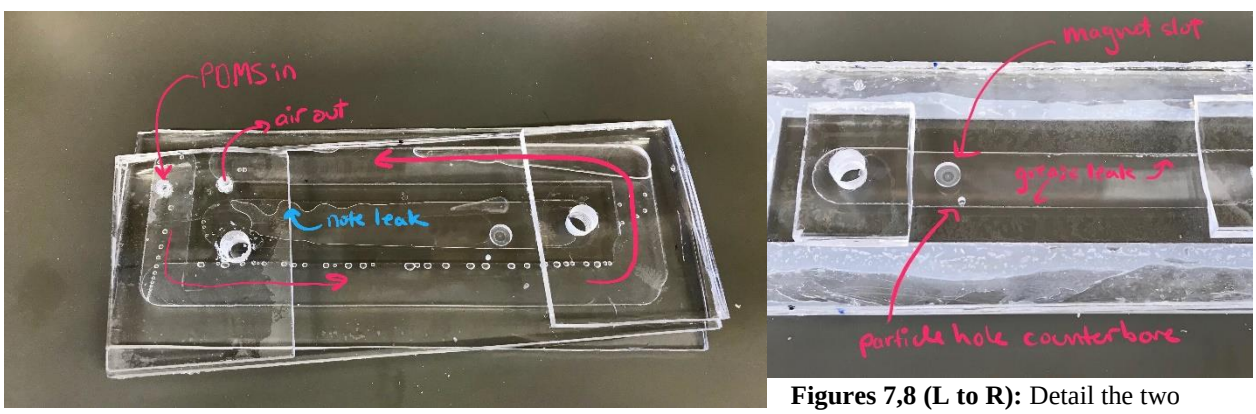


Figure 6: Note the second layer of acrylic and how the hose barb is connected. The green (dye) line represents the particle feed, and the round indents represent different locations for the deflection magnet. This image represents a subsequent version, where the leaking green liquid represents a failure, however through all versions, all inlet junctions were fabricated in the same fashion.

outlet of the chamber. The particle inlet was formed by drilling a 1mm hole through the top plate, and counterboring 2mm deep with a 0.086” drill bit. This allowed for a short length of silicone tubing (Cole Parmer 1/50” ID) to act as a soft adapter, thereby preventing leaks and allowing the line to be easily detachable.

While the inlet and outlet junctions proved to be a useful step toward meeting the objective of sealing the device and would remain, the challenge of the next few versions lay in forming a seal between the plates and gasket. Additionally, forming the chamber from the gasket (by cutting it out) proved a challenge. The gasket was made from a 0.5mm thick sheet of silicone rubber, with the intention of a continued reduction in volume, but its lack of rigidity required it to be cut in place, after having been stuck to the bottom plate. After the gasket was stuck to the bottom plate and cut, a vacuum line was attached to the outlet, and the other elbow connectors were sealed before the plates and gaskets were stuck together using the low air pressure in the flow chamber.

Unfortunately, without a constantly applied pressure, the seal was impossible to maintain, and despite all the effort in forming the gasket and positioning the plates, the seal would fail as soon as the vacuum line was removed. A new approach would be needed, and it would follow the subtractive avenue.

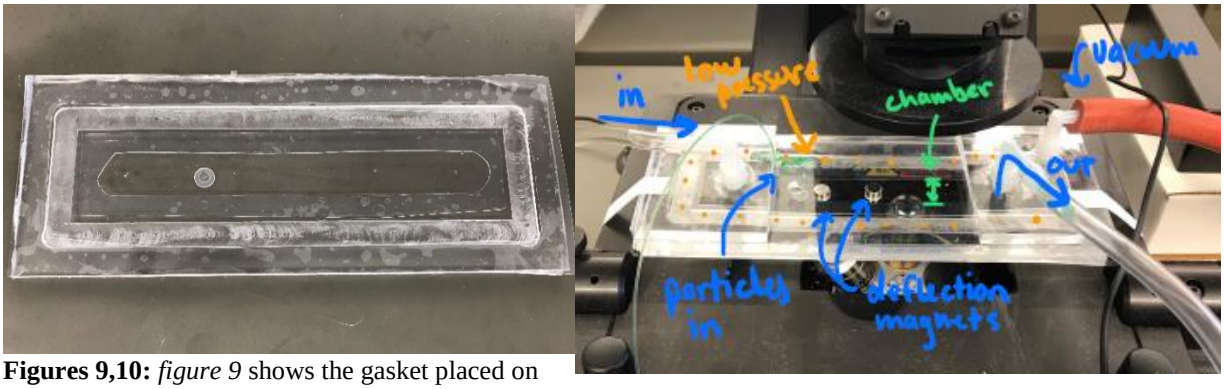


Figures 7,8 (L to R): Detail the two subtractive approaches taken. Note in *figure 7* the failure due to a leak into the chamber (was under vacuum to clamp plates together. Note in 8 the failure due to grease influx. The magnet and particle holes are shown, although the fittings have been reused in subsequent prototypes.

The first subtractive approach can be seen in *figure 7*. In this, vacuum pressure was used in the chamber again to clamp the plates together, and a 3/8” endmill was used to cut a 2mm deep channel around the chamber. The chamber was formed with a ¾” endmill, 0.5mm deep, and 14 cm long. Vacuum grease (Dow Corning 976V) was used to help seal where there was

acrylic/acrylic contact. In the first hole, PDMS (Dow Corning Sylguard 109) was injected with the intent of it curing and sealing the plates together. After failing via leakage into the chamber, a sealant with greater viscosity was chosen (GE5000 silicone sealant). This time, as shown in *figure 8*, a ¾" endmill cut along the boundary of the bottom plate, 2mm deep. After clamping the plates together, the sealant was applied into the gap as can be seen.

This was the first functioning acrylic chamber in that it was sealed, however several problems arose. Firstly, some of the grease infiltrated the edge of the chamber, which induced turbulence. Additionally, due to the minute dimensions required, the equipment at hand could not cut with enough precision, thus again leaving a variable channel depth in much the same way as the second prototype did. In another effect, the mill left tool marks on the bottom of the channel with the potential to induce turbulence. For these difficulties, I elected to abandon the subtractive approach and revisit the additive approach.



Figures 9,10: *figure 9* shows the gasket placed on the bottom plate. The channel cut is under low pressure and again used to clamp and seal the chamber between plates. The bubbles are present because this particular gasket had been taken off and reapplied for the photo. *Figure 10* is annotated to show each part of the prototype.

Above, *figures 9* and *10* show the next prototype. In this, a useful bit of advice from Dr. Peter McFetridge was applied such that a separate channel was created for vacuum pressure. This allowed the clamping force to remain while the flow chamber operated. The vacuum channel was formed 2mm deep with a 3/8" endmill. As can be seen in *figure 9*, the gasket is laid onto the bottom plate. Using a scalpel, the part covering the low-pressure channel is cut away as is the 2 cm wide chamber itself. The top plate was sealed in the same way as the previous prototype, but instead of using the exhaust line, a purpose vacuum line is used.

This approach, featuring an additively formed channel via a silicone sheet gasket and low-pressure seal succeeded in meeting the two objectives described – to seal the chamber and to create a uniform channel. Unfortunately, while these two objectives are necessary to deflect a

stream of magnetic particles in a controlled manner, they are not sufficient to do so. This was illustrated by the difficulties had with the particle stream, whereby preventing pulsation and particle accumulation on the magnet became the primary objective moving forward.

Having realized this, the first and most obvious factor contributing to the pulsation was the proximity of the magnet to the particle inlet which can be seen in *figure 10*. Particle accumulation was visible inside the tube on the side closest to the magnet.

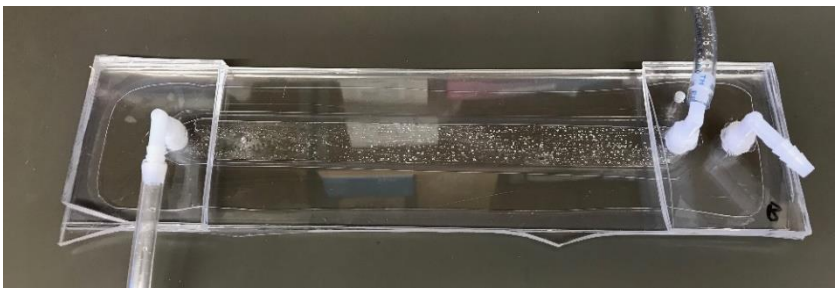


Figure 11 shows the next prototype. This version is 10 cm longer than the previous, and the particle stream flows through the center of the chamber. Additionally, the low-pressure channel was not machined out, but was widened, allowing for more clamping force on a smaller area of gasket, thereby improving the seal.

To remedy this, more space was needed between the magnet and particles to prevent this type of interference. In the next prototype, seen in *figure 11*, the chamber was lengthened by 10 cm and the particle inlet was moved from the edge to the center of the chamber. Together, these prevented interference, but also would allow increased flexibility in magnet placement which was yet to be determined. Additionally, the machined 'low-pressure groove' was foregone, (it was only present because the bottom plate was reused from a previous generation of prototype) thus expediting the manufacturing process.

After further testing, it quickly became clear that pulsation was greatly improved, but the stream could not be deflected because the particles appeared to be settling on the bottom and accumulating near the magnet. This caused them to move slowly regardless of the flow rate and inhibited to formation of a steady state stream. At this point, having mostly overcome the previous prototype's pulsation, the next objective became preventing the particles from settling.

While seemingly trivial, meeting this objective required a fresh look at the particles' behavior. Firstly, with the magnet placed on top of the acrylic sheet, the field gradient, and thus B force direction had a depth component at the stream's location (denoted by the Z direction, where Z=0 at the center of the chamber). This Z component of force would pull particles out of the plane of the center of the channel (X,Y with X being the direction of deflection and Y being along the channel in the direction of flow) and into the acrylic sheet forming its cover.

Compounding this problem was the magnitude of the chamber's shear rate, which drastically slowed the speed of any particles not centered exactly vertically (Z) in the stream (assuming laminar flow), giving them the appearance of having settled on the bottom. This served to increase the amount of time they spend passing the magnet, thus increasing the impulse delivered (in the x direction) and therefore leading to accumulation below the magnet. Because of the previously stated desire to minimize requisite fluid volumes, I had reduced the chamber's thickness repeatedly while holding the linear flow rate constant, with no consideration for the shear rate, which is halved with each halving of thickness. This leads into the final factor confounding these troubles which is the effect of gravity. It causes the particles to settle in the channel (in the negative z direction) and thus slow relative to the flow in the center plane.

To meet this objective, three changes were implemented. First the magnet(s) were moved from the surface of the acrylic to a groove machined between the two plates, which centered the magnet and thus positioned its field gradient in the X,Y plane at Z=0, (or toward Z=0 when deviating from it). This created a theoretically stable equilibrium for the particle stream in the z direction. The second change was to double the thickness (0.5mm – 1mm gasket) thus reducing the shear rate by half. The final change was to orient the chamber such that the flow direction (Y) was pointed vertically, thereby preventing gravity from exerting a force on the particles in the z direction (which confounded the settling/slowing problem). These three changes succeeded in meeting the set objective of preventing the particles from settling, and for the first time allowed for a uniform particle stream to be created in a sealed, geometrically uniform device that could (hopefully) control relevant parameters and produce valid data. Unfortunately, with the magnet in place, even two to double their effects, the deflection did not appear to be measurable, thus setting another objective – increase the magnetic force on the particles.

To increase the B-force, and thus deflection, three routes were available: increase the particles iron oxide loading, strengthen the deflection magnet, or reduce the distance between the magnet and particle stream. For practicality's sake, the third option was taken as the most feasible. It was achieved by halving the channel's width (X direction) to 1cm (from 2cm) which increased the force substantially. This change demonstrated its merit by markedly deflecting the

stream, without allowing for the accumulation of particles on the magnet which afflicted the previous generation of the device.

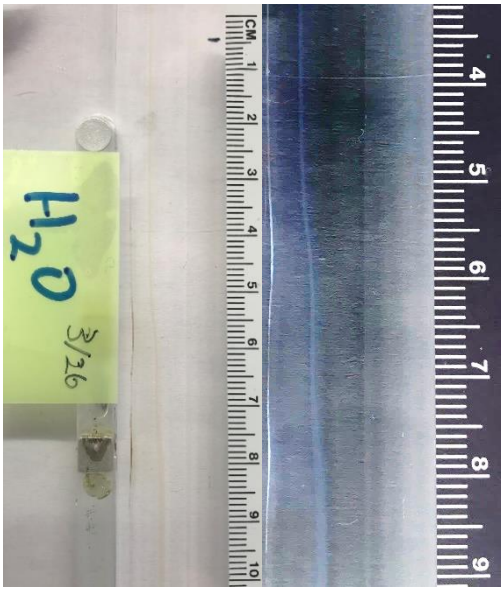


Figure 12 shows the particle stream being deflected by two permanent magnets in water. The image on the right is inverted and enlarged with enhanced contrast for visibility. The success of this design lies in the magnitude of deflection achieved as well as the uniformity of the particle stream.

Protocol for Use

Because of the design's ongoing evolution, the usage protocol was fluid as well, and will be described in this section in its final form, which is the one used to collect data for *figures 16 &17*. The complete setup is shown beside in *figure 13.* It involves two syringe pumps (Cole-Parmer), one for each the particle stream and main flow. The particle pump is run using a 1 ml HSW Norm-Ject syringe (item # 4010.200V0) containing water, with the pump set to a diameter of 4.66 mm and rate of 45 µl/min. The second pump used to power the main flow uses a 30 ml BD syringe (catalog # 309650), with the diameter set to 20.5 mm, and rate set to 6.825 ml/min.

Figure 13 shows the experimental setup used. The clamps and aluminum bars are used to clamp and iPhone (camera). Note the tape marks on the table used to replicate the alignment. The particle pump is left of the frame and was omitted for the sake of clarity.

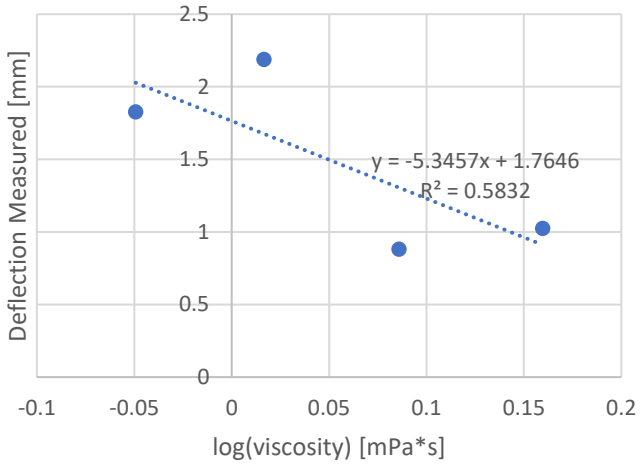
The standard solutions were made (for the final data set, see figures for details on others) by combining glycerol (Fisher Chemical, catalog # G33-4) and water by volume in aliquots of 50 ml, enough for 2 trials, each requiring 25 ml. The viscosity of the standard solutions was calculated using an empirical formula developed by Nian-Sheng Cheng [11]. For each viscosity standard, a particle solution must also be made. Each includes 100 µg of Invitrogen Dynabeads MyOne Streptavidin C1 (ref # 65002) particles suspended in a 40 µl solution of its corresponding viscosity to achieve a concentration of 2.5 µg/µl. After aliquoting, the particles were sonicated,

and used promptly after to avoid particle aggregation. Additionally, a negative control of water/food coloring is aliquoted of the same volume.

With each trial, the chamber is first emptied of fluid. Next, the particles are mixed with a vortex mixer. Using the 1 ml syringe, a small bubble is drawn (< 1cm long) into the particle feedline to separate the particle solution from the water used to push it. Then, the 40 µl particle solution is withdrawn, and again a bubble should be withdrawn, this time ~5 cm long to ensure the particle solution is not wasted in the event the of the plunger being inadvertently bumped. The feedline is then plugged into the chamber and the pump is used to push out the first bubble. Immediately upon the particle front's entry into the chamber, the particle pump is turned off. This will prevent air from entering the chamber during the trial which would induce turbulence and disrupt the stream. Next, the 30 ml syringe is connected to its feedline and filled with care being taken to keep its tip as low as possible while filling. This will ensure that the initial air in the feedline can travel upwards and not bubble. After the feedline has been filled and the standard solution has entered the chamber, the syringe is attached to its pump and started. Once the viscous solution front has reached the top of the chamber, the particle pump is started and the trial can commence. For its duration, pictures are taken approximately every 2 seconds.

Results

To take measurements, the raw images from each trial are analyzed using ImageJ. First, they must be visually inspected to determine when steady state has been reached and particle deflection maximized. This occurs near the end of each sequence. Having selected an example from each trail, they are imported to ImageJ and the measurement standard is taken as 100 mm on the ruler to the right. The image is then zoomed and inverted to enhance visibility and contrast. The deflection measurement is taken from the edge of the ruler at the 4 cm mark to the far edge of the particle stream horizontally (180º in ImageJ). The measurement taken is then subtracted by the measurement taken from the negative control (dye sample) to gain the displacement of the stream due to magnetic deflection.



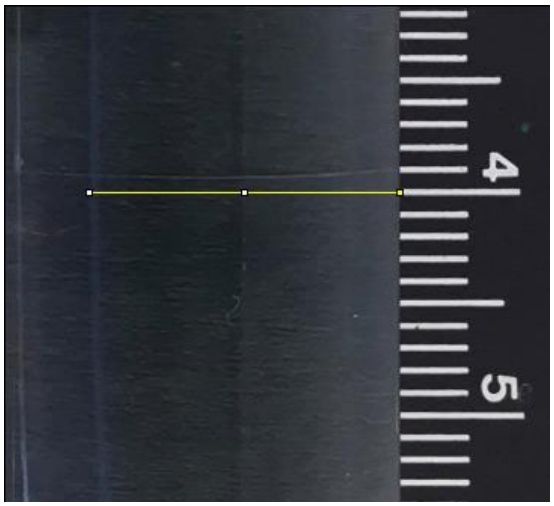


Figure 14: the measurement was taken as shown to the right. To the left shows the data collected from the first working trial of the device using the previously described protocol. The particles used were MagnaBind Goat Anti-Mouse IgG Magnetic Beads (Product # 21354) particles at 2 µg/µl. Note that the particle solutions were all water and standard solutions included 0%, 5%, 10% and 15% glycerol. They were driven by a Fisherbrand™ Variable-Flow Peristaltic Pump (Catalog # 13-876-4) set to 28.

The data displayed in *figure 14* deviates from the protocol as described in the figure label. Being the first data obtained, it served to verify the trend of decreasing deflection as a function of increasing viscosity. Unfortunately, a steady state could not be achieved, thereby necessitating changes in the subsequent trials.

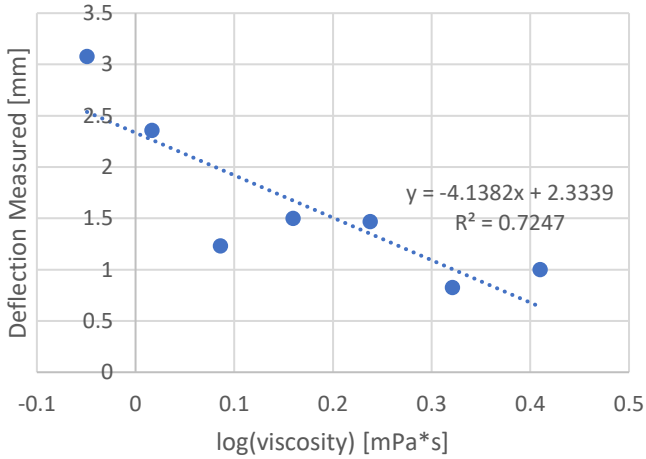


Figure 15: shows data taken in the second full trial run. In this, the syringe pump was adopted with the parameters as described in the *protocol for use* section to drive the particle flow with the hope of steadying the flow. Again, MagnaBind particles were used, this time suspended in their corresponding viscous standards.

In *figure 15*, data from the second trial can be seen. Changes from the first trial are described in the figure label. While this data demonstrated a stronger linear correlation between the measured deflection and log of viscosity, the variability suggests that a steady state assumption cannot be made, and indeed when examining the images that is confirmed.

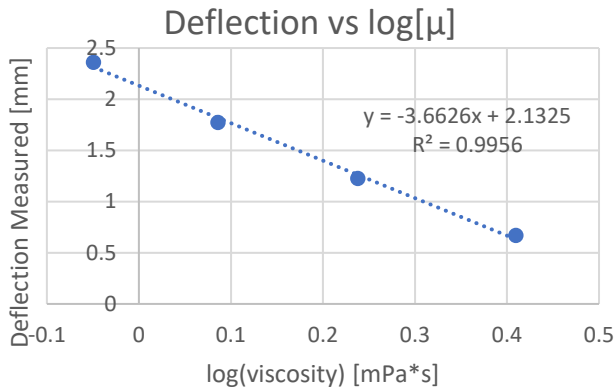


Figure 16 shows the measured deflection of the particles with a strong correlation to the log of the standard solution's viscosity. In this trial, 0%, 10%, 20%, and 30% glycerol standards were used with particle solutions and pump parameters as described in the *protocol for usage* section.

Figure 16 shows the third trial. The strong correlation implies that the steady state assumption should for the first time be validated, and when examining the raw images, that claim can be supported. As such, a further trail should be run to collect measurements over a wider range of viscosities to better characterize the relationship.

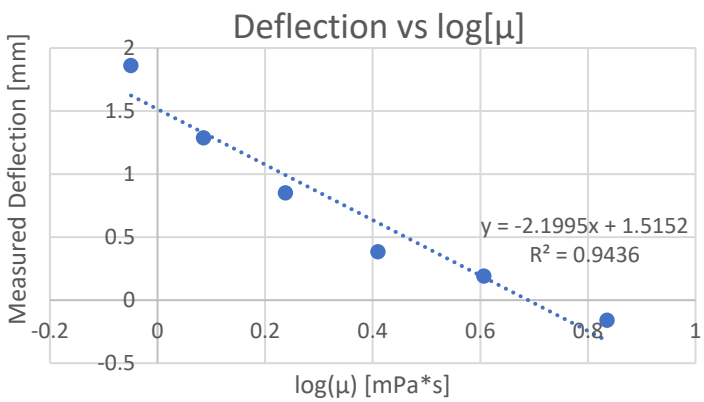
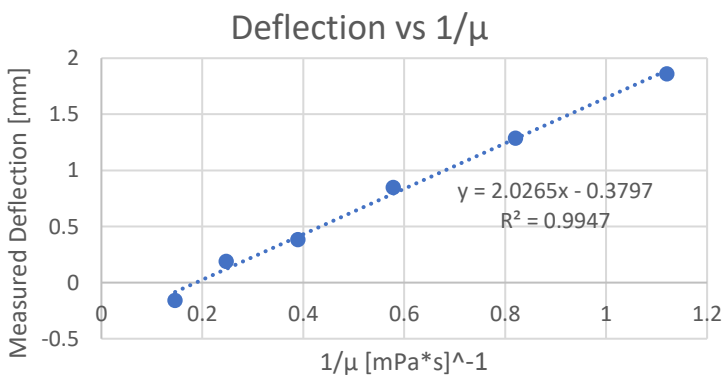


Figure 17 shows the measured deflection as a function of viscosity. Standard solutions used were again separated by increments of 10% glycerol, and included groups from 0% - 50% glycerol. The above plot again attempts to linearize the data with the log of viscosity, however the data suggests otherwise. In the plot below, linearization appears to be achieved using an inverse plot



In the beside plots of *figure 17*, a broader range of solutions are tested and a more robust model of the trend can be found by linearizing the data via an inverse plot as opposed to a semi-log plot. Note the negative deflection measurement of the 50% glycerol solution which suggests the maximum viscosity for this device to detect would be nearly that of the 50% solution. The negative deflection is potentially the result of the stream 'focusing' whereby the magnetic particles are attracted to each other to a greater extent than they are to the magnet;

however more testing should be conducted to determine whether this a result of experimental error or some other phenomenon.

Discussion

In the methodology section, a great deal was done to describe the efforts to build a device which could create a stream of magnetic particles and deflect them with a permanent magnet. In this section, I will delve further into controlling the stream in such a way as to isolate the effects of the solution's viscosity on displacement before then discussing future directions for the project.

The first and perhaps most fundamental assumption is that the stream of particles will remain uniform and not be altered except by the magnetic and drag forces. The first potential challenge to meet this assumption is particulate diffusion. Because diffusion of the particles can be assumed to be uniform, unavoidable within the constraints of this device, and occurring over a relatively small timescale, its effects will be assumed negligible.

The next challenge to achieving uniformity is turbulence in the flow. Below in *figure 18,* a brief calculation demonstrating that at the flow rates utilitzed in this device are an order of magnitude from their transition to turbulent and as such can be assumed laminar.

$$D_h = \frac{4ab}{2a+b} \quad V = \frac{\mu R_E}{\rho D_h}$$

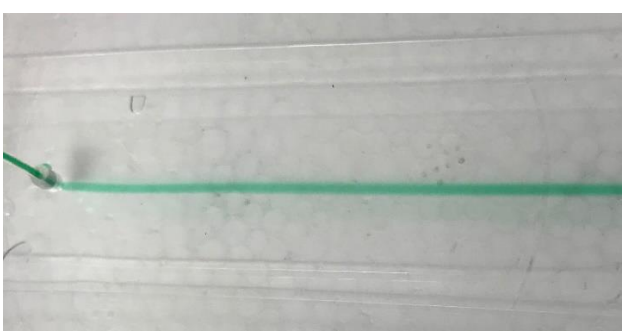


Figure 18: Shows the equation for the Reynold's Number rearranged to solve for linear velocity. Beside it is the equation for the hydraulic diameter of a rectangular conduit, where a = 1 mm and b = 10 mm. For the R_E, 2300 was used as the boundary condition for laminar flow. The dynamic viscosity of water was used as 8.9E-4 Pa*s, with a density of 1000 kg/m^3. This calculation determined the maximum flow rate of 61.4 cm/s with water (the boundary condition), while the linear flow rate used was approximately 1.3 cm/s. In the beside photo, the requisite flow conditions are demonstrated using a green dye.

The other potential source of turbulence is the inlet of the particle stream which flows orthogonally into the main flow at a linear rate of 0.19 cm/sec. This is approximately an order of magnitude below the main flow rate, which along with the qualitative data (images in *figures 12, 14, 17*) will be used to justify the assumption that this induced turbulence is minimal and can be neglected. The final flow characteristic to be considered is pulsation, which would preclude a

steady state from forming. Flow rate pulsation was eliminated largely by switching to a second syringe pump from the peristaltic pump (after the second trial).

The final consideration in achieving steady state is the behavior of the particles themselves as they enter the device. Primarily, aggregation and separation should be considered. As particles aggregate, the cumulative magnetization (of the aggregate) increases with volume, while the drag increases only as a function of the aggregate's increasing diameter. As such, these larger aggregates will have a larger ratio of magnetic force to drag force, thus translating more than an individual. Following the same logic, monodispersity of these particles is also essential. Between the two particle types used, the first (MagnaBind) were used for their lower cost and immediate availability. However, in handling them, it became clear that aggregation was a much more significant problem than with the DynaBeads. Additionally, the DynaBeads are far more monodisperse with a diameter of 1 µm and CV of <3%, while the MagnaBind are specified only as between 1 and 4 µm in diameter. This leads to the next issue, separation. As the particle solution flows through the tubing, its concentration changes spatially, such that the particles move toward the back of the stream and thus concentration increases in the stream as the trial progresses. The effect of this heightened concentration is an increase in deflection, which is thus also time dependent, and contradicts the requisite steady state assumption for the device. For this issue, a larger feedline was used (1/50" ID) to slow the linear flow rate, while the switch to DynaBeads again helped as their reduced size should hypothetically increase their diffusability thus countering their tendency to separate.

With so many factors affecting the state of the particle stream, more work will be required to sufficiently control them to the extent that the steady state assumption can be fully justified. Firstly, improvements must be made to the particle stream to remove its time dependence of concentration (separation) which was still present in the final device tested. This may be remedied by further slowing the flow rate of the particle stream by increasing the tube's diameter. This will require the manufacturing of a new chamber.

Another avenue to reduce these effects may be to drastically reduce the particle concentration in the stream, thereby limiting the interparticle interactions that may lead to the noted variable deflection thought to be caused by the stream's particle concentration. This change will require improvements in lighting and camera to detect the stream, thus a complete

redesign of the experimental setup would be required. If interactions persist, it may be necessary to record the translation of fluorescently tagged particles which could drastically reduce the requisite stream concentration.

Having improved the stability of the stream, it will become necessary to quantitatively confirm the steady state assumption such that it can be validated. This may take the form of a MATLAB code used to process a stream of images taken autonomously at a prescribed interval to select one representative of the steady state and then make the measurement.

Conclusion

In this paper, the concept of magnetic deflection has been proposed, tested and empirically validated by developing a device and methodology capable of creating, regulating, deflecting, and measuring a stream of magnetic particles. Through this paper, a series of devices has been developed, trialed, and improved upon. From the results of *figures 16 and 17*, the empirically determined relationship between deflection and viscosity can be shown. Moving forward, further refinements to the device should be made to fully achieve a steady state deflection, and to quantitatively determine when that state has been reached. Keeping in mind the original objective, the lessons learned in developing these prototypes should be combined with a quantitative model to downscale this technology into a microfluidic chip. If one could be affordably built at minimal complexity, this technology could see the clinical use it was originally intended for.

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