Video Article

Magnetic Levitation Coupled with Portable Imaging and Analysis for Disease Diagnostics

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Abstract

Currently, many clinical diagnostic procedures are complex, costly, inefficient, and inaccessible to a large population in the world. The requirements for specialized equipment and trained personnel require that many diagnostic tests be performed at remote, centralized clinical laboratories. Magnetic levitation is a simple yet powerful technique and can be applied to levitate cells, which are suspended in a paramagnetic solution and placed in a magnetic field, at a position determined by equilibrium between a magnetic force and a buoyancy force. Here, we present a versatile platform technology designed for point-of-care diagnostics which uses magnetic levitation coupled to microscopic imaging and automated analysis to determine the density distribution of a patient's cells as a useful diagnostic indicator. We present two platforms operating on this principle: (i) a smartphone-compatible version of the technology, where the built-in smartphone camera is used to image cells in the magnetic field and a smartphone application processes the images and to measures the density distribution of the cells and (ii) a self-contained version where a camera board is used to capture images and an embedded processing unit with attached thin-film-transistor (TFT) screen measures and displays the results. Demonstrated applications include: (i) measuring the altered distribution of a cell population with a disease phenotype compared to a healthy phenotype, which is applied to sickle cell disease diagnosis, and (ii) separation of different cell types based on their characteristic densities, which is applied to separate white blood cells from red blood cells for white blood cell cytometry. These applications, as well as future extensions of the essential density-based measurements enabled by this portable, user-friendly platform technology, will significantly enhance disease diagnostic capabilities at the point of care.

Video Link

The video component of this article can be found at https://www.jove.com/video/55012/

Introduction

Here, we present a technology platform and a technique which uses magnetic levitation coupled with automated imaging and analysis to analyze the density distribution of a patient's cells as an indicator for disease. This versatile approach for density-based cytometric analysis can ultimately be applied to a range of disease diagnostics. However, in order to be compatible with point-of-care testing and use in developing countries, the technique must satisfy requirements for low cost, portability, and usability. The device and consumables must be easily obtained at a low cost. The sample preparation must be simple, analysis should be automated with minimal requirements for user input or interpretation, and results should be returned quickly. Further, the device must be compact and portable to be useful in clinical settings as well as developing countries. Thus, we have developed a device and method to use magnetic levitation in point-of-care-compatible technology by coupling automated imaging and image analysis to return results regarding the density distribution of a population of a patient's cells.

Point-of-care technologies offer a notable advantage over current clinical laboratory testing procedures. The technology currently available is too expensive to be owned by a clinician or too complex to be carried out by medical staff. Many of these procedures require labor-intensive protocols which must be carried out by a trained technician. For these reasons, patient samples such as blood or urine are generally collected in the physician's office then transferred to a remote, centralized testing laboratory for clinical testing, which may take several days for the physician to receive the results of the test. This can cause delays or complications in the course of treatment in some cases, makes this testing very costly and inefficient (causing a financial burden on insurance payers), and further makes many diagnostics inaccessible in low-resource settings and developing countries.

Here, we present a magnetic levitation technique coupled with automated imaging and analysis in both a device with embedded imaging and processing (**Figure 1**) and a smartphone-compatible device (**Figure 2**). These magnetic levitation-based devices represent a broadly applicable platform technology which has the potential to be applied to a range of different medical diagnostic applications. The magnetic levitation approach functions based on an equilibrium between two forces: a magnetic force and a buoyancy force[1,2,3]. When a particle is suspended in a paramagnetic medium and inserted into a magnetic field generated by two magnets with like poles facing each other, a magnetic force acts on the particle in the direction toward the centerline between the two magnets. The buoyancy force is caused by the relative density of the particle

compared to the suspending medium and is upward in the case of particles less dense than the medium and downward in the case of particles denser than the surrounding medium. Based on these two forces, particles will reach an equilibrium levitation position in the field which balances these two forces; this position is directly related to the density of the particle, with denser particles levitating lower in the field than less dense particles. An imaging module, either a built-in smartphone camera[4,5,6] or independent optical components equipped with a magnifying lens[7,8], are used to visualize the positions of the particles. Image processing, either through a smartphone application[4,5,6] or an embedded processing unit[7,8], then processes the captured images to quantify the spatial distribution and, therefore, the density distribution of the population. In order to analyze larger samples (such as those with only a few particles of interest per milliliter, flow can be integrated directly into the device such the particles are levitated and analyzed as they pass through the imaging region (**Figure 2**).

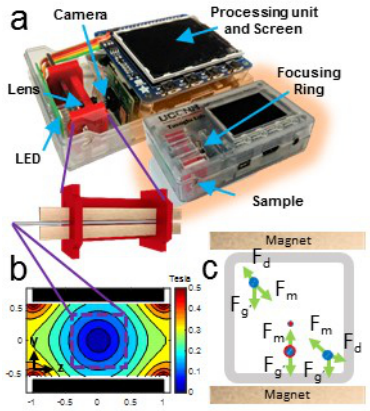

Figure 1: Self-contained Magnetic Levitation Platform. (**a**) Compact magnetic levitation device including a magnetic focusing module, imaging components (a light-emitting diode (LED), an optical lens, and a camera detector), and a processing unit with a display screen. (**b**) Magnetic field strength in the cross-section of the area between the magnets where the sample is inserted. The field strength is greatest at the surface of the magnets and approaches zero at the centerline between them. (**c**) Particles, such as cells, within the magnetic field experience several forces: a magnetic force (F_m) toward the centerline between the magnetics, with magnitude varying based on the position of the particle; a gravitational force (F_g') which depends on the particle density relative to that of the suspending medium, and a drag force (F_d) resisting the particle motion. Reproduced, with permission, from Yenilmez, *et al.*[8] Please click here to view a larger version of this figure.

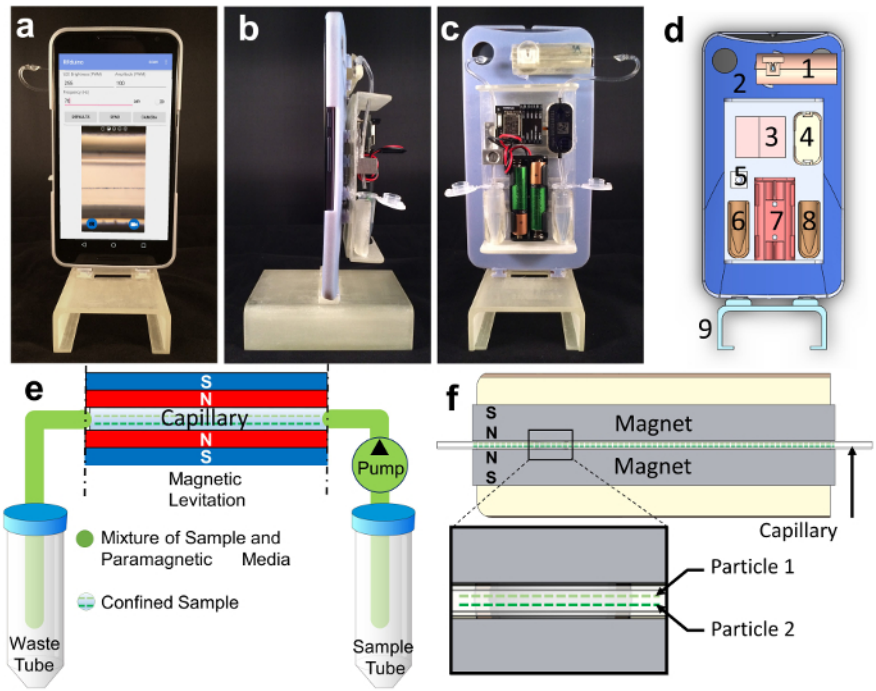

Figure 2: Smartphone-compatible Flow-assisted Magnetic Levitation Platform. (**a**-**c**) Front (**a**), side (**b**), and back (**c**) views of magnetic levitation device (**d**) The components of the device include: 1) Magnetic levitation module, including permanent magnets, a magnifying lens, and an LED and light diffuser, 2) smartphone case, 3) electronics, including a microcontroller, pump driver, and Bluetooth receiver, 4) micro-pump holder, 5) adjustable orifice, 6) waste tube holder, 7) battery holder, 8) sample holder, 9) dual-purpose stand and cover. (**e**) Flow schematic, showing pumping of the sample through the magnetic field. (**f**) Cross-section of the magnetic levitation module, showing how particles of different densities will align as they are pumped through the field; less dense particles, such as Particle 1, will equilibrate at a higher levitation height than denser particles, such as Particle 2. Reproduced, with permission, from Amin, *et al.*[1] Please click here to view a larger version of this figure.

The minimum requirements for use of any sample for density distribution analysis in this system include the ability to obtain a suspension of cells or particles greater than approximately 5 µm and less than approximately 250 µm in size (for imaging and image processing) and its compatibility with mixing in a solution of a paramagnetic solution such as the gadobutrol used here. For disease diagnostics, compatible applications include those in which (i) cells of interest inherently have an altered density when they carry a disease compared to healthy controls, (ii) a density change can be induced in the cell by addition of a reagent or some alternative treatment for a short incubation time, or (iii) different cell types are being identified in a single sample and inherently (or *via* some treatment) have unique characteristic densities.

Sickle cell disease is a genetic disorder causing a mutated form of hemoglobin, HbS, to be produced in a person's red blood cells (RBCs), which can result in intermittent vaso-occlusive events and chronic hemolytic anemia[9]. It is diagnosed using either hemoglobin isoelectric focusing, high-performance liquid chromatography (HPLC) fractionation, or hemoglobin electrophoresis which are highly accurate but must be performed in a clinical testing laboratory because they are incompatible with point-of-care settings. Solubility and paper-based tests for sickle cell disease have been proposed, but generally require subjective user interpretation and confirmatory testing. Here, we use a density-based approach to identify sickle RBCs, which attain a higher density than RBCs from people without sickle cell disease. The mechanism involves polymerization of the mutated form of hemoglobin, HbS, which causes RBC dehydration in sickle cell disease RBCs under deoxygenated conditions[10,11,12,13].

This density-based approach can also be applied to separate cells of different types on the basis of density: white blood cells (WBCs) and RBCs[7]. WBCs are generally responsible for fighting infections in the body. WBC cytometry can be used to quantify the number of these cells in the blood and serves as a useful diagnostic tool. WBC counts higher than normal (generally considered greater than 11,000 cells per µL) may indicate infection, immune system disorders, or leukemia. WBC counts below the normal range (around 3,500 cells per µL) may be caused by autoimmune disorders or conditions which damage bone marrow. Unlike alternative technologies, the process presented here does not rely on lysis of the RBCs or stains in order to identify WBCs. This cell-based test takes advantage of the unique inherent densities of the two cell types to perform separation, as the WBC population density has been reported to be lower than that of the RBC population as calculated previously using density gradient centrifugation[1,5,8].

Compared to alterative testing at remote locations, this test is rapid, with simple sample preparation (**Figure 3**), separation of cells in the device within 10 - 15 min, and automated imaging and analysis which requires less than 1 min. In this way, the device can return results quickly to better inform medical decisions, allow treatment to be administered immediately to alleviate physical and psychological pain, and reduce the risk of complications associated with a delay in medical care. This technique can be performed on-site either in clinical settings due to simple sample preparation and automated imaging and analysis which returns a result with minimal user input or interpretation. Because of the use of a simple approach using permanent magnets for sample analysis and the use of either a smartphone or simple electrical components for imaging and image processing, the device as well as the per-test costs are minimal compared to some sophisticated testing procedures.

Protocol

Ethical Statement: All procedures involving human blood samples were carried out according to the institutional regulations. All protocols were reviewed and approved by the Institutional Review Board. An informed consent was given by all participants.

1. Sample Preparation for Sickle Cell Disease Diagnosis[5,8]

1. Prepare a 50 mM solution of gadobutrol in Hank's Balanced Salt Solution (HBSS).
2. Dissolve 10 mM sodium metabisulfite in the gadolinium solution.
   NOTE: Sodium metabisulfite is toxic by inhalation and strongly irritates skin and tissue. It is a corrosive acid when mixed with water. It may decompose to emit toxic oxide fumes of sulfur and sodium when heated to high temperature.
3. **Obtain blood sample via either fingerstick or venipuncture.**
   1. Draw blood using a lancing device with a clean, disposable lancet. Apply pressure near the pierced site and wipe the blood droplet formed three to four times before collecting blood using a pipette; take care not to "milk" the finger by squeezing the tissue, as this will result in contamination of the sample with tissue fluid.
   2. Alternatively, draw blood using standard venipuncture procedures[14].
      NOTE: If samples will be stored for more than a few hours, collect the blood into a vacutainer with an anticoagulant such as EDTA.
4. Add less than 1 µL of blood to 100 µl of the gadolinium-sodium metabisulfite solution.

2. Sample Preparation for WBC Cytometry[7]

1. Obtain blood sample via either fingerstick or venipuncture, as in section 1.
2. Optional: Lyse RBCs with an RBC lysis buffer. Pipette 5 µL of blood into 500 µL of RBC lysis buffer and incubate at room temperature for 3 - 5 min.
   NOTE: this may be done to confirm the levitation range of an isolated population of WBCs. However, it is not necessary to perform this step, as the results presented here demonstrate that RBCs levitate at a distinctly lower position than WBCs.
3. Dilute whole blood 1:1,000 in 25 mM Gd in HBSS
   NOTE: if cell lysis was performed, dilute the lysed sample 9:1 lysed sample:250 mM Gd to obtain a sample containing 25 mM Gd.

3. Analysis of Samples Using the Magnetic Levitation Platform[4,5,6,7,8]

1. **Start the magnetic levitation device:**
   1. For the self-contained device, plug in the device, allow it to power up, and place on a flat, level surface.

2. For the smartphone-compatible version, launch the smartphone application and swipe left to enter image capture mode, and place on a flat, level surface.

2. **For static magnetic levitation:**
    1. Load the prepared sample into a square glass microcapillary tube by dipping the end into the solution and allowing the sample to fill the capillary via capillary action.
    2. Seal the end with a tube sealant by slowly pushing one end the capillary into the material.
    3. Insert the capillary between the magnets of the magnetic levitation device so that only 1 cm of the tube remains visible (please see **Figure 3** for an illustration the sample preparation) .
    NOTE: This step remains the same for both the smartphone-compatible and self-contained device.
    4. Wait 10 min without disturbing the device or the capillary.

3. **For flow-assisted magnetic levitation:**
    1. Load the sample into the sample tube.
    2. Connect the inlet tubing between the sample container and microcapillary and connect the outlet tubing between the microcapillary and waste container.
    3. Set the LED intensity and flow parameters.

4. Ensure that cells are visible in the field of view, then press the capture button to capture an image (button 3 on the self-contained device and the camera button on the bottom of the screen in the smartphone application).
NOTE: If a USB is used to store the images, create a folder called "images" and insert the USB prior to turning on the device. If no drive is present, the device will store the images in its internal memory and transferred later.
NOTE: Several images may be captured and analyzed to reduce the risk of anomalies by moving the capillary in or out about ½ cm between image capturing.
NOTE: If the number of cells within the field of view is too high or too low (as detected and reported on the user interface), shift the capillary in or out of the device or prepare another sample.
5. Remove the sample and discard the sample according to the institutional or local regulations. Capillaries should be disposed as a sharp.

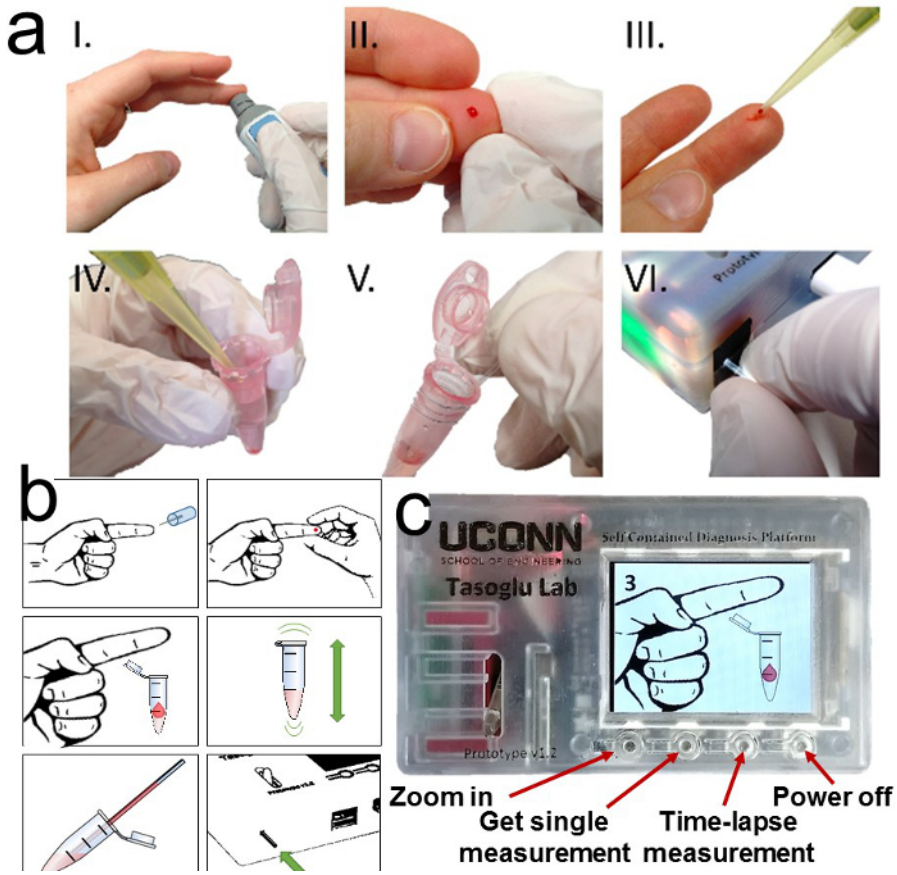

Figure 3: Sample Preparation and User Interface. (**a**) The sample preparation procedure involves lancing the subject's finger, forming a droplet of blood, transferring the blood drop to the sample testing solution, agitating the sample and loading into a capillary tube via capillary action, and inserting the sample into the magnetic levitation device. (**b**) These sample preparation steps are also displayed on the screen of the device to guide sample preparation. (**c**) The device includes four buttons: a button to zoom into the sample image in order to properly adjust the focus using the adjustment knob; a button to obtain a single measurement (a 5 s delay is implemented to allow time for the user to insert the sample); a time-lapse measurement (6 images are taken at 5 s intervals); and a button to power off the device after use. Reproduced, with permission, from Yenilmez, *et al.* [8] Please click here to view a larger version of this figure.

4. Image Analysis[4,5,6,7,8]

1. Run the image analysis software included on the device for the appropriate sample (cell distribution or cell type separation).
   NOTE: For the self-contained device, the analysis is performed automatically and displayed on the graphical user interface. For the smartphone-compatible device, to perform the analysis, go to the gallery and select the desired video file to be analyzed.
2. Observe and record the output of the analysis displayed on-screen.
   NOTE: For cell distribution analysis (such as sickle cell disease diagnosis), the output will be the width of confinement of the cell population.
   NOTE: For cell type separation (such as WBC identification), the output will be an image with the WBC population identified. In order to calculate the number of cells per microliter, multiply the average number of WBCs per image by a factor of 2,000. For example, if 5 WBCs were observed, this would indicate 10,000 WBCs/µL. The normal range is generally considered to be 3,500 - 11,000 WBCs/µL.
3. Repeat the analysis by moving the sample tube in or out of the device about ½ cm and capturing another image to be analyzed as described above.
   NOTE: It is recommended to repeat the analysis 5 - 6 times per sample to avoid errors.

Representative Results

For cell density distribution analysis, which is the technique used for sickle cell disease diagnosis, the aim is to identify the width of the distribution of the cell population. Blood cells from patients without sickle cell disease will be confined within a predictable width. Cells from patients with sickle cell disease will be distributed throughout a wider region, with a downward skew in the cell distribution (see **Figure 4.**) For any particular application, a threshold may be set between the distribution width of control samples versus that of healthy samples as a cutoff between "healthy" and "positive for the disease"[5,8].

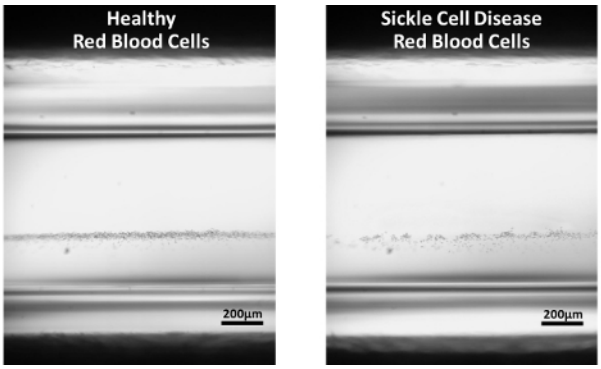

Figure 4: Example of Magnetic Levitation to Analyze Density Distribution as an Indicator for Sickle Cell Disease in Blood Samples. On the left, red blood cells are well confined within a narrow region. On the right, a subset of red blood cells attain a greater density and therefore a lower levitation height, skewing the distribution downward and increasing the width of confinement. Scale bar = 200 µm. Please click here to view a larger version of this figure.

To analyze the density distribution of a sample, a computational algorithm is implemented within the device. First, the pixel intensity gradients along the vertical and horizontal axes are calculated. The magnet edges and the capillary edges are detected as the peaks in the vertical pixel gradient profiles. The distance between the inner capillary edges, in pixels, is known to be 0.7 mm and is therefore used as a scaling factor to convert distances from pixels to millimeters. The pixel intensity gradient along the horizontal axis is greatest where cells are located. This gradient profile is analyzed and fit to a Gaussian curve. The value 4 times the standard deviation of this curve is reported as the confinement width.

Results in **Figure 5** show the confinement widths for both control and sickle cell disease samples. Here, samples with a greater confinement width (over 50 µm) would be considered sickle cell disease positive and those below that threshold would be considered to be negative for the disease. It should be noted that other methods of analysis of the sickle cell distribution have been investigated and reported by Yenilmez, *et al.*[8]

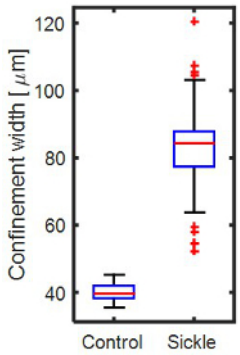

Figure 5: Quantification of the Confinement Width for Sickle Cell Disease Diagnosis. Experimental results for confinement width of control (n = 48 images over 4 subjects) and sickle cell disease (n = 93 images over 10 subjects) red blood cells. Results are statistically significant according to a Mann-Whitney-Wilcoxon two-sided test (normal approximation, $n_1 = 3$, $n_2 = 10$, Z = -2.6764, p = 0.0074). The whiskers represent the minimum and maximum confinement widths from the samples tested and asterisks represent outliers. Reproduced, with permission, from Yenilmez, *et al.* [8] Please click here to view a larger version of this figure.

For particle separation, which may be used to identify WBCs in blood samples, the aim is to identify two distinct populations. If the populations have different densities, they will be observed in distinct regions in the field of view. Thus, homogeneous populations of two or more particles with distinct densities can be levitated and, upon separation, the multiple populations can be observed in the image and detected using the image analysis algorithm[4] (see **Figure 6**).

To analyze the separation of two different cell types, an algorithm is implemented which distinguishes the two separated populations at equilibrium. In a similar manner to that described for sickle cell disease analysis, two Gaussian distributions are fit to the sample, rather than a single curve. Each peak in the pixel intensity gradients represents a different cell population. The Gaussian curves fit to this data give both the average levitation height (relative to the position of the bottom magnet) as the mean of the Gaussian curve and the confinement width as the standard deviation of the curve[7].

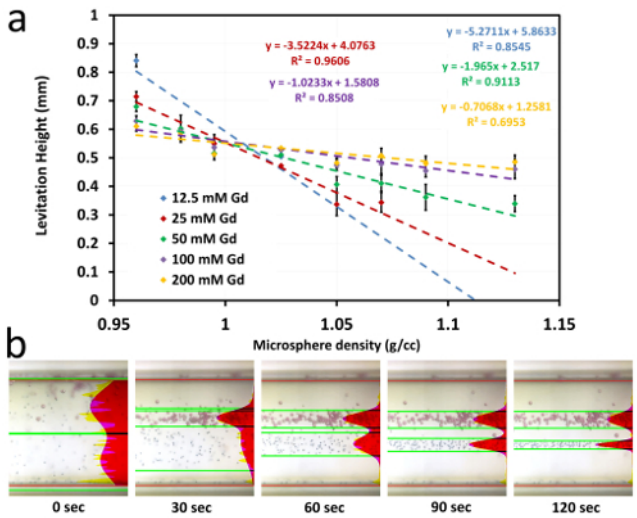

Figure 6: Example of Magnetic Levitation of a Mixed Population of Microparticles with Distinct Densities. (**a**) Calibration curves correlating microsphere density with levitation height in five different Gd concentrations ranging from 12.5 to 200 mM. The slope is greatest at the lowest concentrations of Gd, thus offering a greater resolution (*i.e.* sensitivity to small density differences). The slope is lowest for higher concentrations of Gd, demonstrating the increased range of detection but with lower resolution. (**b**) Time-dependent separation of a homogeneous sample microspheres with two distinct densities over the course of two minutes. At equilibrium (right), two distinct bands are detected by the image analysis algorithm. Reproduced, with permission, from Yenilmez, *et al.*[7] Please click here to view a larger version of this figure.

In order to identify individual cell types with distinct densities for any given application, it is advisable to first levitate one cell type at a time to quantify the expected levitation height. **Figure 7a** shows the levitation height of WBCs from a blood sample in which the RBCs have been lysed. This defines the region of confinement of WBCs for further analysis. The results indicate that RBCs levitate lower than WBCs and, thus, WBCs can be distinguished from blood samples based on the levitation position. The volume within any given field of view is 0.5 µL. In samples which were diluted 1:1,000, the number of WBCs/µL can be calculated by counting the number of WBCs in the field of view and multiplying by a factor of 2,000[7].

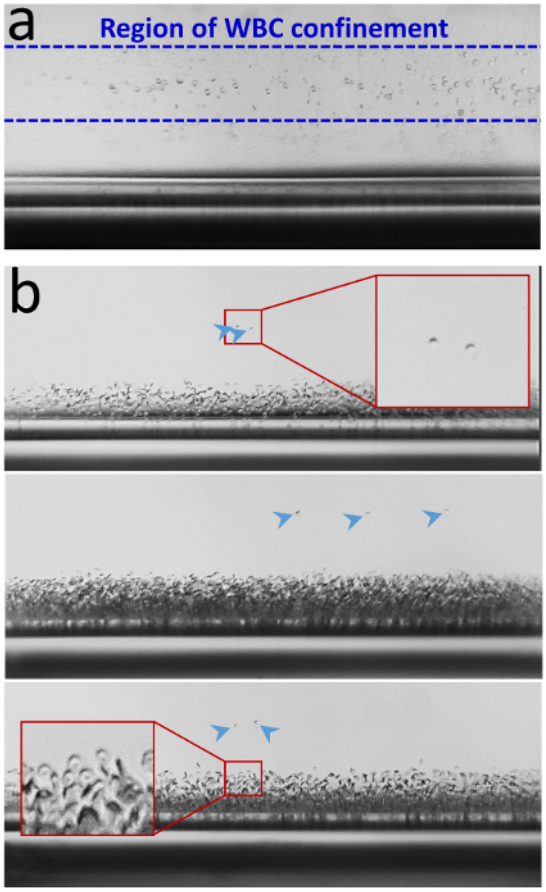

Figure 7: WBC Cytometry in Whole Blood. (**a**) Levitation of WBCs from blood following RBC lysis. This defines the range in which WBCs levitate in the magnetic field in 25 mM Gd. (**b**) Example of WBC counting (WBCs marked by blue arrows). The top frame inlay shows WBCs and the bottom frame and the bottom frame inlay shows the RBC population. Reproduced, with permission, from Yenilmez, *et al.*[7] Please click here to view a larger version of this figure.

Discussion

Critical Steps within the Protocol

Critical factors in this process include the proper alignment of the magnets. If the magnets become dislodged or separated more than normal within the device, this can affect the results. To control for this fault or others in the process, a density-controlled particle, such as polystyrene microspheres, can be used periodically to control for changes over time. Further, levitation time is important to allow the cells to reach equilibrium. For red blood cells, 10 min is sufficient to allow all cells to reach equilibrium. However, it is important to note that smaller particles or cells may require a longer time to reach equilibrium. This can be assessed by taking time lapse images at a 5 s interval and plotting the confinement width over time; equilibrium can be determined as the point at which the change in confinement width is negligible.

Other critical steps within the protocol include the preparation of the gadolinium solution at the precise concentration as this greatly influences sample levitation height. This may be done ahead of time and used from a stock solution, but must be sealed properly to avoid evaporation of the solution and an unintended increase in concentration. Further, care must be taken to maintain the health status of the cells used. For human blood drawn via fingerstick, it should be used within one hour of blood draw and not allowed to dry by storing in a sealed container. For human blood drawn by venipuncture, samples should be stored at 4 °C for no more than one week with anticoagulant (ethylenediaminetetraacetic acid (EDTA), a common anticoagulant, was used here). For adherent cell lines, dead cells should be washed thoroughly from the culture prior to trypsinization and cells should be incubated until use. The health of the cells at the time of levitation is critical because cell health is known to affect density and therefore levitation height.

Modifications and Troubleshooting

We have demonstrated the separation and confinement of cells of two different densities at predicable locations in the magnetic field. In order to extend this technique to other applications, different formulations of the paramagnetic medium may be used to obtain a desired range of detection for alternative applications[3]. The concentration of gadolinium governs the resolution of detection as well as the range (please refer to **Figure 6a**). Because greater concentrations of gadolinium increase the strength of the magnetic force applied to the cells, the greater the concentration of gadolinium in the suspending solution, the smaller the difference in levitation height will be for any difference in cell density. While this limits the resolution, defined as the ability to distinguish between small differences in cell density, it increases the range of densities which may be analyzed. Similarly, decreasing the concentration of gadolinium will increase the resolution but decrease the range of detection. Further, the density of the medium can be altered to shift the limits of detection upward or downward. The second force which controls levitation height is the buoyancy force, which depends on the relative density of the cell compared to that of the suspending medium. Here, a water-based

suspending solution is used, meaning that cells with a density which is the same as that of the medium levitate at the centerline between the two magnets with less dense or denser cells levitating above or below the centerline, respectively (with a range controlled by magnetic force as described previously). Because buoyant force is dependent on relative density, increasing the density of the medium will shift the range of detection to a higher range of cell densities. Similarly, using a lower density medium will shift the range of detection toward a lower range of cell densities.

We have also investigated the performance of flow-assisted magnetic focusing device by quantifying the normalized particle count across the capillary width (*i.e.* probability of a particle to flow at a distance across the capillary width). Lower flow rates have more confinement of particles but result in a lower volume throughput, which can be a drawback for rare object detection in high-volume samples. However, this can be addressed by multiple passes in the magnetic field or via longer magnets. Separation between multiple cell types may also be leveraged in future studies to isolate the particles of different densities by leveraging a microfluidic separator at the end of the magnetic field.

When separating multiple cell types, it may be helpful to levitate each population individually in order to establish the average height and the range of each cell type prior to levitating the homogeneous population.

Limitations of the Technique
The process presented here is limited to the separation of particles of distinct densities. In order to achieve reliable identification of multiple cell types, it is important that they have discrete density ranges that do not overlap. Further, the particles which can be detected are limited in size. They must be able to move freely within the microcapillary tube – 200 µm is the recommended upper limit on the particle diameter. Further, particles must be large enough to be imaged clearly – 5 µm is the recommended lower limit on the diameter.

Significance of the Technique with Respect to Existing/Alternative Methods
This approach to cellular analysis is simple, enabling user-friendly analysis on-site. Many medical diagnostic procedures must be carried out in clinical testing laboratories and require specialized testing equipment and procedures performed by a trained laboratory specialist. However, this protocol requires a simple device which is more accessible to healthcare clinics. The sample preparation is simple and the analysis is automated, minimizing the risk for user error.

This device will enable rapid, on-site testing for a variety of medical conditions. The device is user-friendly, label-free, and portable, making it ideal for point-of-care disease diagnostics. Compared to the current standard of remote clinical laboratory testing, this approach will enable physicians to quickly make informed decisions regarding patient care and potentially prevent complications due to delays in care. The platform has been designed with easily accessible and inexpensive components, allowing widespread use of this method in clinical settings and developing countries and improving worldwide accessibility to healthcare.

Future Applications or Directions after Mastering this Technique
It is important to note that the tests described here are not yet validated on a large-scale patient population. To date, sickle cell disease diagnosis has been confirmed in a small patient cohort[2,5] and WBC cytometry has been demonstrated as a proof of concept. Clinical trials with these applications and those developed in the future must be performed in order to validate this method prior to clinical use, but the results presented here show promise for eventual use of this technology and technique for point-of-care clinical diagnostics.

Using this approach for density-based cytometric analysis may ultimately be extended to additional disease diagnostic applications. This approach of magnetic levitation of single cells for disease diagnostics as described here requires the use of single-cell suspensions of a patient's cells and to cells which can be imaged using the current system with its limitations on resolution due to use of a smartphone camera or low-cost optics. Further, this technique is applicable to diseases which satisfy one of the following conditions: (i) cells of interest must attain an altered density when they carry the disease compared to healthy controls, (ii) a cell density change must be inducible by addition of a reagent (or any available alternative treatment), or (iii) the diagnostic must involve identifying different cells types in a single sample which either inherently or via some treatment have unique densities. Future applications to other diseases using the same platform device can have a tremendous impact on global health. These may include detection of biological components, which are distinguished by density. Certain cell types, cells which are undergoing cell death, and diseased cells have all been shown to have unique density signatures and thus distinct magnetic patterns, and can therefore be quantified and separated using this platform. Cells in very low numbers can also be detected by leveraging fluid flow in the flow-assisted magnetic levitation device.

Disclosures

Authors Stephanie Knowlton and Savas Tasoglu are founders of and have an equity interest in mBiotics, a startup working to commercialize the magnetic levitation platform described herein for point of care diagnostic solutions. A provisional patent entitled "Magnetic Levitation with On-Board Optical Imaging and Image Analysis for Density-Based Separation, Identification, And Measurement" has been filed with UCONN Case No. 16-027 on the technology described here.

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