Recent Development and Applications of Magnetism in Biomedicine

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Abstract. Fluorescence-activated cell sorting (FACS), a cell isolation approach that relies on immunofluorescent signals, is among the most frequently applied approaches. Due to the inherent advantages of microfluidic devices in terms of small size, short detection time and low cost, their application in biotechnology are currently being investigated. Current research by scholars was reviewed by the literature method. Micro-magnet matrices can be used to move multiple cells in cell manipulation, and open tubular with magnetic trapping bead trap beds can be useful in trapping blood cells. The trapping and separation of blood cells have been better progressed, and future studies can concentrate on the concurrent sorting of several targets at high purity, recovery, and throughput levels, label-free continuous separation of cell mixtures, and the sorting of different cells by changing the device environment around the properties of the magnetic device itself.

Keywords: Magnetic cell separations, FACS, cell isolation.

1. Introduction

All of the body's components can only continue to function by receiving oxygen and nutrition through the blood. The lungs, kidneys, and digestive system use the blood to transport carbon dioxide and other waste products for elimination from the body. Humans have a blood volume of around five liters or 7% of our body weight [1]. Erythrocytes, leukocytes, and platelets are the three primary categories of blood cells. In the many different cells, many cells could be studied independently to cure different illnesses. The automation and miniaturization of sample preparation for clinical diagnostics in samples like blood and sperm appear to be made possible by microfluidic devices. Fluorescence-activated cell sorting (FACS), a cell separation approach that relies on immuno-fluorescence signals, is one of the most used methods. Although this method is effective, it has significant disadvantages, such as high instrumentation and operating costs, analysis times that can be hours long, and the possibility of cell damage at high flow rates, when methods such as fluorescence need to be used as markers for pre-experimental processing.

2. Applications of magnetism in biomedicine

Purdon and Westervelt [1] demonstrated a matrix that can control the movement in a cell by influencing the different magnetic field. Controlling the movement of biological cells is usually done by using magnetic beads. Covering up the surface of the bead with different antibodies will move cells around according to their sensitivity. Many magnetizing manipulation tools have been invented and used in different labs in the past. However, a micro solenoid matrix with integrated micro flow paths is can be used in a much larger variety of circumstances and it causes less damage to the cells. In the demonstration, they demonstrated the device by separating a single yeast cell and manipulating it. While individual cells are captured and have consecutive movement, the movement of multiple cells is controlled separately for cell picking and the cells are whirled around in the stream. In the presence of a matrix of micro magnets, individual cells can be assembled into micron-sized artificial tissues or other functional cells, thus allowing various types of cell manipulation in the environment of microfluidic channels, an important direction for novel biomedical research. The findings indicated that the ability of a micro electromagnet matrix to govern individual cells has enabled new forms of biomedical research to be conducted. Figure 1 depicts a design and micrograph of a micro-magnet

matrix made on a Si/SiO2 substrate with wires wrapped in an insulating layer (total thickness of 0.35p) and linked vertically to generate the best magnetic field amplitude between two of the wires. Figure 2 illustrates the complete manipulation of single as well as multiple yeast cells. The cells were manipulated using a micro-magnetic substrate with a sample of baker's yeast at a constant temperature of 25 degrees. Figure 2a shows the capture and transfer of a single cell in the same magnetic field, and in Figure 2b the control of multiple cells, grouping the yeast cells according to their respective characteristics, distorting or rotating the target sample by varying the current, and Figure 2c With a frequency of F=2 Hz, illustrates the rotation of two yeast cells linked to a magnetic bead. For instance, cells can be precisely controlled well enough to form artificial tissue; Magnetic beads linked to cells can be pulled or bent by the matrix's force to assess the mechanical characteristics of the cell membrane. Complex cell manipulation can be carried out inside a microfluidic channel due to the matrix's ability to dynamically adjust its magnetic field patterns throughout tests. When magnetic particles or nanoparticles are guided into a path, they remain confined to that flow path. Future research directions could use microsystems technology for particle, cell, or molecule removal. For example, Nan Xia, Tom P. Hunt et al [1] used a soft magnetic material (NiFe) with low-residual magnetic strength that is magnetized by an extraneous fixed magnet to permit a fast and toggleable process of controlling cell separation. Comparable systems can be micromachined using perpetual flux materials or incorporates components that deliver electromotive power control. In addition, the same micromachining technique can be used to simultaneously deposit more than one magnet layer at various points on the chip. Furthermore, particle thermotherapy is intriguing since it allows for the heating of only the specific target tissue, making it one of the most promising cancer treatment procedures. Rosensweig [2] discussed the theory of directed relaxation of thermally undulated particles in a viscous medium, which leads to dissipation.

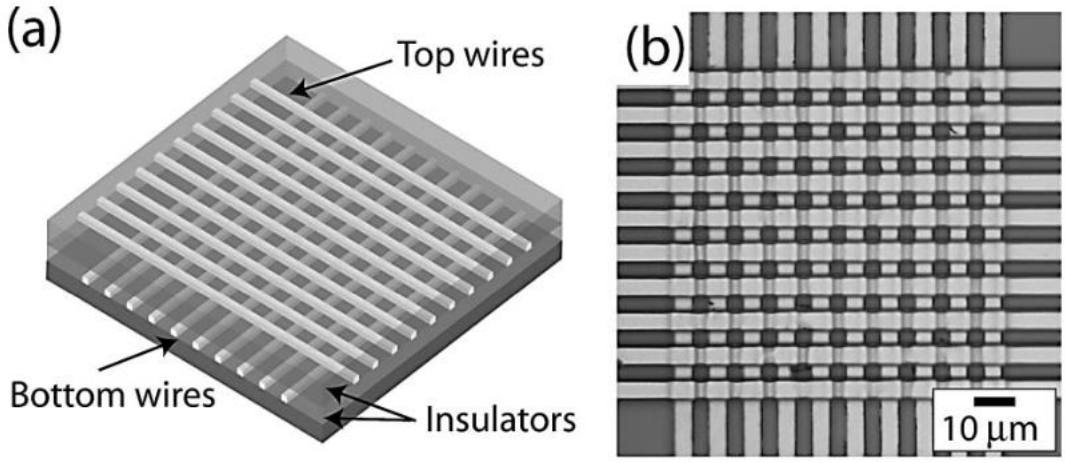

Figure 1. (a)microelectromagnet matrix before attaching channels. (b) Micrograph of a matrix with 10 Au wires in each layer of conductors.

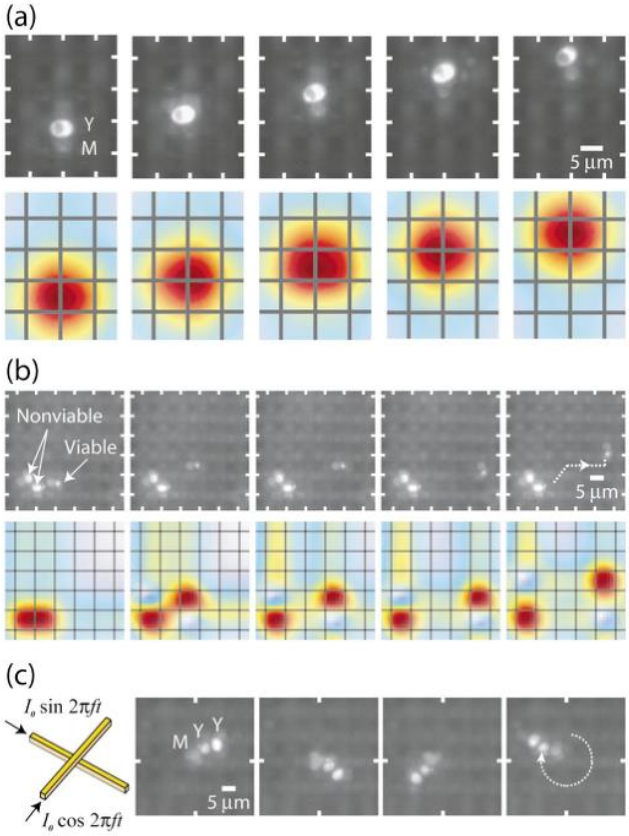

Figure 2. Magnetic field pattern and force profile computed for a 10310 matrix and a magnetic bead

Furdui and Harrison [4] separated T cells from human blood samples using a one-step immunomagnetic separation approach. Despite being only a minor portion of the individual, T cells were able to be isolated successfully from human blood samples. The efficacy of T-cell capture in various flow route designs was evaluated using quantitative polymerase chain reaction analysis of the collected cells. Using 4-8, 50 mm deep narrow tunnels with the same cross-section, the approach proved substantially more effective in trading magnetic beads and separating cells from samples. Compared to a straight eight-way model, the introduction of 8 different bifurcated flow routes raised capture efficiency from around 20% to 37%, demonstrating the requirement for consistent flow distribution into different channels of a flow manifold to achieve efficient cell capture. Figure 3 shows the layout of the Y-crossover apparatus used by the authors to isolate T cells. a,b represents the inlet and c represents the outlet. The device uses certain concentrations of nitric acid, sulfuric acid, and sodium hydroxide in sequential order and for different lengths of time, respectively. Figure 4 shows the operation of the Y-shaped device of the magnetic bead capture bed. First, as illustrated in Figure 2b, the second magnet is deposited below the first opposite chip and an equal amount of blood is stored in the head of the device, respectively, followed by the separation operation. T-cell trapping efficiency is very different under different devices. The channel wall coated with antibodies is the simplest type, and although t-cell capture can be achieved, it may cause some blockage due to the small diameter of the capillaries. The bed of magnetic trapping beads offers a high specific surface area, and by using a magnetic field that is not symmetrical and placing the magnet at the edge of the microchip, bead capture can be maximized. Also, the captured cells can be compared to the cell signals obtained straight into the plasma to gauge the t-cell trapping effectiveness. In these capture beds, up to 3 mL min21 of product stream was measured. What these investigations show is that preparing blood samples for PCR can be difficult. Although electrophoretic investigations employed only diluted or resuspended hematocrit inside the specified dissociation buffer, which requires a change in conductivity, the microfilter was easily clogged by the blood sample. Paramagnetic beads are better for blood cells as the bed may be formed and then reactivated within a wide passage that is

not prone to clogging. Overall, this study evaluated the application of two types of capture beds, open tubular and magnetic capture beads, in blood t-cells. The magnetic bead capture method has the advantage of increased capture surface area, release after washing the cells, and the ability to reduce sample processing time in the bead bed. This study was only used for human cell capture and the test subject was relatively single, which could be used in the future for other animal cells, other human cells, and comparisons between the two. Also, the difference between magnetic and non-magnetic cell separation could be a future research direction. For example, a demonstration of sequential flow separation of magnetically nanoparticle-labeled macropores and neoplastic cells on a microchip revealed that the cells could be segregated among themselves from one another on the grounds of magnetic loading and size. The proposed methodology can not only separate the magnetic units but also separate the magnetically labeled cells away from whatever non-magnetic constituents are present in the specimen compound [5].

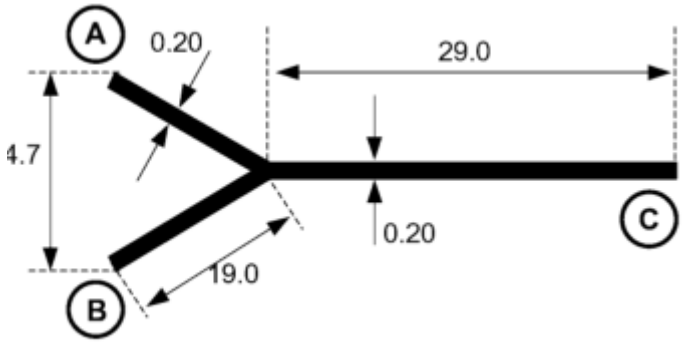

Figure 3. Y-intersection device for blood cell separation

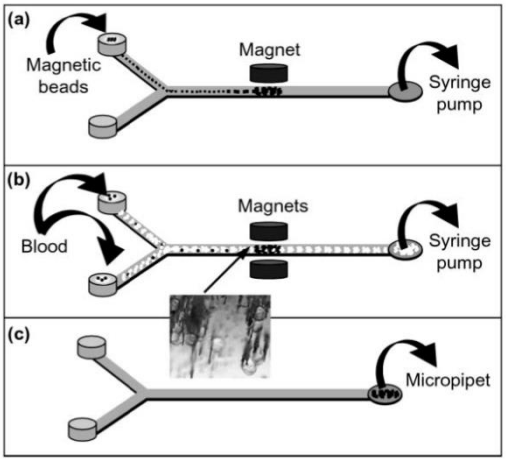

Figure 4. Immunomagnetic separation of T cells

Michael and Robert [6] showed that one method to isolate uniformly shaped cells from tissue or cell solutions is fluorescence-activated cell separation. Figure 5 shows the FACS device and the magnetically separated unit. The microbeads used in the device are composed of ferrous oxide with crystals of adsorbed antibodies attached to the surface. Due to the small thermal fluctuation properties that can lead to spontaneous loss of permanent magnetic moment, superparamagnetic is formed and the microbeads bound in the cells can then be highly magnetized in the presence of an applied magnetic field. Although the 50 nm ferrous oxide particles are super-magnetic, II cannot maintain a stabilizing dipole torque but demonstrate a significant distance within the applied magnetic field. Cell fractionation in this device is achieved by a set of magnetized "wires" with the advantage of an extremely thin ferromagnetic layer and a large magnetic field gradient at the edges so that the mechanism allows to detach of a paramagnetic body and an antimagnetic one. Paramagnetic pearls adherent to cells that get drawn to the conductors have deflected away from the unlabeled cells. The microprocessing device is capable of reaching biological cells' tiny scale of size in length and provides

a sufficiently high-level magnetic field gradient to isolate the cells. In addition, in this device, the liquid flowed fundamentally as a sheet with a much larger two-dimensional space than three-dimensional space. This is in contrast to normal fluid movement, for example in a pipeline, where a single dimension is predominant. Using a fluorescent dye and an antibody from the correct cluster, particular individual cells within the specimen were tagged. The cells are guided across the route of this laser bundle in a monoclinic and thin flow pattern. Each cell is checked for fluorescence as it passes through the beam. Then, as appropriate to whether or not the cells it encompassed were luminescent, a nozzle produced liquid droplets that comprised a solitary unit of cells and applied a magnetic charge, either positive or negative, to each cell. Finally, a strong electric field directs each droplet to a collection chamber. In addition, if the hydrodynamic force is high enough to overwhelm the magnetic deflection, the voltage gradient would have to be reduced in a manner that wouldn't influence the spray breadth. If the droplets instead stick to the electric wire, the pressure may need to be increased. If electrostatic bonding between the beads and the wire is a problem, the SiO2 layer on top of the wire must be thicker. Overall, this article is a technical report and does not enable the separation of bead-labeled cells. However, the device demonstrates that blood samples can be separated in a magnetic environment with different components and that the attachment of white blood cells to the device barrier is under control. However, if the hydrodynamic is large enough to even mask the magnetic deflection, then the pressure gradient of the device must be changed accordingly; On the contrary, if the beads are stuck to the wire, the pressure must be increased, which needs to be achieved by changing the thickness of the coating. The study was likewise not implemented in control of multiple labeling and fluorescence staining. In future studies, the sorting of different cells can be carried out by changing the environment of the magnetic device itself around the characteristics of the magnetic device itself. For example, using the different throughput capabilities of monocytes and macrophages, changing the endocytic capacity in the magnet device can achieve the separation of these two types of cells [7]. Additionally, sorting numerous targets simultaneously at high purity, recovery, and flux levels is still difficult. The multi-target magnet-activated cell sorter apparatus can result in the combined effects of the fluid dynamics generated by laminar flow and the magnetic permeability generated by patterned ferromagnetic structures within microchannels leading to selective purification of differentially marked target cells into various independent outlets [8].

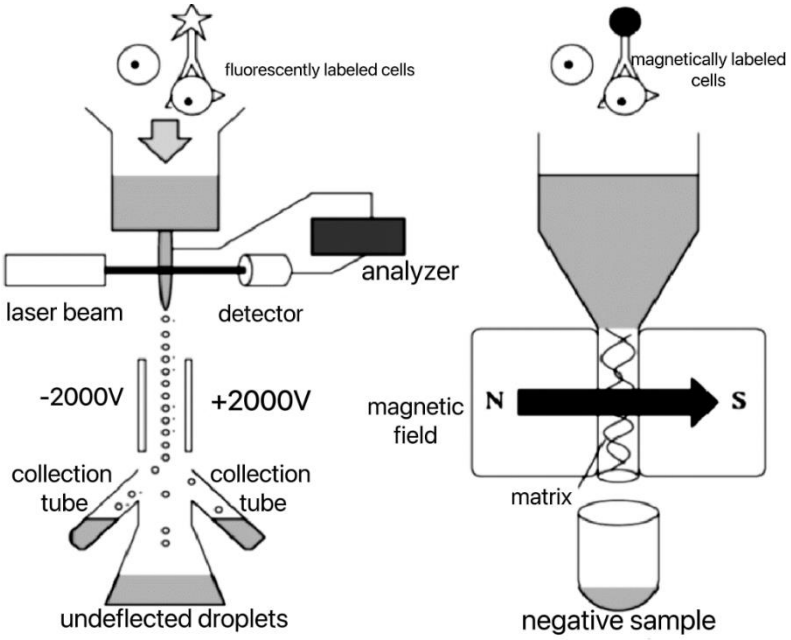

Figure 5. Two conventional ways to sort labeled cells from whole blood

Nicole and Claire[9] came up with another solution for cell sorting. A magnetic field was used to bend the direction of the flow of cells as they operate via a micro-flow cell. Microchip radical flux

magnetophoretic is a means of isolating nuclear microparticles from one another and their non-magnetic counterparts. Figure 6a explains the theory of free stream magnetophoretic: the separation compartment has a combined laminar stream exerted in the X dimension and a magnet field in the Y dimension. Flowing along the surface of the laminate stream of non-magnetized properties, while the magnetic particles/cells deviate from the laminar flow direction. By establishing a laminar flow across the rectangular container, the magnetic field perpendicular to the fluid deflects the magnetic particles. The equivalent microchip design, shown in Figure 6b, was stenciled on a soda-lime glass wafer covered with chromium and photoresist. The microfluidic chip with a cell and buffered intake reservoir is shown in Figure 6c. The findings demonstrate that for a certain cell type and incubation period, the absorption of magnetic particles varies significantly, and these cells are categorized according to their magnetic loading. The deflection of cells is lower at higher flow rates than it is at lower flow rates. As the rate decreases , the wider deflection distribution. The cells are magnetically labeled and then separated. Magnetic particles were deflected from the path of laminar flow based on their size, magnetic susceptibility, and flow rate. Free-flow magnetophoresis allows for the separation of magnetic and non-magnetic cells, as well as cell sorting based on magnetic moments and diameters. The fluorescent albumin was co-internalized with the magnetic cells as detailed in the experimental section to differentiate between the two cell types. The flow velocity of the different cells is the same and all are less than 1 mm/s, and they pass through the microchamber at this speed at a uniform rate. To observe the flow path of the cells, the authors used lenses and fluorescence to enhance the light effect and label the cells as shown in figure 7. The non-magnetic cells flow only to exit 1, while the magnetic cells flow to exit 2 and 3. Overall, this paper demonstrates the effect of continuous mobility separation of two different cells on a slice in the experimental setup under the labeling of magnetic nanoparticles. The method proposed by the authors not only separates different kinds of labeled magnetic cells but also other non-magnetic cells mixed in the liquid along with them. In this paper, when the nanoparticles are small enough, for example with a radius less than 5 nm, they are absorbed into the body by the endocytic mechanism of the cells. Whereas different uptake capacities of cells have different effects, cells with higher uptake capacities can be used to test the effectiveness of the separation method in terms of feasibility and stability. Although the method has a role in isolation, future research could use the method for the diagnosis of diseases and also for the analysis of cell surface markers. Blood is an essential component in the preparation of medical samples, and the cells it contains are extremely important for medical research and treatment. The helical capillary inertial flow control device is capable of achieving labelless sequential isolation of cell mixtures with both high throughput and high efficiency. This robust machine provides greater picking productivity and greater flux than the microfluidic filtering and electro-magnetic vial technologies, and can thereby be applied as a separate workstation for the point-of-service blood testing facilities.[10].

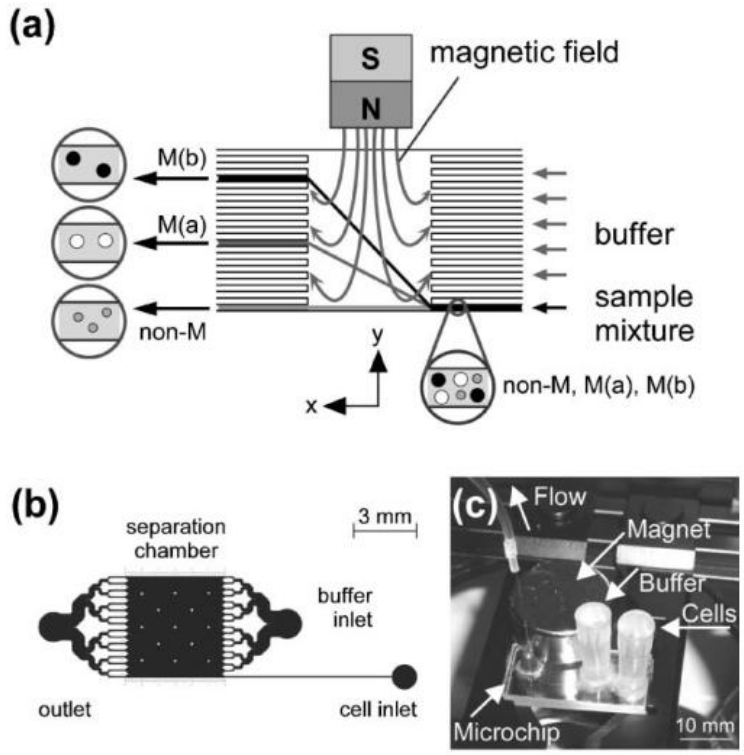

Figure 6. (a) The flow is from the left to right and the magnetic field is comming form above (b)The separation chamber(c) The device as a whole

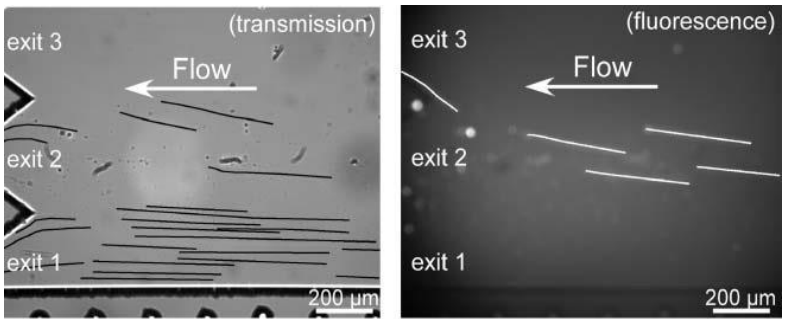

Figure 7. Microscopic view of the flow

3. Conclusion

This paper provides a review of the application of magnetic technology in biomedicine and summarizes the research of scholars using the magnetic moment effect in cell biology by citing four important papers. Firstly, it evaluates the novel application of micro-magnet matrices in cell manipulation, followed by the application of two types of trap beds, opens tubular and magnetic trap beads, in blood t-cells, as well as exemplifying the current status of scholars' research on the use of magnetic technology for biological cell separation. A future study might concentrate on the simultaneous sorting of numerous targets at high purity, recovery, and throughput levels, label-free continuous separation of cell mixtures, and sorting of distinct cells by modifying the device environment surrounding the magnetic device's features.

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