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Applications of Dielectrophoresis in the Field of Medical Sciences

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ABSTRACT

Dielectrophoresis (DEP) is an accurate, fast and a low-costing diagnostic technique that works on the principle of polarization and motion of bioparticles in applied electric field. This technique has brought great revolution in various fields of science such as polymer research, biosensors, medical diagnostics, microfluidics and environmental research. Research in the field of medical science is the major and wide area of interest that could potentially get benefited from DEP technology for its diverse applications. Moreover, many specialized fields of medical science research are yet to be benefited from the technique offered by DEP. This paper will give an overview of recent progress, current challenges, future aspects and potential applications of DEP technique in the field of medical science. This review will also guide the medical researchers and scientists to explore and make utilization of DEP technique in their respective area of research.

Keywords : Dielectrophoresis, Bioparticles Manipulation, Medical Science Diagnostics, Human Health.

I. INTRODUCTION

In recent years, rapid detection of diseases has become very crucial to prevent the loss of human life. It is often too late to take any action on a patient if the disease or infection is at the final stage. The chances of survival of the patients are more if the disease is identified at the primary stage (Jacobs IJ & Menon U, 2004). There are many factors that are responsible for the cause of diseases, such as autoimmune disorders, disruption of the balance in human body, microorganisms such as bacteria, protozoan, virus and fungi (Kassiotis G, 2014). During the diseases, there are some of the complex changes that occurs in all ranging from the molecular integrity to cell morphology (Cravford A, et. al, 2014).There are various technologies and methods involved in detection of diseases, including the use of enzyme-based labelling assays, nucleic acid based assays and dye marker labelling (Bastiat G, et.al, 2013). All these techniques forms basis for the tests performed in pathology laboratories of hospitals. Many assays uses fluorescence substances to label antigen and antibodies to evaluate their quantities. Some makes the use of antibody to label the antigens (Adackapara CA, et.al, 2013).

All of these techniques are highly sensitive. However, the protocols of these tests demands highly trained clinical technicians and expensive equipments (Novak SM & Marlowe EM, 2013). Furthermore, while patients desires for the suitable treatment, these techniques are time consuming which is the major drawback and limitation of these techniques

(Hughes MP, et.al, 2002). These techniques are even considered to be much expensive for small laboratories typically located in slums and village areas. Majority of the samples are sent to highly equipped laboratories for testing at very high cost. This forms a great financial burden on people with low incomes. In addition, there remains great chances of contamination or analytical errors during the process of testing the samples. This leads to false and negative results which places the techniques at great disadvantage (Favaloro EJ, et. al, 2012).

A quick and accurate detection of disease is the first choice for saving human life. This objective cannot be achieved without completely understanding the entire physiology of living cells (Blasi B, et.al, 2012). Differentiating the characteristics and properties of healthy and infected cells have become great area of interest for the researchers to unravel the mystery of disease and its treatment rapidly (Poynard T, et.al, 2013). Recent reports from the researchers have directed their efforts in differentiating the infected cells among healthy cells using the technique of DEP. Dielectrophoresis is the technique which involves the movement of particles in non-uniform electric field by trapping forces when the particles and the medium surrounding have different polarizabilities. The polarization effect of neutral or charged particles is induced by an electric field generated from direct current (DC) or alternating current (AC) potentials. The particles polarized would array in different motions, including repulsion and attraction from electrode by changing the frequency of applied electric field. This particle motion is in response to positive DEP (p-DEP) and negative DEP (n-DEP). These fundamentals were officially named as "Dielectrophoresis" by Dr.Herbert Pohl, a research scientist at the Naval Research Laboratory at Anacosta, USA (Pohl HA, 1951). In his report, he also defined DEP as a phenomenon seen in relative motion of suspensions and media resulting from polarization forces produced by an inhomogeneous electric field. Since then, DEP research got widely expanded in various field of sciences [e.g., Microfluidics (Xuan X , et.al, 2010), Biosensors (Yang L, 2012), Environmental studies (Lafleur P, et. al, 2012), Medical diagnostics (Adekanmbic EO & Srivastava S, 2017)].

This paper will give an overview of present studies and practical applications of DEP in the field of medical science. This paper will start with the brief explanation of background of DEP, theory and its applications. Next the previous DEP investigation in the field of medical sciences are reviewed including eukaryotic and prokaryotic cells, oncology research and mycoses. At the end part of this paper current challenges in DEP and its drawbacks are highlighted along with the potential future applications that can be conducted in the field of medical science through the use of DEP.

Background of DEP

Basic difference between Dielectrophoresis (DEP) and Electrophoresis (EP): Almost everyone gets confused on listening the terms DEP and EP. DEP technique is based on manipulation of particles in non-uniform electric field. Whereas, electrophoresis is based on the response of particles to direct current (DC) voltage to energize the electrode and attract the particles. The motion and movement of the particles in DEP is based on difference in polarizability between the particle and the medium surrounded (Pohl HA,1978). If the particles moves in the direction towards electrode edge, the region of high electric field gradient, then the response is called positive DEP(p-DEP). While if the particles moves in the direction opposite to electrode edge, then the response s called negative DEP (n-DEP)(Morgan H,et.al,1999). In the process of DEP, the particle itself carries electric potentials and response uniquely to different frequencies. On the other side, the particles manipulation in the process of electrophoresis is controlled by density, molecular weight, particle size

and purity. Electrophoresis of positively charged particles (cations) is called cataphoresis. Whereas, electrophoresis of negatively charged particles (anions) is called anaphoresis. Another difference between this two techniques is that DEP can create a trap of particles using electromagnetic fields, while electrophoresis are unable to create stable non-contact traps of particles.

Theory of Dielectrophoresis

DEP force is initiated by applying a non-uniform AC electrical field that manipulates the movements of particles by creating polarizability gradient between the particles and medium surrounded. Technique of DEP is exploiting the mechanical and electrical properties of cells and finding the properties of cell surface and protein for uniquely induced motion of cells. When the cells or particles are suspended into non-uniform electric field, two different forces occurs between cells and the surrounding medium leading to a resultant force. The motion of cells or particles can be in response to positive DEP or negative DEP effects depending on the relative polarizability between the cells and the medium surrounded. (Figure I) will demonstrate the phenomenon of DEP, in which p-DEP effect occurs when cells moves in the direction of high electric field gradient, while n-DEP effect occurs when the cells moves in the direction of low electric field gradient, both of this phenomena depends on Clausius-Mossotli (CM) factor.

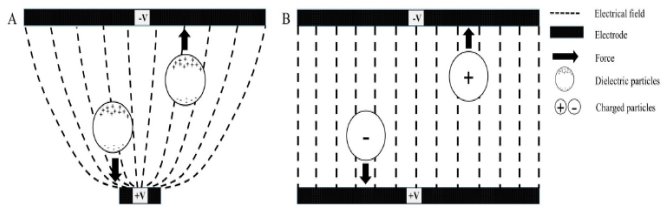

Figure 1. Schematic representation of DEP vs. EP

(A) shows p-DEP and n-DEP effects where dielectric particle move toward the high and low electric field gradient respectively.

(B) shows electrophoresis (EP) in which cation and anion moves toward negative and positive electrode respectively.

The DEP force applied to homogeneous sphere of radius (r) in suspension medium of relative permittivity ε_m can be demonstrated by the formula:

$$< \overrightarrow{FDEP} > = 2\pi r^3 \mathcal{E}_0 \mathcal{E}_m Re[K(\omega)] \nabla E^2 \qquad [1]$$

where,

ω= angular frequency of applied field.

∇E= electric field gradient.

Re[K(ω)]= Real part of the CM factor.

CM factor [K(ω)] is expressed as $\frac{\mathcal{E}^*_p - \mathcal{E}^*_m}{\mathcal{E}^*_p + 2\,\mathcal{E}^*_m}$, $\mathcal{E}^*_p$ is complex permittivity of particles, $\mathcal{E}^*_m$ is complex permittivity of medium. The complex permittivity is given by $\mathcal{E} - j\frac{\sigma}{\omega}$ where $j=\sqrt{-1}$, σ is the material conductivity and ω is the angular frequency.

The direction of DEP forces is dependent on applied voltages, which means that changing the voltage would not interfere with the direction of resultant DEP force. However, the relative polarizability of cells and suspended medium can be manipulated by having control on frequency of applied electric field. The DEP becomes zero at specific frequency and the particle remains stable. This specific frequency is called zero force frequency or crossover frequency (Hughes M, et. al, 2002). This phenomenon takes place when the real part of effective polarizabilities of the particles and surrounding medium are equal to each other (i.e.-Re[K(ω)]=0).

By carefully focusing on the CM factor, it was stated that conductivity controls the low frequency DEP behavior, while permittivity is controlled by high frequency behavior (Ghallab Y & Badawy W, 2004).

Therefore, two main cases are involved in governing the relationship between the applied signal frequency and Re[K(ω)]. This case only occurs when $\sigma_p > \sigma_m$ and $\varepsilon_p > \varepsilon_m$; making Re[K(ω)] positive at high frequency and negative at low frequency. On the other hand, the second case occurs when $\sigma_p < \sigma_m$ and $\varepsilon_p < \varepsilon_m$, then Re[K(ω)] at high frequency and positive at low frequency (Ghallab Y & Badawy W, 2004). [Figure II] will demonstrate the relation between applied signal frequency and Re[K(ω)] with respect to the particle and surrounding medium's conductivity and permittivity.

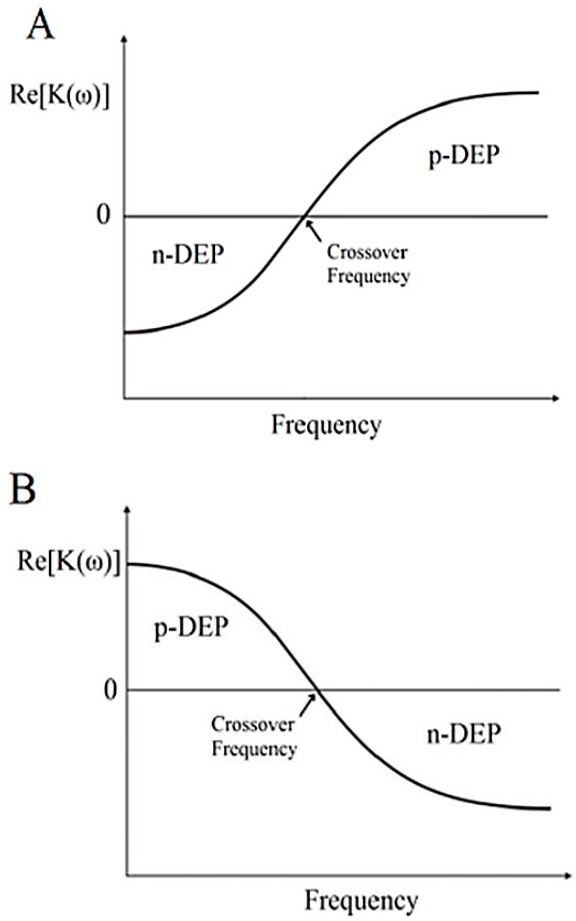

Figure 2. DEP spectrum Frequency vs. Re[K(ω)] of a polarizable particle

[A] When $\sigma_p < \sigma_m$ and $\varepsilon_p > \varepsilon_m$

[B] When $\sigma_p > \sigma_m$ and $\varepsilon_p < \varepsilon_m$.

Geometry of Electrode

The non-uniform electromagnetic fields are needed to generate DEP forces that are generated by microelectrodes patterned using the various methods of micro-fabrication. There are large number of techniques for the fabrication of microelectrodes, including conventional machine, injection molding, laser ablation, in situ construction, wet itching, plasma etching and soft lithography. However, photolithography is considered to be the most basic and important process for these processes. Each microelectrode geometry is designed for the investigation of particular research purpose. Electrode geometry is the most important factor to ensure the sufficient and stable DEP forces that are being applied to induced particles. Since the DEP technique have its direct effect on cell physiology, several electro-physiological effects are needed to be considered when electrode geometry is designed. Factors such as Joule heating (overheating) by electric field may cause dehydration of cells, membrane disruption and death of the cells. [Table I] will describe the electrode geometry with its applications used in previous DEP researches. It can also be concluded that there is no specific electrode geometry that can fulfill all the research applications.

Table I. Geometry and applications of electrodes used in DEP for medical applications.

References	Electrode geometry	Applications	Advantages
Yafouz B, 2016	Circular electrode	Infected cells discrimination	Simple result's interpretation by crossover frequencies
Lin SC,2013	Circular electrode	Particle separation	Low volume of sample
Holzel R, 2002	Cylindrical electrode	Single cell characterization manipulation	Antiparellel DEP field
Laux EM, 2015	Cylindrical electrode	Immobilization of protein molecules	Label free protein molecule quantification

Du E, 2014	Interdigitated electrode	Cell-differentiation	Cell characterization based on bio-electrical properties
Bakewell DJ, 2015	Interdigitated electrode	Nanoparticles quantification	Real time image quantification method of nanoparticles
Wang Y, 2014	Interdigitated electrode	Particle motion prediction	High throughput and low energy consumption
Chrimes AF, 2011	Rectangular electrode	Determination of nanoparticle concentration	Manipulation of particle spacing to observe various conditions of particle
Wu S, 2014	Rectangular electrode	Liquid pumping manipulation in microchannel electrode	Obviate pumping and leakage problems in closed channel
Pesch GR, 2016	Insulator-based(iDEP)	Particle trapping of nanoscale bio particles	High vast localized electric field gradient

iDEP is the technique that deals with the confining of particle based on movement of matter in inhomogeneous electric field that involves insulating structures embedded in microchannel for the production of electric field gradient (Pesch GR, 2016). It has been reported in the studies that polarization of post (obstacles) depends on the ratio of mediums and the post's permittivity (Pesch GR, 2016). The magnitude of the polarization increases with the deviation of permittivity ratio from unity. The optimization of microchannel structures with arrays of post in iDEP may result in only a single particle trapping. Furthermore, it has been illustrated that decreasing the depth of highly constructed channels to submicron sizes, the degree of overheating will get reduced substantially (Chaurey V, et. al, 2013). This will provide a very wide range of media conductivities and voltages that can be applied to achieve rapid enrichment of targeted particles by DEP. While according to the report of (Saucedo-Espinosa MA, 2015), the iDEP showed that particles size and shape of microelectrode have significant effects on the location, magnitude and shape of DEP trapping regions. On the other hand, a report by researchers were able to segregate certain bio-particles by the use of asymmetric shaped insulating posts coupled with the electric potentials of low-frequency (Saucedo-Espinosa MA, et. al, 2017). Moreover, the electrodes used by (Chrimes AF, et. al, 2011) were fabricated on quartz substrates using the technique of photolithography and were used directly for mapping of suspended particle's spatial concentrations. Whereas (Wu S & Hsu W, 2014) used rectangular electrodes that can be selectively and sequentially activated to provide enough DEP force for manipulation of liquids by input frequency modulation. The cylindrical electrodes used by (Laux EM, et. al, 2015) were for the immobilization of proteins. The combination of alternating electric fields with nanometer sized electrodes allowed the proteins to get permanently immobilize by DEP force. A report also stated the characterization of yeast individual by applying different consecutive frequencies (Holzel R, 2002). In this, the electrodes controlled the motion of microscopic particles by DEP for the determination of cell's electrical properties. The most commonly used geometry of electrodes in DEP is Interdigitated electrodes. The interdigitated electrodes used by (Du E & Dao M, 2014) were used to characterize the cells by measuring DEP force by varying the applied frequencies. While the electrode used by (Backewell DJ, et. al, 2015) were used for the calculation of

nanoparticle's density variation by monitoring the distribution of frame pixel intensities. Moreover, report by (Wang Y, et. al, 2014) have replaced the common interdigitated electrode plate by cylindrical interdigitated electrode array to avoid overheating and to also reduce the consumption of power. Microarray dot electrode were used by (Yafouz B, et. al, 2016) was chosen because of its confined area for manipulation in the technique of DEP. Induced cells were either collected at the dot center in case of negative-DEP or move towards the dot edge in case of positive-DEP. The light intensity shifts in the central region of dot were observed and the spectrum of DEP of induced cells were plotted.

Applications of DEP in Medical Sciences

Medical science is an integrated multi-disciplinary field of science that mainly focuses on healthcare diagnostics and its treatment. It deals with the nature of human health and detection of human diseases and achieving the unmet medical needs. Several techniques have been used by medical researchers and scientists for detection of the diseases (Gan SD & Patel KR, 2013). Research in the field of medical science requires great knowledge and understanding of multidisciplinary fields with more innovative research programs to develop better solutions for health related issues (Numamaker JF, et. al, 2013). To support any of the research needs, financial pillars becomes one of the major factor for sustaining of research development. Therefore, well developed rapid diagnostic methods that can be operated with minimal laboratory infrastructures are the crucial need of every researcher.

Bioelectric signals from cells have been proven to carry very useful information about the cell status. There are number of sources of bioelectric signals of cells; one is the sodium potassium pump in the cell membrane matrix. The movements of potassium and sodium ions through the cell membrane creates excitability in membrane and also an electric gradient due to different charges outside and inside the cell membrane matrix (Huang C, et.al, 2013). The effects of chemical analytes and cell-to-cell interactions with the extracellular matrix can be determined by exploiting the dielectric properties of cells without the need of any labels or tags. The following subsection will highlight the applications of DEP in medical sciences which were critically reviewed by our team.

Prokaryotic and Eukaryotic cells

Cells are generally classified into two groups: Prokaryotic and Eukaryotic. This classification is done on the basis of cytology and molecular structures of cells. The most distinct feature between these two cells is the presence of membrane bound nucleus in eukaryotes (Woese C, et. al, 1990). Eukaryotic cells generally have complex membrane bound organelles such as lysosomes and peroxisomes, endoplasmic reticulum, microtubules, mitochondria and histones for DNA wrapping. In comparison to eukaryotes, prokaryotes possess much simple cell structures with small ribosome size and single circular chromosomes (Dell A, et. al, 2011). Human cells can be considered to be eukaryotic cells while bacterial cells are considered as prokaryotes. [Table 2] will give brief description of previous investigations conducted on eukaryotes and prokaryotes using DEP technique.

Reference	Type of cell	Application	Advantage
Yun H, 2013	Eukaryotic: Cancer cells - Erythrocytes HeLa	Sorting and Trapping	More efficient sorting and Trapping.
Sankaranarayanan A, 2016	Prokaryotic: Bacteria	Trapping	Label-free separation of

	(*E.coli, S.aureus & V.cholera*)		microbes.
Pesch GR, 2016	Bacteria: E.coli	Separation	Improve assay sensitivity.
Khoshmanesh K, 2012	Bacteria: Lactobacilli and Yeast	Separation	Independent fingerprinting.

Recently, DEP techniques are only used for prokaryotic and eukaryotic cell separation and trapping. The electrophysiology of cells are being manipulated for the different purposes such as sorting, separation and isolation of cells or microorganisms. DEP involves great features such as label free, fast and inexpensive compared to other techniques. Therefore, DEP has the great potentials to be implemented in future diagnostic techniques that can be commercialized in medical laboratories for its daily usage. Techniques such as immunohistochemistry has high specificity and sensitivity but it requires a specific antibody, a fluorescent dye and a dark-field microscopy in its operation. Furthermore, sometimes due to cell degradation, toxic reactions and fluorescent dye fading during washing steps may lead to false and negative results (Chao WR, et. al, 2015). These problems can be overcome using DEP techniques which are label-free.

Oncology Research using DEP technique

Oncology is the study of diagnosis and treatment of cancer. The main aim of oncology is to detect and identify cancer through screening at initial stage. Cancer is an abnormal malignant cell growth that metastasized and travels to the other nearby tissues and body parts invading organs and systems (Hanahan D & Weinberg RA, 2011). On the other hand, treatment of cancer are multilevel and multimodal depending on its type and stage. Oncology also includes the study and management of side effects of cancer treatment (Aapro M, et. al, 2014). There are several challenges on the research of oncology such as confirmation and differentiation of cancer types, isolation of rare cancer cells from complex samples (i.e., blood) and monitoring the treatment process by continuous assessing the cell morphology. As DEP technique can differentiate between pathological and healthy cells by its dielectric properties, use of DEP has being increasing in the field of oncology investigations.

Different cells have differences in their surface area, morphology and even size. But the main parameter that governs the DEP cell separations are attributed to unique differences of cell electric properties "fingerprints". Each cell at a particular pathological state features a particular crossover which can be used for the characterization of infected cells (Gascoyne PR & Shim S, 2014). Despite, crossing over frequency of DEP, the ionic conductivity of suspending medium also has a major effect on DEP cell differentiation. A particular medium conductivity can be controlled by a narrow AC frequency band (Alshareef M, et. al, 2013). [Table 3] will briefly describe the previous researches of oncology carried out using DEP technique.

Reference	Cell Type	Application	Advantage
Gascoyne PR	CTCs	Isolating CTCs from	Rapid and label-free

& Shim S, 2014)		blood.	method of cell isolation.
Huang C, 2013	Prostate cancer	Very rare cell isolated from blood.	Improved immunocapture performance.
Liang X, 2014	Human oral cancer cells	Cancer cell characterization.	Label-free and rapid characterization method.
Alsharef M, 2013	Breast and colorectal cancer	Differentiation of two cancer cells.	Label-free isolation and separation of cells.
Ismail A, 2015	Osteosarcoma (Bone cancer cells)	Identification and monitoring of tumor heterogeneity.	Label-free cancer subject characterization.

Cancer cells are very difficult to detect and isolate from normal cells because its genes mutate and get differentiated into subsets and a specific biomarker is needed for their detection (Garnett MJ, et. al, 2012). Cell sorting, sequencing and use of flow cytometry in detection of cancer demands highly trained workers and expensive equipments that are of high cost (Galanzha EI, et. al, 2009). According to the above table, DEP is a label-free inexpensive technique that can improve the screening performance of cancer cells when combined with other devices (i.e., microfluidic platforms). For example, (Gasceyne PR & Shim S, 2014) explained that the interdigitated electrode is DEP field flow fractionation (DEP-FFF) allowing high throughput of isolation and characterization of cells. The integrated techniques have also enhanced the recovery of cells for future clinical diagnostics. Therefore, DEP can be used to reduce the complexity and limitations of currently available techniques for identification of cancer cells.

Mycoses

Infections caused by fungi to humans or animals are called mycoses. Fungi can be either eukaryotic or prokaryotic. While its structure can be budding or filamentous. Multicellular complex fungi may have shape of a mushroom. They always favors a dark and humid conditions for their growth. Mycoses can cause severe illness, especially when they enters the internal body system of humans. For example, fungi such as *Aspergillus* can grow in lungs and cause allergy and toxicity, while *Cryptococcus* may cause meningitis and brain damage in auto-immune patients (Chen SC, et. al, 2012).

Detection of fungi is almost the same as that of bacteria. They require their own special media, stains and biochemical reactions (Mehl HL & Cotty PJ, 2013). Cultures of fungi are time consuming and laborious (Moris AJ, et. al, 1996). (Tang S, et. al, 2015) in his research used *S.cereviseae* a type of yeast for investigation of DEP response of lyticase (cell lysis agent). This research used a modular platform of cellular response subjected to apoptosis chemical stimulation as well as physical stimulation down to single cell level. However, (Patel S, et. al, 2012) in their work also used yeast as a platform to check cell availability using reservoir based DEP. Although, mycoses may cause severe infections in humans, there are very limited research work carried out to exploit the advantages of DEP technique in detection of mycoses.

Current challenges and drawbacks of DEP

DEP has been illustrated to have the potentials to be the most convenient assistive POC diagnostic

technique that can be utilized in identification of screening diseases. In the researches of medical science, it helps to isolate, separate, fractionate and concentrate target bioparticles for many research purposes. In addition to the technique of DEP being label-free, they are economical cheaper and saves time compared to other techniques. However, when bringing a new technology, there is always a long and winding road before it comes in recognition to the entire world. There are many obstacles that are faced by researchers to develop DEP electrode to meet their research need. Some researchers faces problems such as bubbles in liquid, which affects the electrical insulations, darkening of electrodes under high conductance conditions in DC and also some problems with microchannels due to high gradients acting only in the vicinity of electrodes (Patel VK & Sayed-Yagoobi J, 2015). Joule heating is also a great challenge for the researchers. Report by Kale stated that Joule heating reduces reservoir DEP (rDEP) focusing and trapping the performance of DEP due to the rise of fluid temperature and also reduces the electric field at the reservoir- microchannel junction (Kale A, et. al, 2014). Furthermore, it was reported that cell viability significantly decreases after iDEP manipulation mainly due to direct damage of cell membrane caused by electric field combined with joule heating (LaLonde A, et. al, 2015).

Besides all the above limitations, there are many other things that need to be considered as limitation for DEP technique such as evaporation of water or liquid during the process, which may cause variations in osmolarity and concentrations. The CM factor K(ω) can be negative or positive depending on the polarizability between the cell and the suspending medium, creating the pDEP and nDEP effects. This can be adjusted by selecting appropriate frequency of applied electric field (Yafouz B, et. al, 2016). In almost every DEP experiments, the typical media used in culture technique [i.e., Dubbecco's Modified Eagle Medium (DMEM) and Phosphate Buffer Saline (PBS)] cannot be used in DEP technique because of their higher conductivities. Therefore, a low conductivity buffer or medium is used as the suspending medium; however, the medium was also reported to have a notable influence on the decrease of cell viability after the incubation period of 6 hours (Khoshmanesh K, et. al, 2011).

Although the techniques of DEP are economically wise, the very first thing to be considered is the user for instance, the clinical laboratory scientists, the medical researchers, the laboratory technicians and the doctors. It is very hard to change the personnel's paradigm that has been well niche by the traditional diagnostic techniques. The technique of DEP needs to be launched after educating, promoting and demonstrating the process by training and seminars to the users so that they can gain confidence in using it.

Potential Applications and Recommendations to DEP

Technique of DEP is label-free, accurate and rapid that can be used for cell sorting, trapping, differentiating and purifications. Furthermore, this technique has the potentials to unbound the research laboratorie's complex and bulky instruments and equipments. Also it does not requires high trained technicians for its operation. Many research experiments have been conducted using the technique of DEP for analysis of biological samples, but investigations are still at the teething phase. This studies mainly focused on understanding the fundamental response of biological particles to DEP forces. Few studies have attempted to link the electrophysiological properties of biological particles to their DEP behavior. However, there is still a great increasing demand to integrate the DEP techniques with miniaturized lab-on-chip platforms to perform various researches of medical science. A complete DEP system should be standardize that should contain several essential components, such as

microelectrode device, a signal generator, an image-capturing device, autograph analyzer and computer software. Such a system should be developed which can conduct the process of sample preparation, detection and robust signal quantification automatically, leading to a complete convenient functional system. The designers should precisely focus on developing a complete system with universal cell suspending solutions, image and graph analysis with standard reference database to make the technique of DEP more user friendly in the field of medical sciences. This technique of DEP can be a potential assistive tool form for making difference between normal cells and damaged cells of fibroblast in anti-aging projects. The effectiveness and delivery of anti-aging plant extract or compound in the cells can be assessed by unique DEP responses of cells. The cells which gets damaged by UVB and UVA can be characterized by DEP since each type of UV will have different effects of electro-physical properties on the cells. Moreover, DEP can also be used as an assessor in the treatment of dermatology industries. With the use of DEP in dermatology industries, the cost of dermatology product testing would be reduced and could save their time and even the use of animal testing in dermatology product development can be stopped. Since the beginning, DEP has being using metal-based electrodes (i.e; Platinum. gold, silver, nickel, etc.) have been used to generate non-uniform electric field needed for DEP.

Planar electrodes have been used widely to induce DEP effects. In order to have electric fields more stronger, a few 3D microelectrodes were proposed according to the literature. However, this microelectrodes used complex machineries to get fabricated which made the process very expensive. Alternatively, 3D microelectrodes may be fabricated using polymer precursors before pyrolyzing them in an inert atmosphere to become carbon (Kamath RR & Madou MJ, 2014). Carbon has very large number of its practical applications as it has wider electrochemical stability window compared to noble metals. This could reduce the risk of sample electrolysis for a given applied voltage. Furthermore, carbon has excellent biocompatibility and chemical inertness.

II. CONCLUSION

Medical science is a multidisciplinary field that involves various studies of mechanism of life and underlying causes of diseases and they need to develop and improve unmet treatment and diagnosis for patients. DEP is one of the most promising technique that can meet all the needs of medical researchers. Researchers should focus towards development of POC devices to be used where high-tech laboratories are unavailable. For e.g.- villages and economically backward areas. This POC devices should be designed such that it would give accurate results in minimum time so that the patient's life could be saved by delivering the right treatment at right time. The technique of DEP can become a helping hand to the global issue of high costs of clinical laboratory tests. This paper has reviewed several research activities that were conducted in the field of medical science utilizing DEP. Finally, future potential directions of DEP in the field of medical sciences were proposed.

In this review, we conclude that DEP is a very powerful, unique, time saving, cost-effective and label-free analytical diagnostic and screening technique. It has been demonstrated that technique of DEP offers a wide range of applications such as isolating, trapping, concentrating, separating and fractionating bioparticles down to nanoscale dimension. With this paper we hope that frontier gap between engineering and medical sciences can be closed and progress to invent better technology to improve human health. It is also expected that DEP technique will change the public health scenarios, especially in developing countries where there is shortage of highly equipped laboratories.

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