ENHANCEMENT OF RING AND RIPPLE MICROELECTRODES DESIGN USING DIELECTROPHORESIS (DEP) FOR BIOCHIP APPLICATION

SITI NURSYAHIRAH BINTI AHMAD LATFI

Master of Science

UNIVERSITI MALAYSIA PAHANG

SUPERVISOR'S DECLARATION

I hereby declare that I have checked this thesis and in my opinion, this thesis is adequate in terms of scope and quality for the award of the degree of Master of Science

_____

(Supervisor's Signature)

Full Name :

Position :

Date :

STUDENT'S DECLARATION

I hereby declare that the work in this thesis is based on my original work except for quotations and citations which have been duly acknowledged. I also declare that it has not been previously or concurrently submitted for any other degree at Universiti Malaysia Pahang or any other institutions.

_____

(Student's Signature)

Full Name : SITI NURSYAHIRAH BINTI AHMAD LATFI

ID Number : MEL14007

Date :

ENHANCEMENT OF RING AND RIPPLE MICROELECTRODES DESIGN USING DIELECTROPHORESIS (DEP) FOR BIOCHIP APPLICATION

SITI NURSYAHIRAH BINTI AHMAD LATFI

Thesis submitted in fulfillment of the requirements
for the award of the degree of
Master of Science

Faculty of Electrical & Electronics Engineering

UNIVERSITI MALAYSIA PAHANG

2018

ACKNOWLEDGEMENTS

Alhamdulillah, all praised to ALLAH s.w.t. First of all, I feel very grateful for all the blessings, mercy, guidance and help, and strength given by ALLAH s.w.t. Appreciation and gratitude also go to my supervisor Dr. Samsuri Fahmi for his guidance, help, encouragement, support, time and patience in supervising me throughout my study. I also thank all academicians and staff of the Faculty of Electrical and Electronics Engineering, Universiti Malaysia Pahang have involved directly or indirectly during my research.

Sincere thanks to all friends and AppECE laboratory colleagues who have contributed ideas, guidance, support, encouragement, and strength to me to cope with the bittersweet journey to accomplish the research goals.

Finally, my deepest appreciation and gratitude are addressed to my parents and siblings for their infinite love, support, encouragement, strength and prayers for my success in completing this study.

TABLE OF CONTENT

LIST OF TABLES

LIST OF FIGURES

LIST OF SYMBOLS

ε	Permittivity
σ	Conductivity
μ	Micro
ω	Angular frequency
N	Newton

LIST OF ABBREVIATIONS

2D	Two-dimensional
3D	Three-dimensional
AC	Alternating current
DC	Direct current
CM	Clausius-Mossoti
DEP	Dielectrophoresis
DNA	Deoxyribonucleic acid
EF	Electric field
EP	Electrophoresis
ID	Interdigitated
LOC	Lab-on-chip
MEMS	Microelectromechanical systems
nDEP	Negative dielectrophoresis
pDEP	Positive dielectrophoresis
RF	Radio frequency
SIBC	Sandwiched insulator with back contact
UV	Ultraviolet
POC	Point-of-care

ENHANCEMENT OF RING AND RIPPLE MICROELECTRODES DESIGN USING DIELECTROPHORESIS (DEP) FOR BIOCHIP APPLICATION

SITI NURSYAHIRAH BINTI AHMAD LATFI

Thesis submitted in fulfillment of the requirements
for the award of the degree of
Master of Science

Faculty of Electrical & Electronics Engineering

UNIVERSITI MALAYSIA PAHANG

2018

ABSTRAK

Pada masa kini, keperluan untuk analisis sel-sel biologi telah menjadi platform bagi para penyelidik untuk membangunkan teknologi dan peranti yang berkaitan untuk melakukan manipulasi yang sesuai seperti menangkap, menyaring dan menyusun. Ini kerana analisis sel-sel biologi boleh memberi manfaat kepada pemahaman yang lebih baik mengenai sifat-sifat sel biologi dalam mencari penyelesaian dan rawatan dalam aplikasi perubatan. Pelbagai teknik manipulasi telah dibangunkan untuk memanipulasi sel-sel biologi seperti teknik manipulasi dalam medan kimia, mekanikal, akustik dan elektrik. Daya DEP digunakan untuk memanipulasi sel-sel terhasil daripada penjanaan medan elektrik AC yang tidak seragam dan corak elektrod memainkan peranan penting dalam menghasilkan medan elektrik yang diperlukan. Reka bentuk semasa mempunyai batasan dari segi corak taburan medan elektrik yang dihasilkan dan data simulasi yang diperlukan untuk pembangunan biochip masih tidak mencukupi. Terdapat dua elektrod baru yang terdiri daripada mikroelektrod corak cincin dan mikroelektrod corak riak telah dibangunkan dalam kajian ini. Objektif utama kerja ini adalah untuk menyiasat pengagihan medan elektrik yang dihasilkan dari mikroelekrod. Semua analisis yang dilakukan dalam kajian ini adalah berdasarkan simulasi. Simulasi telah dijalankan menggunakan perisian COMSOL Multiphysics, yang menyediakan platform simulasi dan analisis yang sesuai untuk kajian ini. Pengoptimuman elektrod telah dilakukan dengan membuat beberapa pengubahsuaian terhadap dimensi elektrod dan disimulasikan dengan nilai potensi elektrik yang berlainan. Ini dilakukan untuk meningkatkan prestasi elektrod untuk memerangkap sel tunggal. Berdasarkan hasil simulasi yang diperoleh, kekuatan tertinggi pengagihan medan elektrik dihasilkan oleh corak elektroda cincin adalah 5.22×10^{6} V/m dan daya DEP adalah 1.42×10^{-13}N. Elektrod corak riak menghasilkan 2.04×10^{7} V/m medan elektrik dan daya DEP yang dihasilkan ialah 4.19×10^{-11} N lebih tinggi daripada elektrod cincin. Adalah didapati bahawa isu kenaikan suhu boleh dikawal berdasarkan hasil simulasi dengan mengurangkan voltan sebanyak separuh, namun medan elektrik dapat menghasilkan kekuatan medan elektrik yang lebih tinggi. Peratusan peningkatan kekuatan medan elektrik mikroelektrik cincin dan mikroelektrik riak masing-masing adalah 86.86% dan 47.55%. Keputusan menunjukkan bahawa jarak antara mikroelektrod dan mikro-rongga memberikan impak yang lebih besar dalam kekuatan pengagihan medan elektrik berbanding dengan perubahan dimensi mikroelekrod. Kekuatan medan elektrik yang dihasilkan adalah tinggi di antara hujung mikroelektrod dan pinggir rongga mikro. Penangkapan sel juga boleh berlaku di bahagian tengah rongga mikro dengan dielekroforesis negatif (nDEP) di mana sel-sel tertarik ke kawasan medan elektrik yang rendah. Sebaliknya, apabila menggunakan dielekroforesis positif (pDEP), sel-sel akan tertarik ke pinggir mikro-rongga di mana kawasan medan elektrik yang tinggi berlaku. Dengan simulasi dan analisis yang diperolehi, mikroelektrod direka mampu untuk memerangkap sel-sel. Kerja penyelidikan ini akan menjadi satu usaha untuk mencari reka bentuk biochip, untuk mendapatkan pola reka bentuk elektrod yang lebih baik yang menawarkan kecekapan yang lebih tinggi dalam memanipulasi dan menjebak sel-sel biologi.

ABSTRACT

Nowadays, the need for the analysis of biological cells has become a platform for researchers to develop related technologies and devices for conducting appropriate manipulation such as trapping, screening, and sorting. This is because the analysis of biological cells can be beneficial to better understand the properties of biological cells and find the solution and treatment in medical applications. Various manipulation techniques have been developed to manipulate biological cells such as manipulation technique in chemical, mechanical, acoustic and electric fields. The DEP was force used to manipulate the cells resulting from the generation of a non-uniform AC electric field and electrode patterns play a major role in producing the required electric field. The current design has limitations in terms of the distribution pattern of the electric field generated and insufficient simulation data required for the development of biochip. There were two new electrodes which are ring pattern microelectrode and ripple pattern microelectrode developed in this study. The main objective of this work is to investigate the electric field distribution resulted from the microelectrodes. All analyses performed in this study were based on simulations. Simulations were carried out by using COMSOL Multiphysics software, which provides suitable simulation and analysis platform for this study. The optimisation of an electrode was done by making some modifications to the dimensions of the electrodes and simulated with different electrical potential values. This was done to improve the performance of the electrodes to trap a single cell. Based on the simulation results obtained, the highest strength of the electric field distribution was generated by the ring electrode pattern 5.22×10^{6} V/m produced and the DEP force was 1.42×10^{-13}N. The ripple pattern electrode generated 2.04×10^{7} V/m of electric field and the DEP force produced was 4.19×10^{-11} N which was higher than the ring electrode. It was found that the temperature rise issues can be controlled based on simulation results by reducing the voltage by half, yet electric field can generate higher electric field strength. The percentage increase in electric field strength of ring microelectrode and ripple microelectrode was 86.86% and 47.55%, respectively. The results showed that the distance between the microelectrodes and micro-cavity provided more impact in electrical field distribution strength compared to the change of the microelectrodes dimension. The resulting electrical field strength was high between the microelectrodes tip and edge of the micro-cavities. Cell trapping may also occur in the central part of the micro-cavities with nDEP where the cells were attracted to the areas of low electric field. On the other hand, when pDEP was used, cells were attracted to the edge of micro-cavities where the high electric field region occurred. With the simulation and analysis obtained, designed microelectrode was able to trap the cells. This research work became an attempt to find a biochip design, in order to get the better electrode design patterns which offered higher efficiency in manipulating and trapping the biological cells.

REFERENCES

Abidin, Z. Z., Baik, D. A., Hafifudin, N., & Markx, G. (2008). Factors Affecting Dielectrophoretic Separation of Cells Using High-Gradient Electric Field. *Science And Technology*, *3*(1), 30 – 39.

Alrifaiy, A., Lindahl, O. a., & Ramser, K. (2012). Polymer-based microfluidic devices for pharmacy, biology and tissue engineering. *Polymers*, *4*(3), 1349–1398.

Arnold, W. M. (2010). Dielectrophoretic Cell Separation : Some Hints and Kinks. *Proc. ESA Annual Meeting on Electrostatics*, *2*(1), 1–11.

Asbury, C. L., Diercks, A. H., & Van Den Engh, G. (2002). Trapping of DNA by dielectrophoresis. *Electrophoresis*, *23*(16), 2658–2666.

Auerswald, J., & Knapp, H. F. (2003). Quantitative assessment of dielectrophoresis as a micro fluidic retention and separation technique for beads and human blood erythrocytes. *Microelectronic Engineering*, *67-68*, 879–886.

Bazou, D., Kuznetsova, L. A., & Coakley, W. T. (2005). Physical enviroment of 2-D animal cell aggregates formed in a short pathlength ultrasound standing wave trap. *Ultrasound in Medicine and Biology*, *31*(3), 423–430.

Becker, F. F., Wang, X.-B., Huang, Y., Pethig, R., Vykoukal, J., & Gascoyne, P. R. (1995). Separation of human breast cancer cells from blood by differential dielectric affinity. *Proceedings of the National Academy of Sciences*, *92*(3), 860–864.

Berger, M., Castelino, J., Huang, R., Shah, M., & Austin, R. H. (2001). Design of a microfabricated magnetic cell separator. *Electrophoresis*, *22*(18), 3883–3892.

Burgarella, S., Merlo, S., Dell'Anna, B., Zarola, G., & Bianchessi, M. (2010a). A modular micro-fluidic platform for cells handling by dielectrophoresis. *Microelectronic Engineering*, *87*(11), 2124–2133.

Burgarella, S., Merlo, S., Dell'Anna, B., Zarola, G., & Bianchessi, M. (2010b). A modular micro-fluidic platform for cells handling by dielectrophoresis. *Microelectronic Engineering*, *87*(11), 2124–2133.

Cao, J., Cheng, P., & Hong, F. (2008). A numerical analysis of forces imposed on particles in conventional dielectrophoresis in microchannels with interdigitated electrodes. *Journal of Electrostatics*, *66*(11-12), 620–626.

Cha, M., Yoo, J., & Lee, J. (2011). Bacterial cell manipulation by dielectrophoresis on a hydrophobic guide structure. *Electrochemistry Communications*, *13*(6), 600–604.

Chen, D., & Du, H. (2007). A dielectrophoretic barrier-based microsystem for separation of microparticles. *Microfluidics and Nanofluidics*, *3*(5), 603–610.

Chen, D. F., Du, H., & Li, W. H. (2006). A 3D paired microelectrode array for accumulation and separation of microparticles. *Journal of Micromechanics and Microengineering*, *16*(7), 1162–1169.

Chen, D. F., Du, H., & Li, W. H. (2007). Bioparticle separation and manipulation using dielectrophoresis. *Sensors and Actuators A: Physical*, *133*(2), 329–334.

Cheng, I. F., Chang, H. C., Hou, D., & Chang, H. C. (2007). An integrated dielectrophoretic chip for continuous bioparticle filtering, focusing, sorting, trapping, and detecting. *Biomicrofluidics*, *1*(2).

Cheng, I.-F., Chen, T.-Y., Lu, R.-J., & Wu, H.-W. (2014). Rapid identification of bacteria utilizing amplified dielectrophoretic force-assisted nanoparticle-induced surface-enhanced Raman spectroscopy. *Nanoscale Research Letters*, *9*(1), 324.

Chronis, N., & Lee, L. (2004). Polymer MEMS-based microgripper for single cell manipulation. *Micro Electro Mechanical Systems, 17th IEEE International Conference on.(MEMS)*.

Chuang, C. H., Huang, Y. W., & Wu, Y. T. (2011). System-level biochip for impedance sensing and programmable manipulation of bladder cancer cells. *Sensors*, *11*(11), 11021–11035.

Chuang, H.-S., Raizen, D. M., Lamb, A., Dabbish, N., & Bau, H. H. (2011). Dielectrophoresis of Caenorhabditis elegans. *Lab on a Chip*, *11*(4), 599–604.

Chung, C. C., Cheng, I. F., Chen, H. M., Kan, H. C., Yang, W. H., & Chang, H. C. (2012). Screening of antibiotic susceptibility to β-lactam-induced elongation of gram-negative bacteria based on dielectrophoresis. *Analytical Chemistry*.

Comsol Multiphysics. (2013). Introduction to COMSOL Multiphysics. Retrieved January 20, 2016, from www.comsol.com/support

Daim, T., & Suntharasaj, P. (2010). Technology Roadmap: Lab-on-a-Chip. *Revista de Administração Da UFSM*, *3*, 160–173.

Dalton, C., Goater, A. D., Drysdale, J., & Pethig, R. (2001). Parasite viability by electrorotation. In *Colloids and Surfaces A: Physicochemical and Engineering Aspects* (Vol. 195).

Dickinson, E. J. F., Ekström, H., & Fontes, E. (2014). COMSOL Multiphysics®: Finite element software for electrochemical analysis. A mini-review. *Electrochemistry Communications*, *40*, 71–74.

Doh, I., & Cho, Y. H. (2005). A continuous cell separation chip using hydrodynamic dielectrophoresis (DEP) process. *Sensors and Actuators, A: Physical*, *121*(1), 59–65.

Duggan, D. J., Bittner, M., Chen, Y., Meltzer, P., & Trent, J. M. (1999). Expression profiling using cDNA microarrays. *Nature Genetics*, *21*, 10–14.

Dürr, M., Kentsch, J., Müller, T., Schnelle, T., & Stelzle, M. (2003). Microdevices for manipulation and accumulation of micro- and nanoparticles by dielectrophoresis. *Electrophoresis*, *24*(4), 722–731.

Evander, M., Johansson, L., Lilliehorn, T., Piskur, J., Lindvall, M., Johansson, S., … Nilsson, J. (2007). Noninvasive acoustic cell trapping in a microfluidic perfusion system for online bioassays. *Analytical Chemistry*, *79*(7), 2984–2991.

Fatoyinbo, H. O., Hoettges, K. F., & Hughes, M. P. (2008). Rapid-on-chip determination of dielectric properties of biological cells using imaging techniques in a dielectrophoresis dot microsystem. *Electrophoresis*, *29*(1), 3–10.

Gallo-Villanueva, R. C., Rodríguez-López, C. E., Díaz-de-la-Garza, R. I., Reyes-Betanzo, C., & Lapizco-Encinas, B. H. (2009). DNA manipulation by means of insulator-based dielectrophoresis employing direct current electric fields. *Electrophoresis*, *30*(24), 4195–4205.

Gascoyne, P. R. C., Wang, X. B., Huang, Y., & Becker, R. F. (1997). Dielectrophoretic separation of cancer cells from blood. *IEEE Transactions on Industry Applications*, *33*(3), 670–678.

Guan, W., Joseph, S., Park, J. H., Krstić, P. S., & Reed, M. A. (2011). Paul trapping of charged particles in aqueous solution. *Proceedings of the National Academy of Sciences of the United States of America*, *108*(23), 9326–9330.

Haeberle, S., Zengerle, R., Le, H. P., Terry, S. C., Jerman, J. H., Angell, J. B., … Haber, C. (2007). Microfluidic platforms for lab-on-a-chip applications. *Lab on a Chip*, *7*(9), 1094.

Han, K., Frazier, a B., & Drive, A. (2005). A Microfluidic System for Continuous Magnetophoretic Separation of Suspended Cells Using Their Native Magnetic Properties. *NSTI-Nanotech 2005*, *1*(Dmc), 187–190.

Han, K. H., & Frazier, a. B. (2005). Diamagnetic capture mode magnetophoretic microseparator for blood cells. *Journal of Microelectromechanical Systems*, *14*(6), 1422–1431.

Heida, T. (2003). Electric field-induced effects on neuronal cell biology accompanying dielectrophoretic trapping. *Advances in Anatomy, Embryology, and Cell Biology*, *173*(III-IX), 1–77.

Henning, A., Bier, F. F., & Hölzel, R. (2010). Dielectrophoresis of DNA: Quantification by impedance measurements. *Biomicrofluidics*, *4*(2).

Hertz, H. M. (1995). Standing-wave acoustic trap for nonintrusive positioning of microparticles. *Journal of Applied Physics*, *78*(8), 4845–4849.

Huang, Y., Hölzel, R., Pethig, R., & Wang, X. B. (1992). Differences in the AC electrodynamics of viable and non-viable yeast cells determined through combined dielectrophoresis and electrorotation studies. *Physics in Medicine and Biology*, *37*(7), 1499–517. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/1631195

Hughes, M. (2003). *Nanoelectromechanics in engineering and biology*. Retrieved from http://scholar.google.com/scholar?hl=en&btnG=Search&q=intitle:Nanoelectromechanics+in+Engineering+and+Biology#0

Hughes, M. P., & Morgan, H. (1999). Dielectrophoretic trapping of single sub-micrometre scale bioparticles. *Journal of Physics D: Applied Physics*.

Ibrahim, S. N., & Alkaisi, M. M. (2012). The octupole microelectrode for dielectrophoretic trapping of single cells-design and simulation. In *2012 10th IEEE International Conference on Semiconductor Electronics, ICSE 2012 - Proceedings* (pp. 119–122).

Ibrahim, S. N., & Alkaisi, M. M. (2015). Microelectrode Design for Particle Trapping on Bioanalysis Platform. *Advanced Materials Research*, *1115*(July), 543–548.

Ibrahim, S. N., Murray, L., Nock, V., Evans, J. J., & Alkaisi, M. M. (2012). The quadrupole microelectrode design on a multilayer biochip for dielectrophoretic trapping of single cells. *Microelectronic Engineering*, *97*, 369–374.

Iliescu, C., Xu, G. L., Ong, P. L., Yu, L., Tay, F. E. H., Iliescu, F. S., & Tressett, G. (2007). Manipulation of Biological Samples Using Electric Field.

Iliescu, C., Yu, L., Tay, F. E. H., & Pang, a. J. (2007). Bidirectional field-flow particle separation method in a dielectrophoretic chip with 3D electrodes. *TRANSDUCERS and EUROSENSORS '07 - 4th International Conference on Solid-State Sensors, Actuators and Microsystems*, *129*, 1837–1840.

J. Kentsch, M. Durr, T. Schnelle, G. Gradl, T. M . uller, M. J . ager, A. N. and M. S. (2003). Microdevices for separation, accumulation, and analysis of biological micro- and nanoparticles. *IEEE Proceedings of Nanobiotechnology*, *150*(2), 82–89.

Jang, L.-S., Huang, P.-H., & Lan, K.-C. (2009). Single-cell trapping utilizing negative dielectrophoretic quadrupole and microwell electrodes. *Biosensors & Bioelectronics*, *24*(12), 3637–44.

Johann, R. M. (2006). Cell trapping in microfluidic chips. *Analytical and Bioanalytical Chemistry*, *385*(3), 408–412.

Kang, Y., Li, D., Kalams, S. a., & Eid, J. E. (2008). DC-Dielectrophoretic separation of biological cells by size. *Biomedical Microdevices*, *10*(2), 243–249.

Khoshmanesh, K., Nahavandi, S., Baratchi, S., Mitchell, A., & Kalantar-zadeh, K. (2011). Dielectrophoretic platforms for bio-microfluidic systems. *Biosensors and Bioelectronics*, *26*(5), 1800–1814.

Khoshmanesh, K., Zhang, C., Tovar-Lopez, F. J., Nahavandi, S., Baratchi, S., Mitchell, A., & Kalantar-Zadeh, K. (2010). Dielectrophoretic-activated cell sorter based on curved microelectrodes. *Microfluidics and Nanofluidics*, *9*(2-3), 411–426.

Kojima, K., Hiratsuka, A., Suzuki, H., Yano, K., Ikebukuro, K., & Karube, I. (2003). Electrochemical protein chip with arrayed immunosensors with antibodies immobilized in a plasma-polymerized film. *Analytical Chemistry*, *75*(5), 1116–1122.

Koklu, M., Park, S., Pillai, S. D., & Beskok, A. (2010). Negative dielectrophoretic capture of bacterial spores in food matrices. *Biomicrofluidics*, *4*(3).

Latfi, S. N. A., & Samsuri, F. (2015). Biochip development for biological cells manipulation using DEP. *ARPN Journal of Engineering and Applied Sciences*, *10*(22), 17091–17094.

Li, C.-W., Cheung, C. N., Yang, J., Tzang, C. H., & Yang, M. (2003). PDMS-based microfluidic device with multi-height structures fabricated by single-step photolithography using printed circuit board as masters. *The Analyst*, *128*, 1137–1142.

Li, H., & Bashir, R. (2002). Dielectrophoretic separation and manipulation of live and heat-treated cells of Listeria on microfabricated devices with interdigitated electrodes. *Sensors and Actuators, B: Chemical*, *86*(2-3), 215–221.

Li, M., Li, S., Li, W., Wen, W., & Alici, G. (2013). Dielectrophoretic manipulation and separation of microparticles in an S-shaped microchannel integrated with multiple hurdles. *International Conference on Advanced Intelligent Mechatronics(AIM), Wollongong, Australia, July 9-10*, 362–366.

Li, M., Li, S., Wu, J., Wen, W., Li, W., & Alici, G. (2012). A simple and cost-effective method for fabrication of integrated electronic-microfluidic devices using a laser-patterned PDMS layer. *Microfluidics and Nanofluidics*, *12*(5), 751–760.

Li, M., Li, W. H., Zhang, J., Alici, G., & Wen, W. (2014). A review of microfabrication techniques and dielectrophoretic microdevices for particle manipulation and separation. *Journal of Physics D: Applied Physics*, *47*(6), 063001.

Li, Y., Dalton, C., Crabtree, H. J., Nilsson, G., & Kaler, K. V. I. S. (2007). Continuous dielectrophoretic cell separation microfluidic device. *Lab on a Chip*, *7*(2), 239–48.

Lilliehorn, T., Simu, U., Nilsson, M., Almqvist, M., Stepinski, T., Laurell, T., … Johansson, S. (2005). Trapping of microparticles in the near field of an ultrasonic transducer. *Ultrasonics*, *43*(5), 293–303.

Liu, J., Kuznetsova, L. A., Edwards, G. O., Xu, J., Ma, M., Purcell, W. M., … Coakley, W. T. (2007). Functional three-dimensional HepG2 aggregate cultures generated from an ultrasound trap: Comparison with HepG2 spheroids. *Journal of Cellular Biochemistry*, *102*(5), 1180–1189.

LR Huang, EC Cox, RH Austin, J. S. (2004). Continuous Particle Separation Through Deterministic Lateral Displacement. *Science*, *304*(5673), 987–990.

Manaresi, N., Medoro, G., Abonnenc, M., Auger, V., Vulto, P., Romani, A., … Guerrieri, R. (2005). New perspectives and opportunities from the wild west of microelectronic biochips. *Proceedings -Design, Automation and Test in Europe, DATE '05*, *2*, 1092–1093.

Manaresi, N., Romani, A., Medoro, G., Altomare, L., Leonardi, A., Tartagni, M., & Guerrieri, R. (2003). A CMOS Chip for Individual Cell Manipulation and Detection. *IEEE Journal of Solid-State Circuits*, *38*(12), 2297–2305.

Mark, D., Haeberle, S., Roth, G., von Stetten, F., & Zengerle, R. (2010). Microfluidic lab on a chip platforms: requirements, characteristics and applications. *Chemical Society Reviews*, *39*(3), 1153–82.

Medoro, G., Manaresi, N., Leonardi, A., Altomare, L., Tartagni, M., & Guerrieri, R. (2003). A lab-on-a-chip for cell detection and manipulation. *IEEE Sensors Journal*, *3*(3), 317–325.

Miltenyi, S., Müller, W., Weichel, W., & Radbruch, A. (1990). High gradient magnetic cell separation with MACS. *Cytometry*, *11*(2), 231–8.

Moghimi, N., Decker, D. R., & Tatic-lucic, S. (2012). Modeling and Measurement of Dielectrophoretic Force and 2-D Trajectories of Microspheres in Quadrupole Electrode Configuration. *IEEE SENSORS*, 1–4.

Mohamed, H., McCurdy, L. D., Szarowski, D. H., Duva, S., Turner, J. N., & Caggana, M. (2004). Development of a rare cell fractionation device: Application for cancer detection. *IEEE Transactions on Nanobioscience*, *3*(4), 251–256.

Molloy, J. E., & Padgett, M. J. (2002). Lights, action: optical tweezers. *Contemporary Physics*, *43*(4), 241–258.

Moorthy, J., & Beebe, D. J. (2003). In situ fabricated porous filters for microsystems. *Lab on a Chip*, *3*(2), 62–66.

Morgan, H., Hughes, M. P., & Green, N. G. (1999). Separation of submicron bioparticles by dielectrophoresis. *Biophysical Journal*, *77*(1), 516–525.

Müller, T., Gerardino, A., Schnelle, T., Shirley, S. G., Bordoni, F., Gasperis, G. De, … Fuhr, G. (1999). Trapping of micrometre and sub-micrometre particles by high-frequency electric fields and hydrodynamic forces. *Journal of Physics D: Applied Physics*, *29*(2), 340.

Nakano, A., & Ros, A. (2013). Protein dielectrophoresis: Advances, challenges, and applications. *Electrophoresis*.

Nedelcu, O. T. (2011). A thermal study on joule-heating induced effects in dielectrophoretic microfilters. *Romanian Journal of Information Science and Technology*, *14*(4), 309–323.

Neve, N., Kohles, S. S., Winn, S. R., & Tretheway, D. C. (2010). Manipulation of suspended single cells by microfluidics and optical tweezers. *Cellular and Molecular Bioengineering*, *3*(3), 213–228.

Nilsson, J., Evander, M., Hammarström, B., & Laurell, T. (2009). Review of cell and particle trapping in microfluidic systems. *Analytica Chimica Acta*, *649*(2), 141–157.

Pankhurst, Q. a, Connolly, J., Jones, S. K., & Dobson, J. (2003). Applications of magnetic nanoparticles in biomedicine. *Journal of Physics D: Applied Physics*, *36*(13), R167–R181.

Patel, S., Showers, D., Vedantam, P., Tzeng, T. R., Qian, S., & Xuan, X. (2012). Microfluidic separation of live and dead yeast cells using reservoir-based dielectrophoresis. *Biomicrofluidics*, *6*(3), 034102–12.

Paweletz, C. P., Gillespie, J. W., Ornstein, D. K., Simone, N. L., Brown, M. R., Cole, K. a., … Petricoin, E. F. (2000). Rapid protein display profiling of cancer progression directly from human tissue using a protein biochip. *Drug Development Research*, *49*(1), 34–42.

Petersson, F., Nilsson, A., Holm, C., & Jo, H. (2004). Separation of lipids from blood utilizing ultrasonic standing waves in microfluidic channels. *Analyst*, *129*(10), 938–943.

Piacentini, N., Mernier, G., Tornay, R., & Renaud, P. (2011). Separation of platelets from other blood cells in continuous-flow by dielectrophoresis field-flow-fractionation. *Biomicrofluidics*, *5*(3), 1–8.

Pioufle, L. (2002). Design of biochip microelectrode arrays for cell arrangement. *2nd Annual International IEEE-EMBS Special Topic Conference on Microtechnologies in Medicine and Biology - Proceedings*, 140–143.

Pohl, H. a, & Crane, J. S. (1971). Dielectrophoresis of cells. *Biophysical Journal*, *11*(9), 711–727.

Pohl, H. A. (1978). Dielectrophoresis: The behavior of neutral matter in nonuniform electric fields. *Cambridge: Cambridge University Press*, *80*.

Primiceri, E., Chiriaco, M. S., Rinaldi, R., & Maruccio, G. (2013). Cell chips as new tools for cell biology - results, perspectives and opportunities. *Lab on a Chip*, *13*(19), 3789–3802.

Qian, C., Huang, H., Chen, L., Li, X., Ge, Z., Chen, T., … Sun, L. (2014). Dielectrophoresis for bioparticle manipulation. *International Journal of Molecular Sciences*, *15*(10), 18281–309.

Ramadan, Q., Samper, V., Poenar, D., Liang, Z., Yu, C., & Lim, T. M. (2006). Simultaneous cell lysis and bead trapping in a continuous flow microfluidic device. *Sensors and Actuators, B: Chemical*, *113*(2), 944–955.

Reyes, D. R., Iossifidis, D., Auroux, P. A., & Manz, A. (2002). Micro total analysis systems. 1. Introduction, theory, and technology. *Analytical Chemistry*, *74*(12), 2623–2636.

Rosenthal, A., & Voldman, J. (2005). Dielectrophoretic traps for single-particle patterning. *Biophysical Journal*, *88*(3), 2193–205.

Samsuri, F., Alkaisi, M. M., & Evans, J. J. (2011). Biochip development using nanoimprint lithography (NIL) and metallic thermal evaporation techniques for biological cells manipulation using DEP. *International Conference on Electrical, Control and Computer Engineering 2011 (InECCE)*, 382–387.

Schnelle, T., Muller, T., Reichle, C., & Fuhr, G. (2000). Combined dielectrophoretic field cages and laser tweezers for electrorotation. *Applied Physics B-Lasers and Optics*, *70*(2), 267–274. Retrieved from <Go to ISI>://000085955900020\nhttp://link.springer.com/content/pdf/10.1007/s003400050044

Sethu, P., Sin, A., & Toner, M. (2006). Microfluidic diffusive filter for apheresis (leukapheresis). *Lab on a Chip*, *6*(1), 83–9.

Shah, J., & Wilkins, E. (2003). Electrochemical biosensors for detection of biological warfare agents. *Electroanalysis*, *15*(3), 157–167.

Shao, B., Zlatanovic, S., Ozkan, M., Birkbeck, A. L., & Esener, S. C. (2006). Manipulation of microspheres and biological cells with multiple agile VCSEL traps. *Sensors and Actuators, B: Chemical*, *113*(2), 866–874.

Solano, B., & Wood, D. (2007). Design and testing of a polymeric microgripper for cell manipulation. *Microelectronic Engineering*, *84*(5-8), 1219–1222.

Su, F., Chakrabarty, K., & Fair, R. B. (2006). Microfluidics-based biochips: Technology issues, implementation platforms, and design-automation challenges. *IEEE Transactions on Computer-Aided Design of Integrated Circuits and Systems*, *25*(2), 211–223.

Sung J.M. (2007). Dielectrophoresis and Optoelectronic Tweezers for Nanomanipulation. Retrieved January 19, 2017, from http://large.stanford.edu/courses/2007/ph210/sung2/

Suzuki, M., Yasukawa, T., Shiku, H., & Matsue, T. (2007). Negative dielectrophoretic patterning with colloidal particles and encapsulation into a hydrogel. *Langmuir*, *23*(7), 4088–4094.

Taff, B. M., & Voldman, J. (2005). A scalable addressable positive-dielectrophoretic cell-sorting array. *Analytical Chemistry*, *77*(24), 7976–7983.

Thomas, R. S., Morgan, H., & Green, N. G. (2009). Negative DEP traps for single cell immobilisation. *Lab on a Chip*, *9*(11), 1534–1540.

Van Hal, N. L., Vorst, O., van Houwelingen, a M., Kok, E. J., Peijnenburg, A., Aharoni, A., … Keijer, J. (2000). The application of DNA microarrays in gene expression analysis. *Journal of Biotechnology*, *78*(3), 271–280.

VanDelinder, V., & Groisman, A. (2006). Separation of plasma from whole human blood in a continuous cross-flow in a molded microfluidic device. *Analytical Chemistry*, *78*(11), 3765–3771.

Voldman, J. (2006). Electrical Forces for Microscale Cell Manipulation. *Annual Review of Biomedical Engineering*, *8*(1), 425–454.

Voldman, J. (2007). Dielectrophoretic Traps for Cell Manipulation. *BioMEMS and Biomedical Nanotechnology*, *4*, 159–186.

Voldman, J., Braff, R. a., Toner, M., Gray, M. L., & Schmidt, M. a. (2001). Holding Forces of Single - Particle Dielectrophoretic Traps. *Biophysical Journal*, *80*(1), 531–542.

Wang, L., Lu, J., Marchenko, S. a., Monuki, E. S., Flanagan, L. a., & Lee, A. P. (2009). Dual frequency dielectrophoresis with interdigitated sidewall electrodes for microfluidic flow-through separation of beads and cells. *Electrophoresis*, *30*(5), 782–791.

Wang, X. B., Huang, Y., Wang, X., Becker, F. F., & Gascoyne, P. R. (1997). Dielectrophoretic manipulation of cells with spiral electrodes. *Biophysical Journal*, *72*(4), 1887–99.

Wang, Y., Rea, T., Bian, J., Gray, S., & Sun, Y. (1999). Identification of the genes responsive to etoposide-induced apoptosis: Application of DNA chip technology. *FEBS Letters*, *445*(2-3), 269–273.

Weigl, B. H., Bardell, R. L., & Cabrera, C. R. (2003). Lab-on-a-chip for drug development. *Advanced Drug Delivery Reviews*, *55*(3), 349–377.

Wu, L., Lanry Yung, L. Y., & Lim, K. M. (2012). Dielectrophoretic capture voltage spectrum for measurement of dielectric properties and separation of cancer cells. *Biomicrofluidics*, *6*(1).

Xiao, Z., Adam, B., Cazares, L. H., Clements, M. A., Davis, J. W., Schellhammer, P. F., … Wright, G. L. (2001). Quantitation of Serum Prostate-specific Membrane Antigen by a Novel Protein Biochip Immunoassay Discriminates Benign from Malignant Prostate Disease Advances in Brief Quantitation of Serum Prostate-specific Membrane Antigen by a Novel Protein Biochip Immu. *Cancer Research*, *61*(15), 6029–6033.

Xing, X., & Yobas, L. (2014). Dielectrophoretic (DEP) separation of live/dead cells on a glass slide functionalized with interdigitated 3D silicon ring microelectrodes. *2014 IEEE 27th International Conference on Micro Electro Mechanical Systems (MEMS)*, 951–954.

Yafouz, B., Kadri, N. A., & Ibrahim, F. (2012). A Numerical Analysis of Electric Field Strength Over Planar Microarray Dot Electrode for Dielectrophoretic Lab-On-Chip Device, *1*(December), 118–121.

Yafouz, B., Kadri, N. A., & Ibrahim, F. (2012). The Design and Simulation of a Planar Microarray Dot Electrode for a Dielectrophoretic Lab-on-Chip Device. *International Journal of Electrochemical Science*, *7*, 12054–12063.

Yafouz, B., Kadri, N., & Ibrahim, F. (2014). Dielectrophoretic Manipulation and Separation of Microparticles Using Microarray Dot Electrodes. *Sensors*, *14*(4), 6356–6369.

Yang, J., Li, C.-W., & Yang, M. (2004). Hydrodynamic simulation of cell docking in microfluidic channels with different dam structures. *Lab on a Chip*, *4*(1), 53.

Yang, L. (2012). A Review of Multifunctions of Dielectrophoresis in Biosensors and Biochips for Bacteria Detection. *Analytical Letters*, *45*(2-3), 187–201. Retrieved from http://www.tandfonline.com/doi/abs/10.1080/00032719.2011.633182

Yang, L., Banada, P. P., Bhunia, a K., & Bashir, R. (2008). Effects of Dielectrophoresis on Growth, Viability and Immuno-reactivity of Listeria monocytogenes. *J Biol Eng*, *2*, 6.

Yang, L., Banada, P. P., Chatni, M. R., Seop Lim, K., Bhunia, A. K., Ladisch, M., & Bashir, R. (2006). A multifunctional micro-fluidic system for dielectrophoretic concentration coupled with immuno-capture of low numbers of Listeria monocytogenes. *Lab on a Chip*, *6*, 896–905.

Yang, M., Li, C. W., & Yang, J. (2002). Cell docking and on-chip monitoring of cellular reactions with a controlled concentration gradient on a microfluidic device. *Analytical Chemistry*, *74*(16), 3991–4001.

Yi, C., Li, C. W., Ji, S., & Yang, M. (2006). Microfluidics technology for manipulation and analysis of biological cells. *Analytica Chimica Acta*, *560*(1-2), 1–23.

Zhang, C., Khoshmanesh, K., Mitchell, A., & Kalantar-Zadeh, K. (2010). Dielectrophoresis for manipulation of micro/nano particles in microfluidic systems. *Analytical and Bioanalytical Chemistry*, *396*(1), 401–20.

Zheng, L., Brody, J. P., & Burke, P. J. (2004). Electronic manipulation of DNA, proteins, and nanoparticles for potential circuit assembly. In *Biosensors and Bioelectronics* (Vol. 20, pp. 606–619).

Zhu, K., Kaprelyants, A. S., Salina, E. G., & Markx, G. H. (2010). Separation by dielectrophoresis of dormant and nondormant bacterial cells of Mycobacterium smegmatis. *Biomicrofluidics*, *4*(2).

Zhu, L., Zhang, Q., Feng, H., Ang, S., Chau, F. S., & Liu, W.-T. (2004). Filter-based microfluidic device as a platform for immunofluorescent assay of microbial cells. *Lab on a Chip*, *4*, 337–341.