proceedings

MDPI

Abstract

Optically Induced Dielectrophoresis and Machine Learning Algorithms for the Identification of the Circulating Tumor Cells †

Joanna Filippi [1,2,*], Francesca Corsi [3], Paola Casti [1,2], Gianni Antonelli [1,2], Michele D'Orazio [1,2], Francesco Capradossi [3], Rosamaria Capuano [1], Giorgia Curci [1,2], Lina Ghibelli [3], Arianna Mencattini [1,2] and Eugenio Martinelli [1,2]

[1] Department of Electronic Engineering, University of Rome Tor Vergata, 00133 Rome, Italy; casti@ing.uniroma2.it (P.C.); g.antonelli@ing.uniroma2.it (G.A.); michele.d.orazio@uniroma2.it (M.D.); capuano@ing.uniroma2.it (R.C.); giorgia.curci@uniroma2.it (G.C.); mencattini@ing.uniroma2.it (A.M.); martinelli@ing.uniroma2.it (E.M.)
[2] Interdisciplinary Center for Advanced Studies on Lab-on-Chip and Organ-on-Chip Applications (ICLOC), 00133 Rome, Italy
[3] Department of Biology, University of Rome Tor Vergata, 00133 Rome, Italy; francesca.corsi@uniroma2.it (F.C.); francesco.capradossi@uniroma2.it (F.C.); ghibelli@uniroma2.it (L.G.)
* Correspondence: filippi@ing.uniroma2.it
† Presented at the XXXV EUROSENSORS Conference, Lecce, Italy, 10–13 September 2023.

Abstract: Detecting circulating tumor cells (CTCs) is a challenge in cancer research. Their dissemination into the blood stream represents a crucial event in the formation of the metastases from the primary tumor. For this reason, targeting CTCs in human liquid biopsies is a warning event for cancer invasiveness, progression, and prognosis. In this regard, by means of the optically induced dielectrophoresis (ODEP) technique, we investigated the response to the electric field, at different frequencies, of human prostatic carcinoma PC3 cells, which mimic CTCs derived from prostate cancer, and human leukemia monocytic THP-1 cells, which simulate circulating monocytes. The obtained spectra of the cell motion descriptors represent the unique identification signature of each cell type.

Keywords: optically induced dielectrophoresis; machine learning; Lab-on-Chip; CTCs

Citation: Filippi, J.; Corsi, F.; Casti, P.; Antonelli, G.; D'Orazio, M.; Capradossi, F.; Capuano, R.; Curci, G.; Ghibelli, L.; Mencattini, A.; et al. Optically Induced Dielectrophoresis and Machine Learning Algorithms for the Identification of the Circulating Tumor Cells. *Proceedings* **2024**, *97*, 71. https://doi.org/10.3390/proceedings2024097071

Academic Editors: Pietro Siciliano and Luca Francioso

Published: 21 March 2024

1. Introduction

The high-purity isolation and analyses of CTCs are crucial in developing targeted therapy [1]. Additionally, these cells are rare and heterogeneous, so identifying them is difficult. Their detection with common epithelial markers that are not expressed in normal blood cells can fail when some cell subtypes miss the markers mentioned above [1]. In this regard, we explored the potential of using ODEP-based multi-spectral analysis to distinguish between PC3 [2] and THP-1 cells [3] in a label-free manner. The proposed method highlights the dielectric signature of every cell population, allowing for the identification of different cell types by exploiting their response to the DEP force.

2. Materials and Methods

Cell manipulation was performed using an ODEP-based Lab-on-Chip device and an optical platform [4], as shown in Figure 1. An AC potential was applied between the ITO layers, and a light pattern was projected on the a-Si. The generated non-uniform electric field induced a dielectrophoretic (DEP) force on the cells by producing three different cell motions: attractive (pDEP), repulsive (nDEP), or steady-state cell motions. Single cells were measured at different frequencies in a range 25–150 kHz with steps of 5 kHz and an amplitude of 10 Vpp. Videos of the DEP-induced motion were acquired, and the cell tracking procedure allowed us to extract a set of cell parameters for each n frequency: the

cumulative displacement $CD(f_n)$, the maximum velocity $v_{max}(f_n)$, and the maximum DEP force $F_{DEP\_max}(f_n)$ were used as inputs to build a classification model [4].

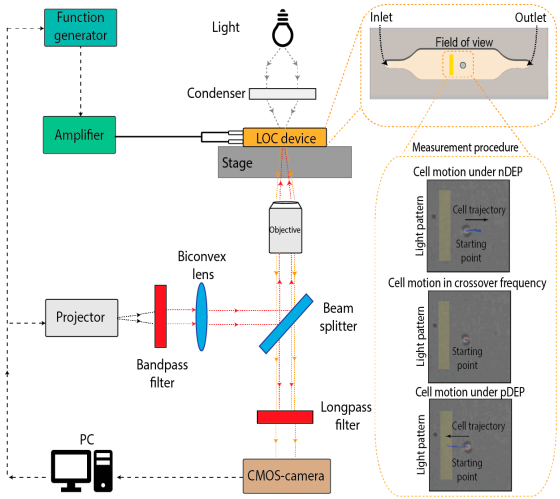

Figure 1. Schematic representation of the ODEP system setup with details on the cell measurement strategy.

3. Discussion

The response spectra of $CD(f_n)$ and $F_{DEP\_max}(f_n)$ for both PC-3 and THP-1 cells are shown in Figures 2a and 2b, respectively. As shown, the two cell populations exhibited different crossover frequencies: 30 kHz for PC-3 (blue dotted line) and 50 kHz for THP-1 (green dotted line). The extracted features have been used to build an LDA classification model whose confusion matrix and total accuracy value obtained in the 5-fold cross-validation are shown in Figure 2c. The high discrimination rate suggests that the proposed system, with the appropriate operating conditions, can sort cells and isolate CTCs in a label-free manner under continuous flow.

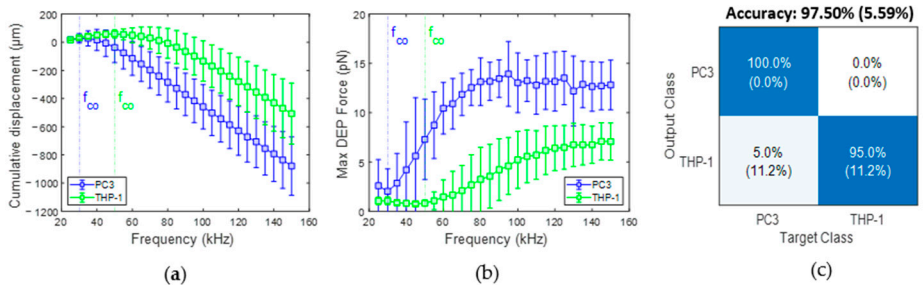

Figure 2. Spectra of cumulative displacement (**a**) and maximum DEP force (**b**). Average values and standard deviations are reported. Dotted lines indicate the crossover frequency (f_{co}). (**c**) Confusion matrix of the LDA model.

Author Contributions: Conceptualization, methodology, and formal analysis, J.F., P.C. and E.M.; data curation, J.F., G.A., M.D., R.C., G.C. and A.M.; biological experiments, J.F., F.C. (Francesca Corsi), F.C. (Francesco Capradossi) and L.G.; writing—original draft preparation, J.F., P.C., A.M. and E.M.; writing—review and editing, all authors. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Data are available on request.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Plaks, V.; Koopman, C.D.; Werb, Z. Circulating Tumor Cells. *Science* **2013**, *341*, 1186–1188. [CrossRef]
2. Chen, H.-H.; Lin, M.-W.; Tien, W.-T.; Lai, C.-P.; Weng, K.-Y.; Ko, C.-H.; Lin, C.-C.; Chen, J.-C.; Tiao, K.-T.; Chen, T.-C.; et al. High-purity separation of cancer cells by optically induced dielectrophoresis. *J. Biomed. Opt.* **2014**, *19*, 1. [CrossRef]
3. Chanput, W.; Mes, J.; Vreeburg, R.A.M.; Savelkoul, H.F.J.; Wichers, H.J. Transcription profiles of LPS-stimulated THP-1 monocytes and macrophages: A tool to study inflammation modulating effects of food-derived compounds. *Food Funct.* **2010**, *1*, 254–261. [CrossRef] [PubMed]
4. Filippi, J.; Di Giuseppe, D.; Casti, P.; Mencattini, A.; Antonelli, G.; D'Orazio, M.; Corsi, F.; Della-Morte Canosci, D.; Ghibelli, L.; Witte, C.; et al. Exploiting spectral information in Opto-Electronic Tweezers for cell classification and drug response evaluation. *Sens. Actuators B Chem.* **2022**, *368*, 132200. [CrossRef]