

Label-free Biomarker Detection Using Dielectrophoresis and Localized Surface Plasmonic Resonance

K . A. S. Lakshan

Department of Electrical and Computer Engineering,
North Dakota State University,
Fargo, ND, USA.
k.sameeralakshan@ndsu.edu

Dharmakeerthi Nawarathna

Department of Electrical and Computer Engineering,
North Dakota State University,
Fargo, ND, USA.
dharmakeerthi.nawara@ndsu.edu

Abstract: We have utilized the dielectrophoretic force of short single-stranded DNA molecules to manipulate molecules around Au nanoparticles and studied the effects of the localized plasmon resonance response of Au nanoparticles.

Keywords—Localized surface plasmonic resonance, Dielectrophoresis, DNA, Au nanoparticles

I. INTRODUCTION

Detection of disease biomarkers is a common method used in screening and diagnosis of diseases. Moreover, disease stage and severity can be identified by quantifying the concentrations of biomarkers. Biomarker detection using localized surface plasmon resonance (LSPR) is promising concept as it provides label-free detection. LSPR is produced when incident light interacts with surface electrons of conductive nanoparticles. This interaction produces localized plasmon oscillation with a resonance frequency. The resonance frequency is dependent on variable such as nanoparticle size, and geometry. Au and Ag nanoparticles exhibit LSPR in visible range [1]. When nanoparticles experience LSPR, it produces high molar extinction coefficient for absorption that is many orders higher than without LSPR. Small changes to environmental conditions (e.g., concentration of biomarker molecules) produces red shift in extinction spectra, which can be used to detect biomarkers. LSPR techniques have been widely utilized to develop biosensors. However, the issue is the lack of strategies for concentrating biomarker molecules near nanoparticles prior to detection by LSPR.

To address this issue, we have used dielectrophoretic (DEP) force of biomarker molecules. The DEP force is exerted on biomarker molecules when molecules are placed on a non-uniform electric field. By selecting the appropriate frequency of the external electric field, DEP force can be used to concentrate molecules on electrodes or away from electrodes. Dielectrophoretic behavior of common biomarkers such as DNA, microRNA and protein are well studied [2], [3]. In this work, we have investigated integration of dielectrophoresis and LSPR to improve the LSPR detection. Moreover, we have used DEP force of biomarker molecules to manipulate them near the nanoparticles and studied the effects of LSPR peak absorbance wavelength. To demonstrate the proof of concept, we have used short single stranded DNA molecules (ssDNA; ~22 nt) in experiments. We have recently demonstrated that ssDNA molecules can be concentrated near electrodes or away from electrodes using the DEP forces produced at MHz frequencies [3].

II. EXPERIMENTS

Fig. 1(a) shows the picture of the device used in experiments. The sample was pipetted to the middle rectangle that has T-shape gold interdigitated electrode arrays (TIEs). Earlier, we have demonstrated that TIEs electrodes can efficiently manipulate biomarker molecules using DEP force [2]. Fig 1(b) shows a picture of the TIEs. Fig 1(c) illustrates scanning electron microscope image of an individual T-electrode. During experiments, first, we have pipetted about 10 μL (8.7×10^{11} nanoparticles per mL; Nanopartz Inc., Loveland, CO) nanoparticles on the electrode area and let the particles dry in normal laboratory conditions. These

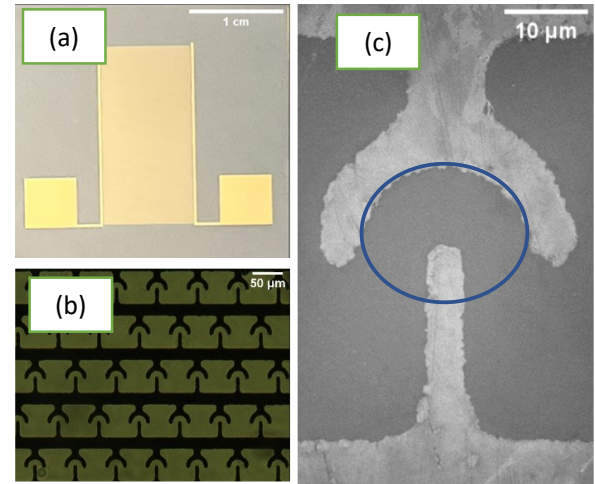


Figure 1: The device and electrodes used in the experiments. (a) Picture of the device used in experiments, (b) section of TIE electrodes, and (c) Scanning electron microscope image of a T-electrode. ssDNA molecules were concentrated in the circle area drawn in blue color.

nanoparticles are cylindrical shape with 10 nm in diameter and 30 nm in length and have absorbance peaks around 730 nm and 520 nm due to the longitudinal and transverse oscillations of electrons, respectively.

Next, 10 μL of ssDNA (5'-AACTATACAACCTACTACCTCA-3'; Midland Certified Reagent Co, Midland, TX) from 10 μM concentration was pipetted on the TIEs, and the AC electric potential of (10 V_{pp}) was applied to the electrode and waited until dry. Normally, it took about 15 mins to dry the sample. Then the absorption

spectrum (200 -1100 nm) of the electrode with nanoparticles and ssDNA was recorded (Cary 60, Agilent Technologies, Santa Clara, CA). Data were imported to Python for analysis and interpretation. Experiments were conducted at frequencies of 0, 1 MHz, 3 MHz and 5 MHz. Figure 2 illustrates the normalized absorbance spectra.

III. RESULTS AND DISCUSSION

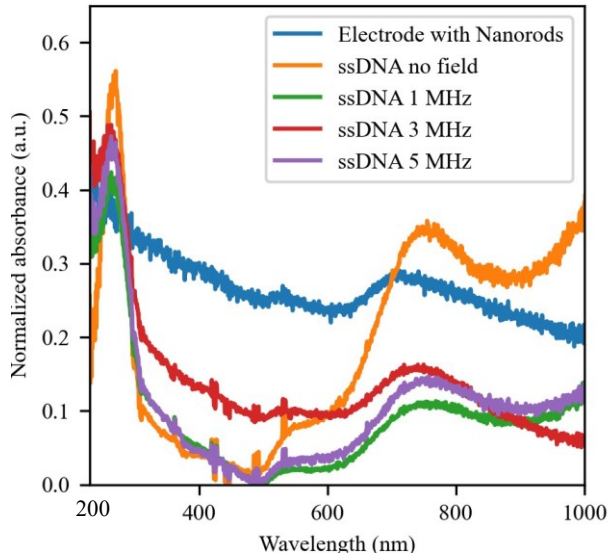


Figure 2: Normalized absorbance spectra of concentrated ssDNA using 0, 1, 3 and 5 MHz electric fields.

The selection of frequencies for this study was based on our previous finding about DEP force of short ssDNA molecules (~22 nt) [3]. In our previous study, we have found that ssDNA molecules can be concentrated in the electrodes using DEP force at 3 MHz and 5 MHz. There was very weak DEP force on ssDNA molecules at 1MHz [3]. There are significant absorptions in the wavelengths ~ 260, 520 and 730 nm (Figure 2). As, Au nanorods exhibit absorbance peaks in two plasmonic wavelengths corresponding to transverse and

longitudinal electron oscillations, absorptions ~ 260, 520 and 730 nm is due to ssDNA, longitudinal plasmon band and transverse plasmon band, respectively.

We have found that when ssDNA is present, there is a shift in absorption wavelength at 730 nm. The largest shift was recorded for the sample that did not use electric fields or no DEP force. When DEP force concentrates ssDNA molecules in the electrodes, ssDNA concentration outside (or around the nanoparticles) the electrodes are decreased. As the shift in absorption frequency of nanoparticles is depended on the dielectric properties of its surroundings, samples with concentrated of ssDNA with DEP forces (1-5 MHz) produces smaller shift (Fig. 2).

IV. CONCLUSION

We have utilized DEP force of ssDNA molecules to concentrate them in the electrodes and studied its effects in LSPR. We have found that red shift in extinction spectra is dependent on the frequency of the DEP force. We will conduct additional studies in future to further develop this technique toward biomarker detection for wide range of diseases.

ACKNOWLEDGMENT

DN would like to thank financial support from National Science Foundation grant no:1941748.

REFERENCES

- [1] E. Petryayeva and U. J. Krull, "Localized surface plasmon resonance: Nanostructures, bioassays and biosensing-A review," *Analytica Chimica Acta*, vol. 706, no. 1, pp. 8–24, Nov. 07, 2011. doi: 10.1016/j.aca.2011.08.020.
- [2] L. Velmanickam, M. Bains, M. Fondakowski, G. P. Dorsam, and D. Nawarathna, "ILLuminate-miRNA: Paradigm for high-throughput, low-cost, and sensitive miRNA detection in serum samples at point-of-care," *Journal of Physics D: Applied Physics*, vol. 52, no. 5, Jan. 2019, doi: 10.1088/1361-6463/aaed97.
- [3] L. Velmanickam, V. Jayasooriya, and D. Nawarathna, "Integrated dielectrophoretic and impedimetric biosensor provides a template for universal biomarker sensing in clinical samples," *Electrophoresis*, vol. 42, no. 9–10, pp. 1060–1069, May 2021, doi: 10.1002/elps.202000347.