

Dielectric Analysis of Single Biological Cells at Both Microwave and Optical Frequencies

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Dielectric measurement of a biological cell at microwave frequency or optical frequency provides unique yet distinct information about its physiological state. Microwave dielectric spectroscopy gives information on plasma membrane complexity and permeability, cytoplasm and nucleoplasm ion concentration, and the presence of smaller membrane-bound organelles. Optical holographic imaging and reconstruction provides complementary information on cell morphology and refractive index, which reflects cytoplasm and nucleoplasm mass density. As shown in Fig. 1a, we use a microfluidic device for dual-modality RF dielectrophoresis (DEP) and optical scattering measurements of single biological cells while in flow. (E. Kovacs, et al., “Light-Emitting Diode Array with Optical Linear Detector Enables High-Throughput Differential Single-Cell Dielectrophoretic Analysis,” *Sensors*, vol. 24, issue 24, 8071, 2024). Cells flow through a channel and over electrodes, which induce an RF frequency-dependent DEP force that translates them vertically to higher or lower velocity regions in the channel. Multiple LED semi-coherent optical sources above the channel illuminate the cells. A linear CMOS imaging array below the channel captures the resulting inline incident-scattered field interference patterns. The captured holograms are analyzed to reconstruct each cell’s size and optical refractive index. Simultaneously, the cell’s DEP induced velocity trajectory, obtained by particle tracking, is used to analyze selected RF dielectric properties. (S. Afshar, et al., “Full Beta-Dispersion Region Dielectric Spectra and Dielectric Models of Viable and Non-Viable CHO Cells,” *IEEE J. Electromagnetics, RF, Microwaves in Medicine and Biology*, vol. 5, issue 1, 2021).

Chinese hamster ovary (CHO) cells are a mammalian cell line widely used in vaccine and therapeutic drug production, and monitoring their viability during bioprocessing is crucial. We study a CHO cell culture during starvation and use our device to evaluate the cells’ viability and obtain RF and optical dielectric properties of both viable and non-viable cells. Fig. 1b shows the average measured Clausius-Mossotti factor, K_{CM} , spectra for viable and non-viable cells. Selected cell dielectric parameters, such as cytoplasm conductivity, can be extracted from the K_{CM} response at a specific frequency. Fig. 1c shows measured inline interference patterns at 630 nm for a mixture of viable and non-viable CHO cells, along with the corresponding simulated patterns using a single homogeneous sphere model.

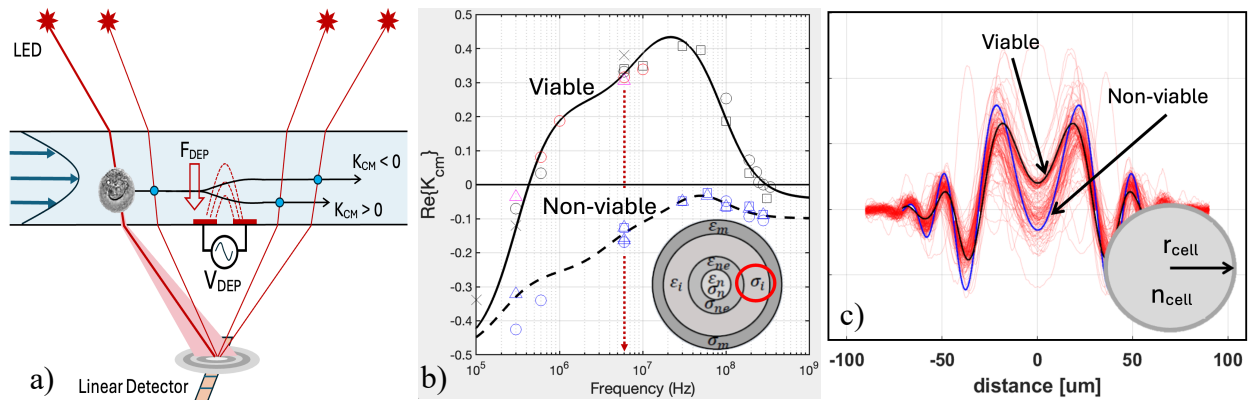


Figure 1. a) Microfluidic device for combined RF dielectrophoresis and optical holographic imaging analysis of single cells, b) measured and simulated $K_{CM}(f_{RF})$ for viable and non-viable CHO cell dielectric models, and c) measured and modeled inline interference patterns.