Broadband Electrical Detection of Individual Biological Cells

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Overview

Purpose

- Develop a miniaturized lab-on-a-chip electrical sensor for portable, real-time, and label-free detection of live versus dead biological cells

Methods

- Designed coplanar waveguide electrode for broadband radio frequency measurement
- Integrated with microfluidics for single cell handling

Results

- Single cell trapping and detection
- Capable of differentiating cell viability
- Single cell sensitivity achieved
- Signal intensity scaling with cell number

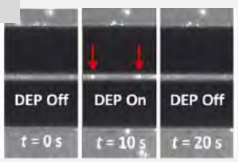
Introduction

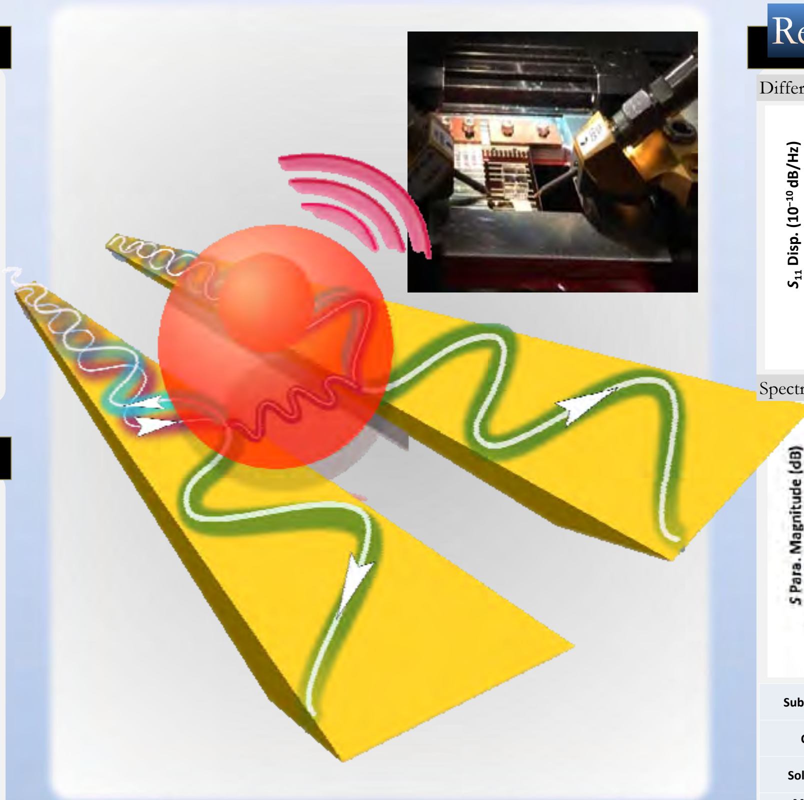
Cell detection is traditionally accomplished through chemical or optical means for which sophisticated instruments such as DNA sequencers or flow cytometers are commercially available, but neither is applicable for point-of-need differentiation of live vs. dead pathogen [1]. In comparison, electrical cell detection can be label-free and nondestructive with high throughput. To this end, cytometers capable of measuring the electrical properties of single cells are also commercially available as Coulter counters [2]. However, they can suffer from the dilemma of cell clogging or solution parasitics [3]. Additionally, Coulter counters typically use discrete frequencies on the order of MHz or lower, which made them unduly sensitive to the size and shape variations of individual cells, as well as the polarization layers formed in the solution between the cells and electrodes [3].

Broadband electrical detection has been found to overcome some of the challenges of using Coulter counters and yields richer information about cells [4]. For example, based on the different dispersion characteristics [5], live and dead cells can be differentiated at MHz frequencies, cell types can be identified at GHz frequencies, and surface functionality can be detected at THz frequencies. However, many challenges remain for broadband electrical detection, such as impedance matching, calibration, modeling, and data analysis. This research addresses these challenges and uses broadband electrical detection to differentiate viability of single mammalian cells [6].

Cell Trapping

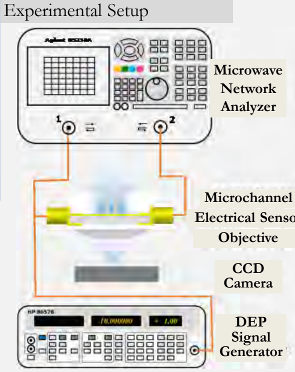
Dielectrophoresis (DEP) is used to immobilize cell temporary for cell sensing. The cells are released afterwards for checking the background signal.



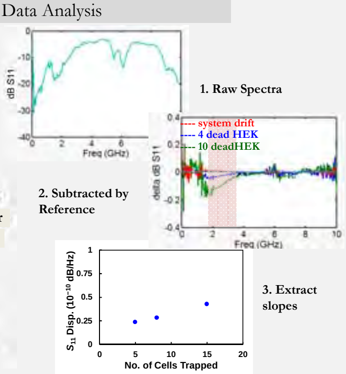


Experimental

Experimental Setup

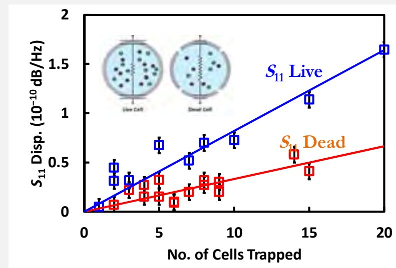


Data Analysis

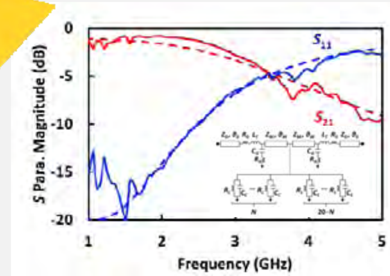


Results

Differentiation of Jurkat Cell Viability



Spectral Fitting



Subcircuit	Parameter	Symbol	Jurkat Live	Jurkat Dead	HEK Live	HEK Dead
Cell	Cyto. Resistance	R_C (kΩ)	190	860	120	500
	Cyto. Capacitance	C_C (fF)	29			
Solution	Unit Resistance	R_S (kΩ)	480			
	Unit Capacitance	C_S (fF)	30			
Micro-chamber	Char. Impedance	Z_M (Ω)	28			
	Length @ 3 GHz	θ_M (º)	5			
Ground	Resistance	R_G (Ω)	4.1			
	Capacitance	C_G (fF)	420			
Transition	Inductance	L_T (nH)	1.7			
Stripline	Char. Impedance	Z_0 (Ω)	55			
	Length @ 3 GHz	θ_0 (º)	12			
	Loss	R_0 (Ω)	6.5			

Outlook

- Further improving signal to noise ratio by on-chip probing and calibration.
- Extending the frequency range to THz for cell-specific chemical signatures.
- Applying detection system to microorganisms and biofilms.
- Fundamental understanding of signal contribution from different cell compartments and organelles.

Acknowledgement

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