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Ultra-wideband Systems for Single Cell Sensing

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Electrical sensing of live biological cells can be fast, compact, and label-free. Recently, the bandwidth of electrical cell sensing was expanded to the ultra-wide bandwidth (UWB) of 9 kHz–9 GHz, so that cellular as well as intracellular properties could be sensed in one setup [1]. Whereas cell impedance can be directly measured, cell permittivity can only by inferred with assumptions of cell morphology and field distribution. Therefore, to extract the cell permittivity from the measured cell impedance, numerical analysis of the field distribution must be performed iteratively.

The UWB measurement setup comprises a homemade microwave probe station on top of an inverted fluorescence microscope [1]. On the probe station is the device-under-test (DUT) connected to a vector network analyzer (VNA) for two-port measurement of scattering (*S*) parameters from 9 kHz to 9 GHz in a single sweep. The DUT comprises a gold coplanar waveguide (CPW), approximately 1-cm long and 0.5-μm thick, on top of a 0.5-mm-thick quartz substrate. A microfluidic channel intersects the CPW at a right angle. The *S* parameters measured on the VNA are de-embedded to the microfluidic channel as shown in [2]. The width of the center electrode of the CPW is precisely tapered from 120 μm outside the channel to 10 μm inside the channel, while maintaining a constant spacing of 16 μm from the ground electrodes both inside and outside the channel. Inside the channel the CPW is modified in a series or shunt configuration. In the series configuration, the center electrode has a 10-μm gap in the middle, whereas in the shunt configuration, a protrusion on one ground electrode narrows the lateral spacing from 16 μm to 10 μm. These 10-μm gaps are used to trap a Jurkat human lymphocyte cell by dielectrophoresis. Live Jurkat cells are used due to their relatively large size (≅10 μm in diameter), simple structure, and non-adherent nature. The cells are suspended in a sucrose solution before injection through the microfluidic channel. Both series and shunt configurations of the DUT are simulated in the electromagnetic module of COMSOL Multiphysics v. 5.3 from 50 MHz to 10 GHz. The Jurkat cell is modeled as a two-layered sphere with only membrane and cytoplasm whose electric properties are modeled using the dispersive Debye formula. To evaluate the sensitivity of the proposed technique to the Debye parameters, we consider two membrane permittivity values (ε_s = 11.7, ε_∞ = 4; ε_s = 5, ε_∞ = 3.39) and three cytoplasm conductivity values (σ_s = 0.32, 0.55, and 1.00 S/m) [3], [4].

Simulated *S* parameters with a cell trapped in the series configuration are significantly different from that of sucrose alone. S_{21} is much more sensitive than S_{11} to the presence of the cell and to variations in its cytoplasm conductivity, especially at frequencies below 1 GHz. With a cell trapped in the shunt configuration, we can see the opposite behavior. However, both S_{11} and S_{21} are affected by variations of cytoplasm conductivity and membrane permittivity: S_{11} change increases logarithmically with frequency with its slope dependent on cytoplasm conductivity and its value dependent on membrane permittivity. By contrast, the S_{21} change increases linearly with frequency with its slope dependent on membrane parameters and its value dependent on cytoplasm conductivity. These simulation results are in general agreement with analytical analysis and experimental finding [5], confirm that the proposed setup is sensitive enough to extract dielectric properties of the cell compartments from measurement of *S* parameters and provide a useful guide for the optimization of the experimental design.

References

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