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A BIOPARTICLE DETECTOR AND ENRICHMENT PLATFORM USING INTEGRATED INSULATOR-BASED DIELECTROPHORESIS AND BIOIMPEDANCE MEASUREMENTS

Pierre Ponce, Blake A Simmons, Michelle Khine and Rafael V Davalos*

Sandia National Laboratories, Livermore, CA 94550 USA
*rvdaval@sandia.gov

Abstract

We have developed a bioparticle detection platform which combines insulator-based dielectrophoretic (iDEP) concentration with impedance feedback. The system continuously and selectively accumulates particles while electrical responses of the suspension at the trapping site are recorded. The operating conditions for trapping are determined by the physical and electrical properties of the target particle type. Recordings of phase offset, relative to the reference sensing signal, act as the principal monitoring indicators. These measurements enable us to detect the presence and the approximate concentration of biological contaminants in a sample. This system is the first to combine iDEP concentration with impedance measurements. The results obtained from fluorescent beads and viable *B. subtilis* spores demonstrate the feasibility of using iDEP concentration with active impedance monitoring to detect biological pathogens collected from dilute samples.

Keywords: concentration, impedance, bacterial spores, bioMEMS, microfluidics

1. Introduction

Devices that detect health hazards in air and water supplies must be sensitive enough to detect low concentrations of pathogens. For example, less than a microgram of botulinum toxin is lethal to an average adult human [1]. Moreover, knowledge of the concentration of such particles can determine the toxicity level of a water supply and the appropriate measures needed to quickly resolve health crises.

In this study we developed a self-contained platform that integrates the ability to concentrate bioparticles with a reliable method for detecting their presence. The trapping methodology is based on insulator-based dielectrophoresis (iDEP) [2]. This is a new iDEP device architecture that minimizes the trapping area to enhance the detection limit of the system. The small volumes of solution in the trap during detection makes the tracking of impedance changes a practical solution for detection [3,4]. Detection is enabled by monitoring impedance changes through sensing electrodes located in the vicinity of the trapped particles. This publication demonstrates the feasibility of iDEP concentration coupled with impedance-based monitoring for rapid and sensitive detection of biologicals.

2. Experimental methodology

The microfluidic channel in our testing platform is fabricated on a polymer substrate Zeonor® (Zeon Chemicals, Louisville, KY). The insulating structures that facilitate particle trapping are formed by injection molding using a Ni stamp fabricated from a Si master, as detailed in [5]. The device used is depicted in Figure 1.

Baseline impedance measurements were taken to determine the electrical responses to different particle concentration levels. All sample solutions use a low-conductivity (1.52 µS/cm) buffer. Impedance measurements and AC sensing signals were done using an SR830 DSP lock-in amplifier (Stanford Research Systems, Sunnyvale, CA).

Initial experiments are conducted in a rectangular control channel to compare our results to those obtained in the literature and our bulk measurements. The fluidic channel is 1 mm wide and 30 µm deep. The detection site within the platform consists of two 50-µm coplanar rectangular electrodes, separated by 150 µm. The electrodes are composed of Au thin film with a Ti adhesion layer. Their surfaces are passivated with a ~0.4-µm oxide layer (SiO_2) to prevent the occurrence of electrolysis in the solution and protect the sensing electronics.

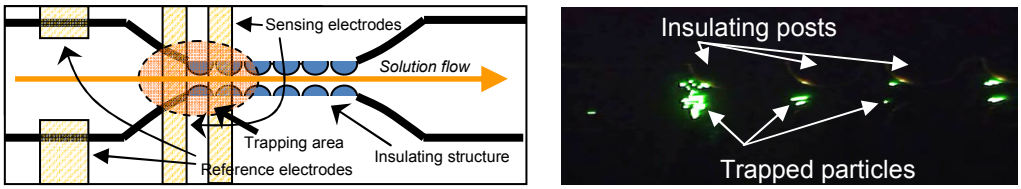

Figure 1. System layout. (a) Labeled schematic of the channel. (b) Image of trapping with iDEP.

3. Theory

The collection of individual particles within the encompassing medium can be modeled as a variable parallel resistance/capacitance pair, as shown in Figure 2(a). As the concentration of particles increases, the displacement of solution by those particles leads to changes in C_{Trap} and R_{Trap}. The cell constant, which affects measured resistances and capacitances, is affected by the dimensions and geometry of the electrodes and channel [6,7]. Figure 2(b) illustrates the test circuit used for measuring phases and currents.

Based on our trap circuit model, we derive a formula that helps determine capacitive changes from introduction of particles. In our calibration tests using 20-mL glass vials, we used stainless steel electrodes without passivation. The phase response is given by Equation (1). We used an AC probe signal of 50 mV amplitude (rms) at a frequency of 2 kHz for our trials. We placed the resistance of the clean solution (R_{Trap}) at approximately 2 MΩ. R_{src}, which accounts for parasitics and resistance chosen to protect sensitive electronics, was chosen to be 10 MΩ.

$$\phi = \tan^{-1}\left(\frac{\omega C_{Trap} R_{Trap}}{(\omega^2 C_{Trap}{}^2 + 1)R_{src} + R_{Trap}}\right) \approx \tan^{-1}\left(\frac{\omega C_{Trap} R_{Trap}}{R_{src} + R_{Trap}}\right) \quad \text{(valid for low frequencies)} \qquad (1)$$

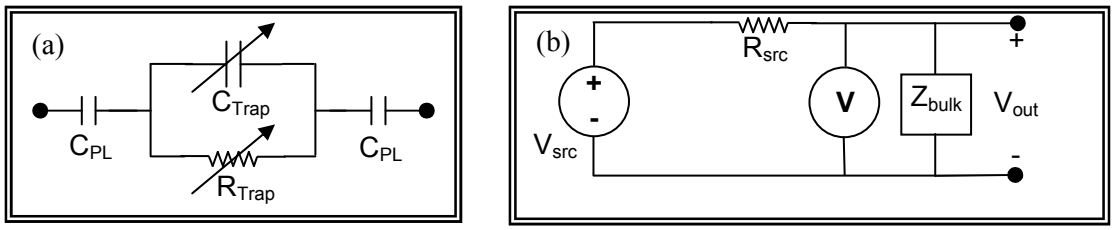

Figure 2. (a) Equivalent circuit depicting the changes in resistance and capacitance within the sensing region of the detection platform. (b) Test circuit used to monitor phase changes in the bulk solution. Z_{bulk} is the overall impedance modeled in (a).

4. Results and discussion

Table 1 summarizes the findings from experiments run on our control detection platform and compares them to experiments conducted in bulk solution using the 20 mL vials. Both sets of experiments display trends that correlate phase offset with particle concentrations in solution. This detection method can detect concentrations as low as 10^3 spores/mL. Past work on iDEP has demonstrated the capability of concentrating particles by a factor of 1000 within minutes [2]. We have exhibited a system that should be capable of detecting low concentrations of bioparticles (~1 spore/mL) from large test samples. The goal of our effort is to eventually develop a system capable of detecting low concentrations of bioparticles from large test samples.

Table 1. Baseline impedance measurements for *B. subtilis* in bulk tests (*n=5*)

Particle Concentration	Peak Phase Offset Relative to Clean (degrees)	
	Bulk Tests	30µm x 50µm x 150µm channel
clean (no spores)	0.00 ± 0.04	0.00 ± 0.02
10^3 spores/mL	16.75 ± 0.15	0.05 ± 0.02
10^5 spores/mL	32.20 ± 0.14	0.19 ± 0.05
$5x10^6$ spores/mL	38.72 ± 0.25	0.24 ± 0.06
$5x10^7$ spores/mL	39.23 ± 0.08	0.33 ± 0.07

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