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Microfluidic Platform for Specific Capture, Release, and Impedance Based Quantification of Microparticles for Protein and Cellular Quantification

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Electrical affinity based biosensors generally consist of an electronic transducer surface functionalized with probe molecules. These types of sensors are limited in sensitivity due to the inherent contradicition between transducer sensitivity which requires small size for high signal to noise ratio, and analyte capture rate which requires large surface area for high capture efficiency. Our solution is to pre-concentrate the target molecule on a separate capture surface selectively, and then transfer the preconcentrated particles to a separate sensing region.

We present a microfluidic electronic platform for specific capture, release, and quantification of microparticles. An image of the fabricated chamber and micropore is shown in Figure 1. An image of the downstream impedance sensor is shown in Figure 2. This platform is applicable to quantifying a wide range of biomarkers including proteins, nucleic acids, and whole cells. In this presentation we will discuss the design, fabrication, and implementation of our system.

The optimal performance of the device requires optimization of several parameters such as test sample injection flow rate, bead size and material, bead wash flow rate, and elution buffer, and also elution flow rate. Application of flow during the test sample injection step results in improvement in analyte capture rate compared to no flow. The size of the bead affects the sensitivity of the assay. Beads that are too large result in poor sensitivity due to dead area on the surface in between the beads not getting interrogated. Beads that are too small have a slow settling time also hurting sensitivity. Optimal elution flow rate is limited by the crowding of beads in the micropore and also the bandwidth of impedance sensor.

Optimal pore dimensions and electrode configuration allow for single bead detection (Figure 3). We use a three electrode configuration to perform a differential impedance measurement. Impedance is measured between electrodes 1 and 2 (Z_{12}), and also between 2 and 3 (Z_{23}). Electrode 2 is connected to a signal generator. A current pre-amplifier is connected to electrodes1 and another one is connected to electrodes 3 converting the current from each into a voltage. The voltage from each is then fed into a differential amplifier which is then fed into a mixer which shifts the signal down to baseband and a low pass filter which allows only the DC component of the signal to pass through. As a result of this differential measurement, a negative and then positive peak is observed as a result of each bead passing through. A matched filter can be used to enhance the signal to noise ratio thus allowing detection of smaller particles compared to a two electrode measurement. Figure 3 shows representative data of single beads passing through the micropore.

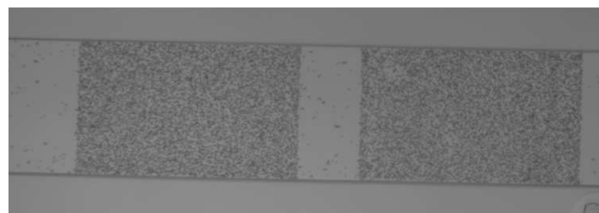

Figure 1. Image of fabricated capture chamber. Beads have been captured along a single channel patterned with antibodies in array format.

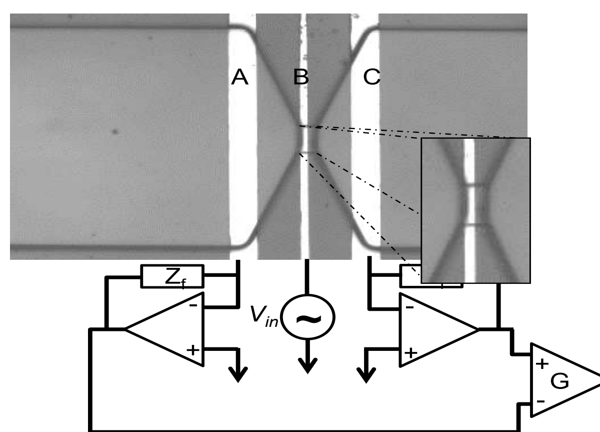

Figure 2. Image of fabricated micropore impedance sensor. (Inset) Zoomed in image of micropore. Differential lock-in amplification technique is used to measure impedance across micropore. Single bead detection has been achieved.

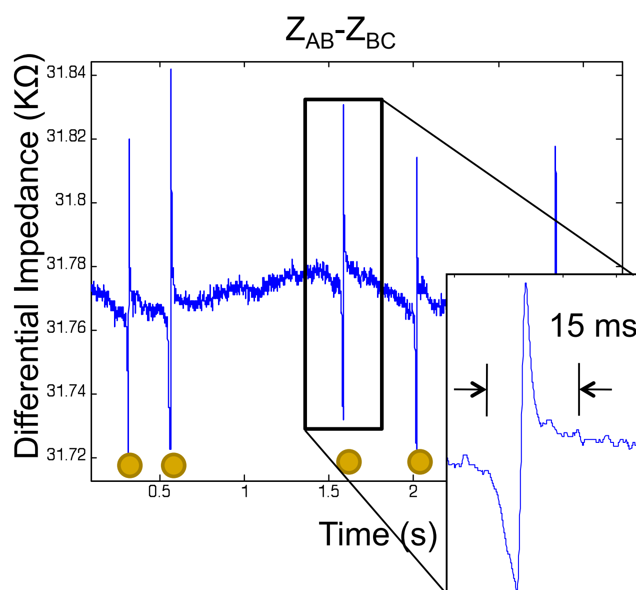

Figure 3. Representative data of differential impedance measurement. Single beads passing through results in unique signature with a negative and then positive peak.