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Detection of Single Gold Nanoparticle in Liquid with Nanopore-Integrated Microwave Resonators

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***Abstract*— Here, we propose a nanopore integrated microwave resonator to detect single nanoparticles in real time. In contrast to existing nanopore-sensors relying on detection techniques like resistive pulse sensing, and current-voltage measurements, the presented coplanar-waveguide sensor detects the passage of gold nanoparticles through a nanopore on a thin film membrane. Resonance frequency of the sensor, which is around 7 GHz, is tracked by a custom-built close loop circuitry. Gold nanoparticles are electro kinetically driven through the pore: as each nanoparticle passed the pore, it induces a shift in the resonance frequency of the resonator. The presented method is not limited by the specific design of the pore, alleviating the stringing condition on pore size and shape with respect to the target analyte.**

Keywords*— *nanopore, microwave sensors, electrokinetics, nanoparticle detection

I. INTRODUCTION (*HEADING 1*)

In the past two decades, the field of nanopore sensing has received wide attention due to the high sensitivity and versatility offered by this technique [1]. Two widely used sensing modalities used in nanopore platforms are resistive pulse sensing, and current-voltage (I-V) measurements. In these modalities, it is critical to match the size of the pore and the analyte of interest, so that the analyte blocks almost the entire nanopore and induces a large change in the conductivity across the nanopore. To avoid this stringent condition between the size of the nanopore and the analyte, we investigate the use of resonant microwave sensors in this work. Here, we build a coplanar waveguide (CPW) sensor integrated with a nanopore solid state structure (SiN) to detect the passage of individual gold nanoparticles, nominally 20 nm in size. As the key components of any nanopore/channel-based application, solid state type membrane is used in measurement process due to its advantages of excellent durability, robustness, as well as seamless integration with existing semiconductor and microfluidics systems. Moreover, the presented sensor benefits from a relatively simple fabrication technique compared with others such as those employing suspended graphite [2] and nanoribbon [3] sheets, as well as, mechanically controlled break junctions (MCBJ) [4-6]. To enhance the sensing resolution [7], the microwave resonator is equipped with a custom designed control circuitry based on a phase-locked loop reaching a frequency stability level of 1×10^{-8} and detecting GNPs passing through the sensing region.

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II. METHOD

A. Fabrication Procedure

The CPW sensor shown in “Fig. 1” is fabricated on a $Si_3N_4/SiO_2/Si$ wafer (double side deposited). A 2 µm layer of SiO_2 is sandwiched between top Si_3N_4 layer (of 220nm thickness) and silicon substrate to reduce the parasitic capacitance and the dissipative characteristics of mobile charge carriers in Si at room temperature. The sensor is fabricated in three steps: first, the creation of a membrane, second the fabrication of the gold electrodes forming the CPW resonator, and finally the ion milling of the nanopore on the membrane.

The thin part is formed by suspending the top-most Si_3N_4 layer by backside etching of the wafer. A window is patterned on the backside of the wafer using optical lithography to plasma etch a section of nitride film. Then the wafer is left for wet etching of 500 µm Si wafer and 2 µm SiO_2 layer in KOH solution to open the back window. Etching continues until the top nitrate layer is fully suspended, creating a high-aspect-ratio membrane of 200 x 200 µm in size and only 220 nm in thickness.

In the second step of fabrication, Electron Beam Lithography (EBL) is used to pattern the CPW resonator on the front side of the wafer, taking care to align the metal paths with the membrane fabricated in the first step. Both signal and ground electrodes are tapered toward each other to create effective region in the bow-tie design where the distance between electrodes is reduced to a few hundreds of nanometer. Metallization of the electrodes is accomplished by thermal evaporation of gold with 100 nm layer thickness. Thereby, the designed sensor is also compatible to work with biological samples due to the inert nature of gold and silicon nitride. In the last step, Focused Ion Beam (FIB) is used to open a nanopore on the membrane, positioned critically between the converging signal and ground electrodes. "Fig. 1" depicts scanning electron microscopy image of the completed sensor.

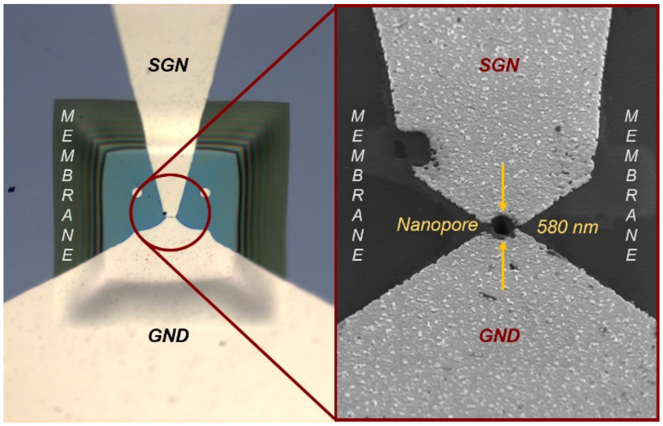

Fig. 1. Optical (left) and SEM image (right) of the fabricated device. Two gold electrodes are separated by few hundreds of nanometers with a pore having diameter of 580 nm. Fabricated dimensions match to 50 Ω impedance to reduce noise due to impedance mismatch.

B. Experimental Setup

In the presented system, a Vector Network Analyzer (VNA) is used solely for initial characterization: rather, a dedicated system based on phase-locked loop (PLL) architecture was constructed to track the resonance frequency of the sensor in real-time ("Fig. 2"). Initial measurements (with S11 parameter) shows the device has resonance frequency around 7 GHz.

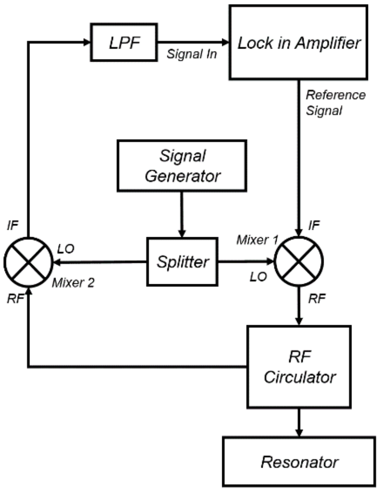

Fig. 2. Electronic detection circuitry. Closed loop system keeps the resonator at its resonance frequency. A reference signal is generated from lock in amplifier and read in each cycle. Then, signal generator is updated in accordance with the response of the resonator.

For measurements, a narrow-band detection circuitry is employed to enhance the sensitivity of the microwave sensor. Phase-sensitive detection is performed with a lock-in amplifier. Due to the frequency upper limitation of the lock-in amplifier, we constructed an external heterodyne circuitry to continuously track the resonance frequency. With PLL, the phase of the resonator is locked to 0 degrees with a PI controller. Any deviation from 0 degrees emerges as an error signal which then updates the frequency of the signal generator. One can continuously track the shifts in resonance in real-time [8] using this technique.

Top side of the fabricated device is immersed into a large reservoir and a smaller reservoir is attached to bottom side. Both reservoirs are initially filled with DI water and they are separated from each other by the film membrane of 220 nm thickness. Then, an aliquot containing GNPs are added to smaller reservoir ("Fig. 3").

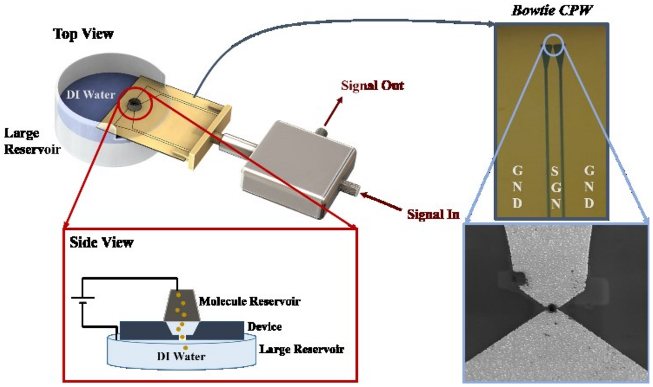

Fig. 3. Sensing region of bowtie shaped CPW resonator is immersed in the DI water and another reservoir is attached to the sensing region. Microwave signal is transmitted through a RF circulator. GNPs are transported electro-kinetically through the nanopore by applying a bias voltage between the two reservoirs.

Two probes are employed in the experimental setup to sustain a voltage difference between the two reservoirs and inducing the electro kinetic transportation of the molecules. One of the probes is placed into the large reservoir; the other one is placed into the smaller reservoir. When the voltage source is on, GNPs are forced to transit through the pore ("Fig. 3"). Translocation of GNPs through the effective region modulates the resonance frequency of the sensor.

III. RESULTS AND DISCUSSION

We have tracked resonance around 7.06 GHz with a resolution of ten parts per trillion. Examples of the recorded data comparing with control experiments are illustrated in "Fig. 4" demonstrates the comparison between actual GNPs run and control run.

In both the control run and actual experiment, both reservoirs are filled with deionized (DI) water and the PLL parameters are adjusted to be identical. In the control run, no large, spike-like signals were observed. Then, GNPs were added to the smaller reservoir. As they pass through the hole, upward frequency shifts are observed. It is well discussed in literatures that microwave resonators are susceptible to any ambient factor changes (temperature and humidity) occurs in their vicinity. Thereby, after the addition of nanoparticles to the reservoir, the temperature equilibrium of the resonator and set-up is changed. This is the reason to the level difference between control and particle run in "Fig. 4".

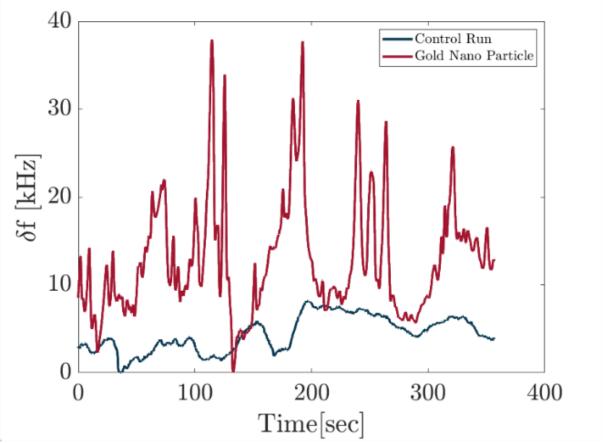

Fig. 4. Sample from the recorded data. Blue data is taken when no GNPs are added to the reservoir and red data is taken after GNPs are added and electro kinetically driven through the nanopore. Clear upward shifts are observed which are induced due to particle transition.

The histogram of frequency shifts indicates accumulations of events around specific values ("Fig. 5"). Therefore, we interpreted the different amount of frequency modulations to the number of GNPs passing the nanopore, rather than positional dependence. The analysis of the same sample in a different study employing nanoelectromechanical systems in vacuum indicates a similar degree of dispersion for the nanoparticle sizes [9]. Degree of sensitivity presented here using nanopore-integrated microwave sensors (NIMS) shows that the device is potentially sensitive enough for resolving large biological structures such as single exosomes and viruses in the GHz regime.

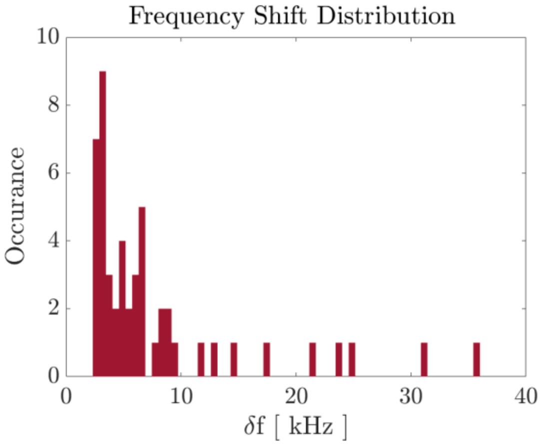

Fig. 5. Histogram of the frequency shifts induced by GNPs. Single particles seem to induce shifts around 3-3.5 kHz, while less numerous, larger shifts (e.g. 36 kHz) are interpreted to be induced by aggregates of gold nanoparticles.

IV. CONCLUSION

Herein, a coplanar waveguide microwave resonator integrated with nanopore is presented to detect 20 nm gold nano particles. To enhance the microwave resolution, microwave resonator is equipped with a custom designed control circuitry (PLL) operating around 7 GHz and reaching a frequency stability level of ten parts per trillion. Proposed sensor benefits from standard fabrication steps compared to suspended 2D sheet of graphite or nanoribbon structures. As the key components of any nanopore/channel-based application, solid-state type membrane is used in measurement process due to its advantages of excellent durability, robustness, as well as compatibility with existing semiconductor and microfluidics systems. The presented data in detecting GNPs of 20 nm paves the way for future works including detection of single molecules, viruses and DNA chains using the nanopore-integrated microwave sensors (NIMS) with some minor changes in device design.

ACKNOWLEDGMENT

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