Enhancement of High-Performance Graphene Biosensors for Cancer Detection

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Abstract:
Current alpha-fetoprotein (AFP) sensing technologies such as enzyme-linked immunosorbent assays (ELISA) require a lot of equipment, time, and skill. Still, they would be less sensitive than our proposed graphene biosensors, which in theory could detect a single AFP. Graphene’s unique material properties and sensitivity to the surrounding environment are exploited in our sensor for the detection of AFP. A U-shaped gold electrode containing a small gap for the sensing area would then be patterned using photolithography. The gap would be closed by covering the bare substrate with our few-layer-graphene (FLG) structure. We tune the thickness, and thus the properties, of graphene through a unique layer-by-layer self-assembly process that uses graphene solution and polyelectrolytes. The graphene sensing area is further prepared with poly-L-lysine and then functionalized with anti-AFP. Also, due to the fact that the ability to detect AFP is heavily limited by the signal-noise ratio, we redesigned the basic interface between gold and graphene in multiple ways to achieve a better signal-noise ratio in our sensors. The sensors that were fabricated were successful in detecting alpha-fetoprotein even in concentrations as low as 1 pg/ml. Lastly, the redesigned gold/graphene interface showed promising results and seems to have only been limited by our fabrication procedure.

Introduction:
Graphene, the two-dimensional counterpart of graphite, has been extensively studied in terms of its properties and manufacturing since its discovery in 2004. Since its discovery a plethora of techniques have been developed for creating this new material [1]. Though popular methods produce quality graphene, they are not scalable to meet industry demand. However, this work uses layer-by-layer self-assembly to produce few-layer-graphene (FLG), which is indeed scalable.

This bio-sensor would be a candidate for phasing out and replacing the current bio-chemical assay known as ELISA, which is the industry standard for antigen screening. ELISA is a great tool, however it is complicated to screen antigens, it requires great technician skill, and takes hours to run. Conversely our sensor is simple to prepare for testing, the screening is simple, and data is visible in a matter of seconds/minutes.

We wanted to enhance our sensor sensitivity as well by reducing 1/f noise in our sensors. In order to do this we decided to try reducing the overall contact resistance present, thus we reduced the contact area between the graphene and gold [2,3].

Methods and Techniques:
Fabrication. We fabricated our sensors using a photolithography process, as demonstrated in Figure 1, which involves the patterning of the gold electrode, patterning of graphene onto the sensing area, and the patterning of a protective KMPR coating.

Modified Gold-Graphene Interface. In order to reduce contact area between gold and graphene, the junction at which they meet was redesigned. This work used three different designs, as seen in Figure 2 — a 31 strip design, 95 strip designs, and 950 strip designs that reduced the contact area between the graphene and gold [2,3].

Figure 1: Process scheme.

Figure 2: The 31 strip design, 95 strip design, and 950 strip design.
surface area to 33%, 50%, and 50% respectively. The small feature size lead to occasional complications with fabrication, especially in the 950 strip design due to the 2 µm strip width.

**Graphene Self Assembly.** Next we facilitated the layer-by-layer self-assembly of few-layer-graphene onto the entire wafer. This was done by alternating immersion of the graphene wafer between a solution of poly(diallyldiamine chloride) (PDDA), which is positively charged, and poly(styrene sulfonate) (PSS), which is negatively charged; it enabled us to create a thin layer of polymer that distanced the graphene, once formed, away from the silicon oxide. Next we alternated immersion into PDDA and a solution of suspended negatively charged graphene platelets for five cycles to form FLG.

**Graphene Charge Sensitivity and Debye Length.** If there is a charge within the Debye length of the sensing area, the graphene’s carrier mobility and resistance will be affected, however the affects vary depending on the charge present. Since graphene in our sensing area was P-doped, a negative charge within its Debye length would decrease resistance throughout the material, whilst contrariwise, a positive charge would increase the resistance in the graphene.

**Functionalization.** The sensing area was prepared in the following progression: immersion in poly-L-lysine, cleaned with distilled water, immersed in a solution of anti-alpha fetoprotein (anti-AFP), cleaned with Dulbecco’s phosphate-buffered saline (DPBS), and finally immersed in diluted 1% bovine serum albumin (BSA).

**Results:**

**Alpha-Fetoprotein Sensing.** We allowed the sensor to calibrate when exposed to DPBS with no AFP and then began to slowly increase the concentration of AFP, as can be seen in Figure 3.

**Noise Reduction.** This approach of 1/f noise reduction by reduction of contact area between gold/graphene was successful. Though poor performance is seen in the 950 strip design, which can be attributed to poor fabrication of electrodes, the 95 strip and 31 strip designs had less 1/f noise than the original sensor design, as is seen in Figure 4. If applied to our sensors we would surely surpass sensitivity of tests such as ELISA.

**Future Work:**

We would like to focus on two areas for future work. We would want to apply our work to flexible substrates to prove the potential application of our sensor as an *in vivo* bio-sensor, which is the consummation of our work. Lastly, we want to better understand the graphene-gold interface by finding the optimal value for contact area reduction and number of gold strips, in order to further improve the signal-to-noise ratio.

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**References:**

