**A Fully Electric DNA Detection using CMOS integrated CNT network Sensor**

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**ABSTRACT**

A fully CMOS integrated carbon nanotube (CNT) sensor platform that consists of a 32X32 array of unitary CNT elements for electric bio material detection is presented. For digital conversion of the analog voltage of CNT sensor elements, a correlated double sampling (CDS) type Successive Approximation Register (SAR) analog/digital (A/D) converter has been used. Also, each sensor cell of the sensor array contains a buffer circuit which provide independent sensing signal. The CMOS chip presented in this research is applied to a DNA sensor after functionalization with a 25mer ss-DNA. Because of its small size and low power features, this sensor can be easily used for the ubiquitous sensor networks. The chip is fabricated on the basis of a 0.18μm CMOS process.

**Keywords**: CMOS Integrated Circuit, Carbon Nanotube, DNA sensor

1 INTRODUCTION

Carbon Nanotubes (CNTs) have become one of the most preferred materials for biological sensors because of their superb sensitivity [1], [2]. The convergence of these sensors and CMOS chip technology has been emerged to be one of the most promising candidates to overcome the barriers of current medical issues such as single molecule analysis, real time detection, low power dissipation and miniaturization to be used as in vivo application [3]. The electrical biosensors, in particular, have additional advantages in sensing speed, detection accuracy, and semiconductor device integration possibility. However, integration of the sensor devices into CMOS chip with signal processing capability is the key to attain sensitivity, capability in multiple target detection.

In addition, capability to measure in different voltage biases for the same sensor is necessary to increase SNR (signal to noise ratio) and dynamic range since binding events of the target molecules such as toxins, DNA strands, and proteins have specific voltage dependent dissociation constants pKa, pKb. Our group has reported an easy and reliable integration scheme of the CNT network on the CMOS chip by introducing ELP (Electroless Plating of Au on Aluminum) [4]-[6] and self gating effect using concentric electrode structure [7], [8].

In this paper, we present a fully CMOS-integrated CNT sensor array platform that consists of a 32X32 array of unitary CNT elements, self-reference voltage gating, flexible transducer circuits, and a CDS type SAR A/D converter for signal processing [10]. Also proposed is a sensing scheme with a buffer circuit for sensor isolation, and demonstrated the actual array sensor operation through statistical measurement data.

2 CMOS INTEGRATION

Fig. 1 show the conceptual diagram of the proposed post processing steps. The CMOS chip is fabricated using the standard 0.18μm CMOS process (Magnachip, Korea). The top metal layer of the chip is Al and exposed to ambient by pad-open process.

The first step of post processing is Au electroless plating (ELP) on the Al electrode [6]. There are two distinctive processes of Au ELP on the Al surface, which are chemical Pd activation, and Au ELP. For the chemical Pd activation, the chip is immersed into the Pd activation solutions at room temperature for 2min. The mixture's components are 3.5mL deionized (DI) water, 0.4mL 0.1g/L PdCl2 solution, 0.5mL of polyethylene glycol, 3mL of methyl gallate, and 1mL 85% phosphoric acid. After dipping into the solution for activation the chip was rinsed with DI water and dried with a N2 gun. The Au plating solution was prepared by the addition of 50mL DI water, 0.05g KCN, 0.913g citric acid, 0.128g KAu(CN)2, and 2mL...
The second step of post processing is a drop-coating of single-walled CNT (swCNT). The swCNTs (ASP-100F produced by Il-jin Nanotech, Korea) were ultrasonicated in nitric acid at 50°C for 30min to purify and simultaneously exfoliate from bundles. The swCNTs are then neutralized with DI water and trapped on the membrane filter (Millipore, 0.2μm pore size, 47mm diameter) by a vacuum filtration method. The swCNTs on the filter were dried in a vacuum oven chamber at 80°C for 48h. The prepared swCNTs were dispersed in 1,2-dichlorobenzene solution with a concentration of 0.05 mg/mL, and then an ultrasonication process is performed for 10h. The swCNTs were dispersed in 1,2-dichlorobenzene solution with a volume of 20 solution made of swCNTs dispersed in a 1,2-channel formation between the two electrodes, we drop the ultrasonication process is performed for 10h. For the vacuum oven chamber at 80°C for 48h. The prepared filtration method. The swCNTs on the filter were dried in a vacuum oven chamber at 80°C for 48h. The prepared swCNTs were dispersed in 1,2-dichlorobenzene solution with a volume of 20μL on the chip.

The last step of post processing is Au deposition on the swCNT to provide a docking place for the probe molecules and to enhance the attachment of the swCNT to the Au electrode during the overall swCNT sensor device integration. Deposition of Au nanoparticle on swCNT network is performed by thermal evaporation method. The deposition rate and thickness is monitored using a quartz crystal microbalance (QCM). The diameter of Au on the swCNT is about 7nm. After deposition of Au nanoparticle, the CMOS chip was annealed at 350°C about 30min for enhancing Au nanoparticle attachment to swCNT network. We will call a Carbon nanotube network with Au particles as CGI. The last step of post processing is Au deposition on the swCNT to provide a docking place for the probe molecules and to enhance the attachment of the swCNT to the Au electrode during the overall swCNT sensor device integration. Deposition of Au nanoparticle on swCNT network is performed by thermal evaporation method. The deposition rate and thickness is monitored using a quartz crystal microbalance (QCM). The diameter of Au on the swCNT is about 7nm. After deposition of Au nanoparticle, the CMOS chip was annealed at 350°C about 30min for enhancing Au nanoparticle attachment to swCNT network. We will call a Carbon nanotube network with Au particles as CGI.

The scheme for the A/D converter adopting the auto offset cancellation is shown in Fig. 2. The operation of the comparator is a CDS process. The timing scheme is given in Fig. 2(c). Firstly, S1 and S2 are switched on, and S3 and LATCH are switched off. The residual offset of the static latch is memorized in series of capacitor C1 and A/D converter capacitors. Secondly, S1 and S2 are switched off, and S3 is switched on. The difference of the selected sensor cell level and the reference level is stored in C1, and automatically compared with the level of the A/D converter capacitors. LATCH activates and makes the static latch to enter its latch step and a successive output logic signal is maintained for 8clock cycles. The implanted A/D converter has 10bit accuracy; 8bits from binary capacitor arrangement, and 2bit from A/D converter voltage range selection without complicated sub-A/D converter scheme.

3 CHIP ARCHITECTURE

The top-level chip architecture and its timing diagram are shown in Fig. 2. The CMOS chip consists of the a timing controller which controls each part of CMOS chip, sensor array which is coated by swCNT network and CDS type SAR A/D converter [10]. Fig. 3 is a buffer circuit in every microarray sensor which removes the parasitic capacitance effects from other sensors. Vbias is the bias voltage between swCNT node and common enclosing electrode. Operational amplifier keeps the bias voltage through negative feedback and the upper and lower path of feedback is determined by the Vbias polarity denoted as Vmode. Current mirror circuit which is isolated from sensing part transfers the sensing result to open drain type output circuits. Rext is the load resistance, and amplification factor is determined by the ratio of Rext to swCNT resistance.

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4 MEASUREMENT & DISCUSSION

Fig. 4(a), and 4(b) show the chip photograph and the tested result of 32X32 CMOS integrated CNT biosensor, respectively. To confirm the operation of the CMOS chip, we compared the resistance distribution from a 32X32 array to the 12cell resistance distribution from same chip.
manually measured by Agilent 4145 parameter analyzer. As shown in Fig. 5(a), this result confirms that the measurement result of CMOS chip is identical to the actual swCNT resistance.

As an example application, we tested the standard DNA sequence detection [13]. Selectivity of swCNT electric sensors was demonstrated on CGI systems with four different probe-DNA. The random sequenced 25mer target-DNA, it’s completely complementary probe-DNA (C), and it’s also random generated partially mismatched probe-DNA (single nucleotide polymorphism (SNP), half mismatch (HM), noncomplementary (NC), Table 1). The sensor array located in the center region of the chip were exposed to 10µM thiolated probe-DNA solution in Tris-EDTA (TE) buffer for 12h to allow surface immobilization of capturing probe oligos. The probe-DNA immobilized on the surface of CGI by formation of covalent bonding between the Au nanoparticle and the thiol group end of oligonucleotide. The sensor surface was then flushed with multicopies of TE buffer to remove unbound probes. 20µL droplet containing 5µM of target-DNA was added onto the surface of CGI coated with various probe-DNA for 30min during hybridization process. The electrical sensing of DNA hybridization was carried out in real time by monitoring the resistance of sensor array in response to the addition of target-DNA oligos in TE buffer, pH 7.4, using a CMOS chip. After 30min, sensor array was then rinsed with

![DNA sequences](image)

<table>
<thead>
<tr>
<th>DNA</th>
<th>Sequences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target</td>
<td>3'-CGGTAAGAGT GGCCTAAGTCACAGCAG-5'</td>
</tr>
<tr>
<td>Probe C</td>
<td>5'-HSC6-C18-GCCATCTCAC CGGATTCAGTGCTC-3'</td>
</tr>
<tr>
<td>Probe SNP</td>
<td>5'-HSC6-C18-GCCATCTCAC CCGATTCACTGCTC-3'</td>
</tr>
<tr>
<td>Probe HM</td>
<td>5'-HSC6-C18-GCCATCTCAC CCCTAAGTCCGCCAG-3'</td>
</tr>
<tr>
<td>Probe NC</td>
<td>5'-HSC6-C18-GGCCGTAAAGGT GGCCTAAGTCAGCAG-3'</td>
</tr>
</tbody>
</table>

Table 1 : DNA sequence used in the experiments

![Graph](image)

Fig. 5. Electrical characteristics of the CMOS chip. (a) Cumulative distribution of the CGI resistance from 12 cell using the CMOS chip and Agilent 4145 parameter analyzer. (b) The change of electrical resistance of each sensor cell in the sensor array depending upon the sensing conditions. (c) Sensitivity of fabricated sensor IC with various probe-DNA.

TE buffer. After the addition of 20µL TE buffer droplet onto the surface of sensor array, the DC measurement was performed. The electrolyte potential is determined by the enclosing electrode due to large capacitance between the electrode and electrolyte.

A 0.3V source-drain bias was maintained at all times during electrical measurements, while the electrolyte potential was grounded to reduce electrical noise. This self gating effect [8] is one of important advantages of our
sensing approach to other approaches in the label free electrical sensing of DNA hybridization in that we can measure various hybridizations on the chip without electrolyte potential variations. The result of Fig. 5(c) shows that almost 30% sensitivity was measured in the case of hybridization between complementary probe-DNA and target-DNA, a very negligible small sensitivity (~ 10%) was observed in the presence of hybridization of NC, HM probe-DNA with target-DNA. However, no difference was measured between C and SNP, which necessitates more accurate sensing condition to detect the small DNA sequence difference.

5 CONCLUSION

In this paper, a fully CMOS integrated swCNT sensor array platform that consists of a 32X32 array with the swCNT network-Au nanoparticle combination as the sensing element has been demonstrated. Using a 0.18μm commercial CMOS technology, we realized a CMOS swCNT integrated bio-sensor platform. As an application of DNA sensor, we have confirmed the response of the sensor to DNA hybridization. The platform can be a good candidate for a general sensor platform for bio molecule detection if further efforts are made to understand interactions between specific molecules and swCNT network Au used in our sensor device.

ACKNOWLEDGEMENT

This research was supported in part by the Smart IT Convergence System Research Center funded by the Ministry of Education, Science and Technology as Global Frontier Project (SIRC-2011-0031845), by a grant from the Industrial Source Technology Development Program (10033590) of the Ministry of Knowledge Economy of Korea, by the Pioneer Research Center program (20110002126) of the National Research Foundation of Korea, which is funded by the Ministry of Education, Science, and Technology of Korea, by the BK21 Program, and by the IC Design Education Center (IDEC).

REFERENCES