Fabrication of interdigitated nanogap devices for biomolecular detection

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ABSTRACT

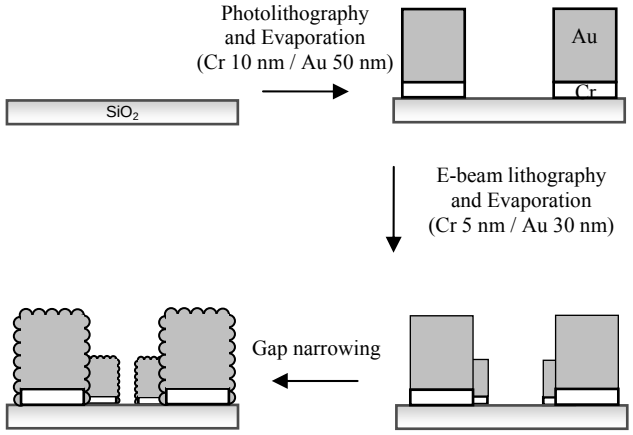
Interdigitated nanogap devices (INDs) were fabricated by the combination of conventional photo/e-beam lithographic techniques and surface-catalyzed chemical deposition (SCD) process. Lithographically-defined gap distances of initial devices were reduced to designed values by simply dipping the devices into the aqueous solution of gold ions and a mild reducing agent. The gross yield of the SCD process was found to be over 50%. The gap distances were controlled by the number of repetition of the SCD process. The INDs that include the minimum 20 nm gap distances, which are hard to form by using conventional lithographic techniques, could be successfully fabricated by using the gap narrowing processes. We also confirmed that the devices could be used for the detection of biomolecules by monotoring the jump of electrical conductance induced by the probe-labeled Au nanopaticles introduced into the gap region. To detect the target biomaterials at low concentrations, the design of INDs was selected as a shape of interdigitated electrodes presenting large active area. We believe that the INDs would be one of the promising platforms useful in the detection of biomolecules.

Keywords: interdigitated nanogap, nanoparticle, electric detection, immobilization, nanobiosensor, biomolecule.

INTRODUCTION

Numerous studies have been attempted to develop devices capable of detecting biomolecules such as DNAs, peptides, and proteins, aiming clinical or immunological applications.[1] Highly-sensitive bioassays are necessary for the early-stage disease diagnosis since the biomolecular markers of the disease are often present at an extremely low concentration, particularly in its early-stage.

Nanotechnology offers unique opportunities for creating highly sensitive and miniaturized biosensing devices. So far, various biosensing systems using the nanostructured materials such as carbon nanotubes, nanowires, nanoparticles, and nanogap devices, have been successfully demonstrated to detect various target biomaterials in recent years.[2-6] The majority of the nanoelectronic devices for biomolecular sensing were based on the field effect transistors made of semiconducting nanowires and nanotubes because their conduction properties should change sensitively in response to the changes in surrounding electric charges induced by the binding of target biomolecules.[2-4]



Scheme 1. Schematic diagram showing the fabrication processes of a nanogap device.

Herein, as an alternative format of nanoelectronic devices for biomaterial detection, we report the fabrication of the INDs, where the jump of electrical conductance is derived by introducing the probe-labeled Au nanopaticles, metallic connectors, via specific recognition processes at the nanogap of two electrodes separated by a few tens of nanometers. The IND system would provide efficient detection characteristics such as enhanced sensitivity because the effective length of the nanogap region increases. The gap narrowing processes were necessary because the detection of the incorporation of Au nanoparticles in the gap regions would be straightforward in the devices presenting narrower gaps. The pre-defined electrodes with

large gap distances were fabricated by photo/e-beam lithographic techniques and the gap distances were narrowed by applying SCD process to the pre-defined electrodes.[7] The INDs with a large active area fabricated by the SCD process were used in the electric detection of the existence of interested biomaterial. Briefly, in this paper, we describe the method for controlling gap distances of INDs, which can be used in the effective detection of biomaterials.

EXPERIMENTAL DETAILS

The fabrication process of INDs is schematically shown in scheme 1, where three individual processes: photo lithography, e-beam lithography and the gap narrowing process were included. Micro-/millimeter-sized and nano-/micro-sized structures were fabricated by photo and e-beam lithography, respectively. Finally, the SCD process was performed on the lithographically-defined devices to reduce the initial gap distance varying the number of repetition as a control parameter.

Photo lithography.
A 1.2 μm thick layer of positive photoresist, AZ-5214, was spin-coated on thermally-grown silicon oxide on a Si(100) substrate at 5000 rpm for 30 s and baked at 90 °C for 3 min on a hot plate. Photo exposure was carried out for 45 s and then development for 30-60 s. Prior to the lift-off process, metal layers of Cr and Au were successively deposited by e-beam evaporation with the thickness of about 10 nm and 50 nm, respectively.

E-beam lithography.
Polymethyl-methacrylate (PMMA), e-beam resistor, was spin-coated on the substrate with photolithographic pattern at 5000 rpm for 30 s and baked at 170 °C for 2 min. Scanning electron microscope (SEM) operating at 30 kV was used to expose the PMMA. The development was performed with using PMMA developer and isopropyl alcohol. The average gap distances were in range of 90-110 nm and the electrode thickness was about 35 nm after metal deposition and lift-off process.

Gap narrowing process.
Initial devices fabricated by conventional lithographic techniques were first immersed into the piranha solution [H_2SO_4 (30%): H_2O_2 = 5:1 (v/v)] at 60 °C for 1 hour to remove possible polymeric residues. 1 ml of 400 μM $HAuCl_4$ was added into 10 ml water containing the devices with initial gap and the gap narrowing reaction, the surface-catalysed chemical deposition, was initiated by adding 1 ml of 640 μM NH_2OH. The reaction temperature was kept at 28 °C for 2 min and this process was repeated several times. The number of repetition determines the final gap distance of INDs. The dependence of the gap narrowing process upon Au ion concentration and reaction temperature was also examined in the range of 200 μM – 1.5 mM and 300-330 K, respectively.

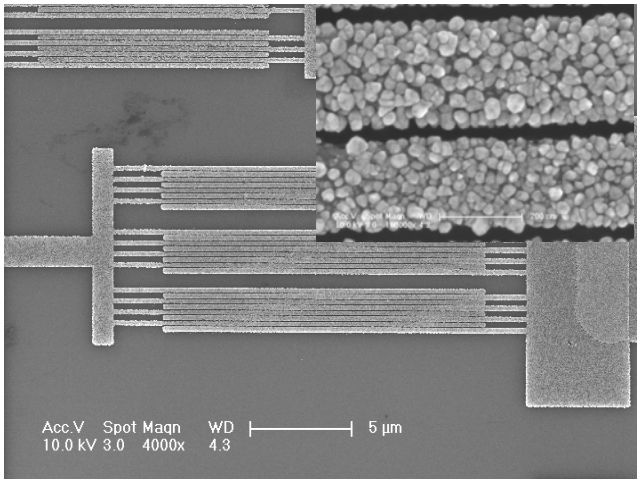


Figure 1. Field Emission Scanning Electron Microscope (FESEM) images of INDs after the surface-catalyzed chemical deposition. The inset is a magnified FESEM image of the nanogap device.

Electric detection of Prostate Specific Antigen (PSA) using a interdigitated nanogap device
On the SiO_2 surface between two Au electrodes of an IND, monoclonal anti-PSA (antibody) molecules were immobilized via a series of surface organic reactions while the Au electrode surfaces were passivated with a self-assembled monolayer (SAM) of polyethylene glycol. After immersing the device into a PSA sample solution and a colloidal solution of Au nanoparticles modified with polyclonal anti-PSA, the conductance between the electrodes was measured after a gentle N_2 drying. The conductance change of the IND was readily measurable with a simple multimeter because of the great difference of the device conductance before and after the Au nanoparticle immobilization. Further electric properties of the device was measured with a Probe Solution Incorporate-100 probe station connected to a Hewlett Packard-4156A precision semiconductor parameter analyzer using connecting cables with guard shield.

RESULT AND DISCUSSION

Figure 1 shows a Field Emission Scanning Electron Microscope (FESEM) image of an IND after the whole fabrication process. Since the SCD process includes Au ion reduction on the pre-defined gold surface, the electrode surface became rugged with densely-packed gold islands. However, the whole length of about 300 μm was not made in contact between two electrodes of the IND and the gap distances are maintained at about 20 nm on average. The gap distance of the IND is quite difficult to be obtained by conventional photo or e-beam lithography, not only because of the small gap distance compared to the lithographic limit but also because of the complicated design with a highly extended length of the nanogap.

The gap distance of INDs can be controlled by adjusting the reaction parameters during the SCD process. Higher concentration of Au ions results in the narrower gap in a given time of the reaction because the narrowing reaction proceeds faster at higher concentrations. However, the enhanced rate of narrowing process sometimes resulted in a wide distribution of the gap distance. The dependence of the gap distance on the reaction temperature is not so evident. When the reaction temperature was raised, the number of the gold islands grown on the initial device surface was increased while their size became smaller. The simplest parameter of adjusting the gap distance can be the number of repetition of the SCD process. The INDs having the gap distance of 20-100 nm were obtained by simply varying the number of repetition

Figure 2 shows FESEM images after the SDC processes and the relation between gap distance and the number of repetition. It was observed that the gap distances was changed to be about 84.6±6.3 nm, 50.4±4.6 nm, 43.1±4.2 nm, and 24.6±7.7 nm, after repeating the SCD process once, five times, nine times, and thirteen times, respectively. In general, the gap distance of the INDs decreases with increase in the repetition number. In other words, the gap distance can be controlled to have a designed value by a simple process.

Various designs of INDs were also examined to verify the usefulness of the SCD process for the fabrication of complex-structured devices. When the device structure is very simple, e. g., two facing electrodes with a point contact, the gross yield of the SCD process was over 90 %. However, the yield gets lower with higher complication of the device. In the case of the INDs as shown in Fig. 1, the yield of the SCD process was slightly above 50%.

The INDs can be used in the electric detection of a biomolecule. Since the gap distance between the two electrodes is comparable to the diameter of a nanoparticle and the effective length of the nanogap is highly-extended, the immobilization of metallic nanoparticles in the gap region is readily measurable by simply monitoring the conductance change between the electrodes. If the surface of the gap region has antibodies, specific binding between the antibody and antigen will leads to the immobilization of antigen in the gap region. On introducing antibody-labeled Au nanoparticles, the formation of the sandwiched structure of antibody-antigen-antibody will results in the nanoparticle immobilization in the nanogap of the IND, which in turn increase the electric conductance of the IND. We have confirmed that the INDs can be used in the detection of PSA upon anti-PSA labeled nanoparticle immobilization in the anti-PSA functionalized gap region.

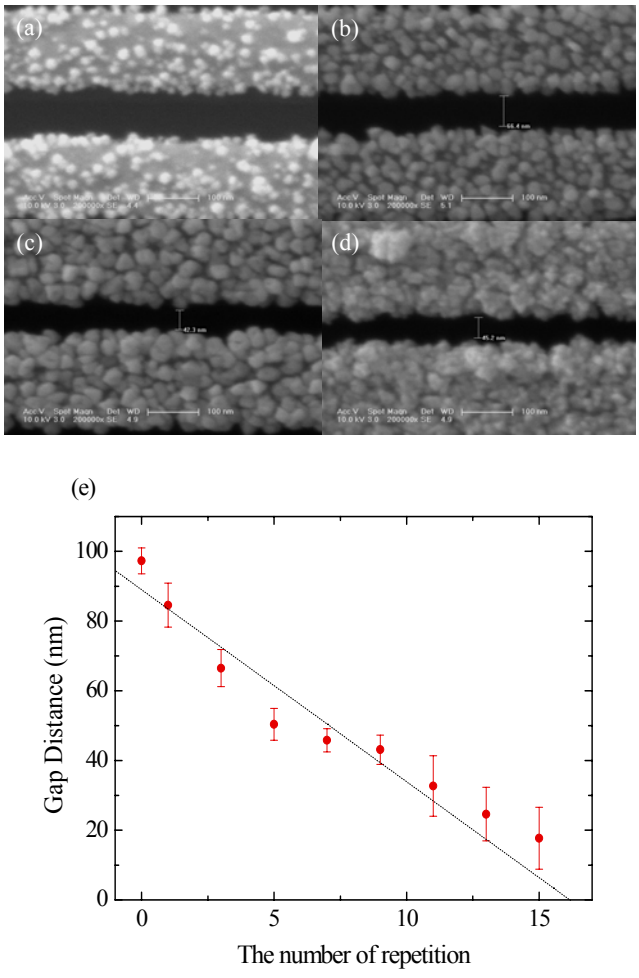


Figure 2. FESEM images of gap regions in the INDs as a function of the number of repetition of the SCD process. (a) ×1, (b) ×3, (c) ×5, (d) ×7 of the SCD. (e) Relation between the gap distance and the number of repetition.

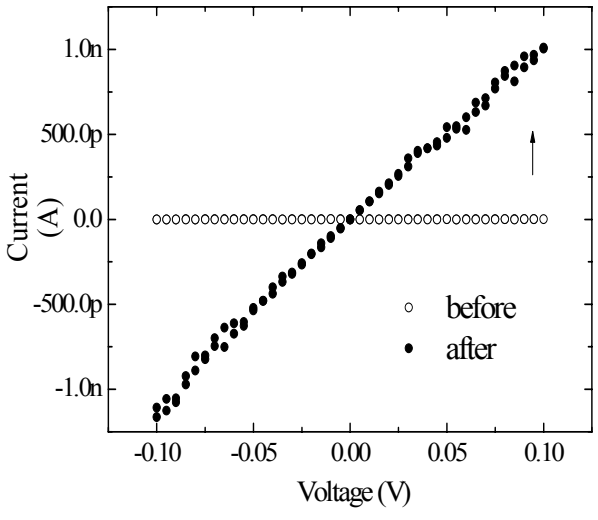


Figure 3. Current-voltage (I-V) curves of an IND before and after the immobilization of the gold nanoparticles modified with polyclonal anti-PSA.

To demonstrate the biomolecular sensing capability, the gap region of INDs and Au nanoparticles were modified with monoclonal and polyclonal anti-PSA, respectively. To reduce the loss of antigen through non-specific binding onto the electrodes, a SAM of polyethylene glycol was formed on the surface of the gold electrodes. Figure 3 shows current-voltage (I-V) curves of INDs before and after dipping into colloidal solution of polyclonal anti-PSA modified Au nanoparticles after immersing into the solution of 1 μg/ml PSA. The voltage was varied from -0.1 V to 0.1 V with 5mV steps to minimize the possibility of unintended voltage-induced processes such as electromigration.[6] Before immersing the device in PSA solution, the resistance of the INDs was over the detection limit (> 10 GΩ) of our system. However, the device conductance was dramatically increased after dipping into the Au nanoparticle colloid, which was attributed to the formation of electric conduction channel upon the immobilization of Au nanoparticles.

CONCLUSION

We have fabricated interdigitated nanogap devices by the combination of conventional lithographic techniques and the surface-catalyzed chemical deposition process. The gap distance was dependent upon the SCD parameters such as concentration, temperature, and the number of repetition. By varying the number of repetition of the SCD process, the gap distance of INDs was controlled in the range of 20-100 nm. Since the effective length of the nanogap is extended to be over 300 μm, the INDs can be used as a very sensitive platform of electric detection of biomolecules as demonstrated by detecting PSA in this paper.

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