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Gamma radiation effects on hydrogen-terminated nanocrystalline diamond bio-transistors

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ABSTRACT

Diamond is considered as a promising tissue equivalent material in radiation therapies as well as for bio-electronic sensors due to its unique set of properties. These features are combined in this work where effects of gamma irradiation (^{60}Co, up to 300 Gy) on function and stability of microscopic (60 × 20 μm^2) hydrogen-terminated diamond (H-diamond) solution-gated field effect transistors (SG-FETs) are studied. The H-diamond SG-FETs were prepared using 300 nm thin diamond films deposited on glass from methane and hydrogen gas mixture by microwave plasma. Prior to gamma irradiation they were interfaced to proteins (fetal bovine serum) and cells (human sarcoma osteogenic cell line — SAOS2) in cell growth medium. Blank H-diamond SG-FETs did not degrade after the irradiation. With adsorbed proteins and cells they showed specific changes in gate current characteristics (about 100% increase) after the irradiation. These current changes are attributed to modified protein layer and cell morphology on the diamond surface. The presented results establish a first step towards real-time electronic monitoring of cell growth during the irradiation by therapeutically relevant doses.

1. Introduction

Diamond exhibits a unique combination of intrinsic properties (i.e. electrical, optical, mechanical, chemical, biocompatibility) [1,2] which make it a perspective material for bioelectronics [3,4] including electrical and optical monitoring of cell cultivation and cell functions [5–8]. Owing to high radiation hardness diamond is recognized as the most suitable material for radiation medicine where it can be used in one of three principal modalities — radiotherapy, radiation oncology or therapeutic radiology. The use of diamond in counters of radiation particles or gamma rays has been studied since the late 1940s [9]. For monitoring medical irradiations diamond offers an excellent tissue equivalence due to its atomic number (Z = 6) which is close to the human tissue (Z_{muscle} = 7.42) [10–13]. In radiation detector devices diamond electrical resistance is inversely proportional to the absorbed dose [14].

Number of scientific works focused on radiation resistance of diamond to different sources (electron, neutrons, X-ray, gamma, etc.). Structural changes of microcrystalline diamond films after high gamma irradiation doses of 26 Mrads (260 kGy) have been reported by Gupta et al. [15]. Nanocrystalline diamond films were more radiation resistant due to the saturated transformation of sp^3 to sp^2. Both film types revealed an enhanced electron field emission after the irradiation. Similarly to intrinsic diamonds, boron doped diamond films have been studied too. The change from metallic to semiconducting like properties was studied as a function of the gamma radiation dose (up to 10^3 kGy) and boron doping level [16,17]. The mechanism was explained by the compensation of electrically active boron by hydrogen or boron-hydrogen complexes induced during the irradiation. Diamond nanoparticles added to multiwall carbon nanotubes enhanced their radiation resistance to the gamma irradiation at doses higher than 50 kGy [18]. The radiation resistance of diamond devices, namely lateral field emission vacuum microelectronic devices in two- and three-terminal (diode vs. transistor) configurations, has been demonstrated by Subramanian et al. [19]. The tested devices did not reveal any structural or electronic changes after the device exposure to X-ray and neutron radiation for 15 Mrad (150 kGy) and 4.4 × 10^{13} neutrons/cm^2, respectively. Diamond has been also investigated as the radiation protective layer integrated in standard electronic devices. Diamond film employed as the dielectric in MOS devices [20] or as the p-type conductive layer in 4H SiC detectors [21] was helpful to preserve the device reliability after the irradiation.

Most of the works have been focused on employing diamond in monitoring of radiation beams. However, little is still known about

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using diamond as biosensor for real-time monitoring of bio-chemical processes during radiation treatments. In this work we investigate the influence of gamma irradiation on function and stability of planar diamond based solution-gated field effect transistors (SG-FETs). We show that the nanocrystalline diamond SG-FETs based on H-terminated surface conductivity are radiation resistant. Moreover, we shows that changes in the SG-FET transistor characteristics after the irradiation can be attributed to the radiation-induced modifications of bio-layer (proteins, cells, etc.) on the diamond surface.

2. Experimental part

2.1. Fabrication of diamond transistors

Prior to the diamond deposition, fused silica substrates (10 mm × 10 mm × 1 mm in size) were ultrasonically cleaned in isopropanol and deionized water and were subsequently immersed for 40 min into an ultrasonic bath of a water colloidal suspension with a nanodiamond powder of nominal particle size 5 nm (NanoAmando, New Metals and Chemicals Corp. Ltd.). The ultrasonic treatment resulted in the formation of thin layer of nanodiamond powder in a total thickness of 5–25 nm [22].

Diamond thin films were grown in the thickness of about 300 nm by large area linear antenna pulsed microwave plasma system [23]. A multi-step CVD procedure was employed to grow diamond film with good electronic quality and good adhesion to the glass substrate. The process parameters were as follows: microwave power 2000 W, pressure 0.1 mbar, and substrate temperature approx. 600 °C. The gas mixture consisted of methane and carbon dioxide diluted in hydrogen (>80%). An average diamond grain size was 250 ± 50 nm as estimated from SEM images.

After the CVD process, the diamond films were partially overgrown and hydrogen terminated by employing focused microwave plasma with the ellipsoidal resonator cavity in order to improve surface electronic quality [24]. The hydrogenation process was done at microwave power 2500 W, total pressure 30 mbar, hydrogen flow 300 sccm, substrate temperature around 510 °C and total time 10 min. This treatment induced p-type surface conductivity on the nanocrystalline diamond films when exposed to air or solution [25].

Diamond planar SG-FETs were fabricated using standard lithographic steps, involving the lift off process and surface plasma treatments. Details on the device design and fabrication can be found in our previous study [26]. The opened gate area (60 × 60 μm^2) consisted of electrically conductive p-channel (H-terminated diamond, 20 × 60 μm^2) surrounded by the O-terminated areas (electrically insulating areas).

2.2. FBS adsorption and cell growth

The 15% fetal bovine serum (FBS) protein solution in McCoy's 5A supporting medium was prepared according to the protocol [27]. The FBS was adsorbed on the surface of H-terminated nanocrystalline diamond (H-NCD) FETs or H-terminated monocrystalline diamond for 10 min. Protein solution was removed from the substrate by rinsing in water and the sample was dried by compressed air.

SAOS-2 cells (sarcoma osteogenic, human osteoblast-like cell line; DSMZ GmbH) were grown in McCoy's 5A medium (Bio-Concept) supplemented with heat inactivated 15% FBS (Biowest), penicillin (20 U/ml) and streptomycin (20 μg/ml). HEPES buffer was added to the medium because of the absence of CO_2 atmosphere during electrical or optical measurements. Prior to the cell plating, sterilization of SG-FETs was performed by UV-C irradiation for 10 min. We used a standard germicidal low-pressure mercury lamp (TUV 15 W/G15 T8, Philips) which emits UV-C radiation with the peak at 253.7 nm. The distance of sterilized sample from the lamp was 20 cm.

Cells were plated in the densities of about 100,000 cells/cm^2 using a droplet technique: substrate surface was covered by 100 μl droplet of cell suspension in the medium. After 1 h incubation, 1.4 ml of the medium was added and cells were cultivated for 2 days in 5% CO_2 at 37 °C. Stable 5% CO_2 concentration in the atmosphere during the cell cultivation helps the bicarbonate buffer in cultivation media to maintain the optimal pH (7.1–7.4).

2.3. Gamma irradiation procedure

Blank SG-FETs, SG-FETs with adsorbed FBS and SG-FETs with cells were irradiated by up to (5 ± 0.05) Gy of gamma radiation (Chisostat, Chirana, ^{60}Co source, dose rate of 6 Gy/min at the sample position). The uncertainty in dose can come from uncertainty of exposure time (determined uncertainty below 1%) and sample position (incorrect sample positioning of 1 mm from defined position corresponds to dose change of 1%). The dose of 5 Gy was used as it corresponds to about 10% survival of human fetal osteoblasts in vitro [28] and it is similar to typical therapeutic doses.

During the irradiation, the SG-FETs were inserted upright into plastic bottles filled with cell medium used for preceding cell cultivation. The diamond surface was faced to the gamma radiation source. A schematic drawing of the experimental setup during the irradiation is shown in Fig. 1. AFM measurements confirmed that proteins were adsorbed on monocrystalline diamonds which were then irradiated in the same configuration. The irradiation dose was up to (300 ± 3) Gy in this case in order to corroborate the observed trends.

2.4. Measurement procedures

Electrical characteristic of SG-FETs before and after gamma irradiation were measured by the setup composed of K237 source-measure units [26]. Gating of SG-FET was realized by immersing H-terminated channel into electrolyte solutions which were in contact with Ag/AgCl gate electrode. As solutions we used (a) blank HEPES buffer and (b) heat inactivated 15% fetal bovine serum in HEPES buffer.

Transfer and gate current characteristics were measured in amplification regime at $U_{DS} = -0.6$ V for all samples. The sweeping rate was 50 mV/s and initial delay time was 5 s. All experiments were performed at room temperature. For data collection we used our own measurement software that was built upon measurement and control libraries developed under Delphi programming language.

AFM measurements were performed using Multi75Al cantilevers (Budget Sensors) in tapping mode on ICON AFM (Bruker). The AFM

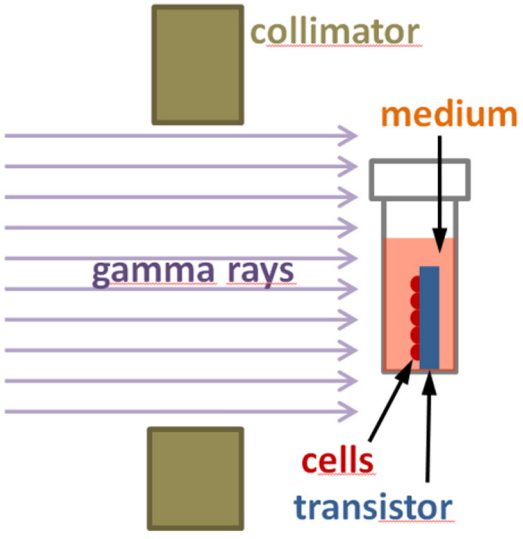

Fig. 1. Schematic drawing of the experimental setup during gamma irradiation experiments.

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