Graphene integrated optical biosensor for detection of breast cancer cell media

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ABSTRACT

We report a graphene oxide integrated optical biosensor for the detection of breast cancer cell media. The graphene oxide nanosheets-coated long period grating (GO-LPG) serves as an optical transducer where the GO acts as a bridging interface between optical sensor and external medium. The principle of the optical biosensor is based on alerting the optical signal as a change of local refractive index caused by different analyte concentrations. The proposed biosensor has been implemented to detect the breast cancer cell media with ultrahigh sensitivity, opening the path as a bio-nano-photonic platform for biosensing and early diagnosis.

Keywords: Graphene oxide, optical biosensor, breast cancer, long period grating

1. INTRODUCTION

Cancer is the second leading cause of death worldwide, accounting for an estimated 10 million deaths in 2020 [1]. Breast cancer causes one in six of all cancer deaths among women. Breast cancer survival five years after diagnosis now exceeds 80% in most high-income countries. However, survival rates in low-income countries remain lower as large numbers of cancer patients do not have access to early detection, timely quality diagnosis and successful treatment.

Here we propose a highly sensitive optical biosensor based on graphene oxide-coated long period grating (GO-LPG) for the detection of breast cancer cell media. The GO nanosheets were deposited on a long period grating, then the optical microscope, scanning electron microscope and atomic force microscopy were used for the surface morphological characterisation of the GO overlay. The sensitivities of the sensors were compared by monitoring the spectral changes with or without GO coating. The proposed GO-LPG biosensor was implemented to detect the breast cancer cell media demonstrating an ultrahigh sensitivity.

2. METHODS

2.1 Fabrication and principle of LPG

The LPG with a period of 400 μm and a length of 15 mm was fabricated in a hydrogenated single-mode fiber by the use of a CW frequency-doubled Argon laser at 244 nm wavelength and point-by-point technique. When the light was launched to the LPG, the fundamental core mode would be coupled to the forward-propagating cladding modes resulting in several attenuation bands in the transmission spectrum. The wavelengths of the attenuation bands satisfy the phase matching condition [2]:

$$\lambda_{res} = (n_{co}^{eff} - n_{cl,i}^{eff})\Lambda \tag{1}$$

where n_{co}^{eff} and $n_{cl,i}^{eff}$ are the effective refractive indices of core and ith cladding mode respectively, Λ is the LPG's period. The transmission power T_i of the ith attenuation band is given by [2,3]:

$$T_i = 1 - \sin^2(\kappa_i L) \tag{2}$$

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where κ_i is the coupling coefficient of the ith cladding mode and L is the grating length. The changes of surrounding-medium refractive index (RI) will result in the fluctuation of the effective refractive indices of cladding modes, hence the wavelength shifts of the attenuation bands [2-6]. For the thin film-coated LPGs, due to the electric field distribution changes rapidly, the coupling strength would consequently change making the GO-coated LPG as an intensity-based sensor [7-10].

2.2 Deposition of GO nanosheets on LPG

We developed the deposition technique by conjunction of the chemical bonding and multiple physical adsorption [9]. The fiber sensor was firstly cleaned with acetone, then immersed in 1.0 M NaOH reagent for 1 hour followed by washing with deionized (DI) water and drying thoroughly. The OH-enriched LPG was silanized by incubating into 5% (3-Aminopropyl)triethoxysilane (APTES) solution for 20 min at room temperature, then washed with ethanol and baked in an oven at 70°C for 30 min to stabilize the Si-O-Si bonding. The APTES-silanized LPG was immersed in 1 mL 0.1 mg/mL GO colloidal suspension contained in a custom-made mini-bath, which was placed on a hotplate at ~ 42°C for 40 min. During the evaporation of GO suspension, the GO nanosheets were chemically bonded on the sensor surface due to the reaction between epoxy groups of GO and amino groups of APTES-silanized surface. After the suspension evaporated thoroughly, the 2nd coating cycle was applied by pipetting 1 mL 0.1 mg/mL GO suspension into the container to accomplish physical adsorption of new GO nanosheets onto former GO overlay. After 4th deposition cycle, the GO-coated LPG was washed with DI water to remove the unbonded nanosheets and baked in an oven at 35℃ for 12 h.

2.3 Characterization of surface morphology

The surface morphology of GO-coated fiber samples were characterized by the use of optical microscope, SEM and AFM.

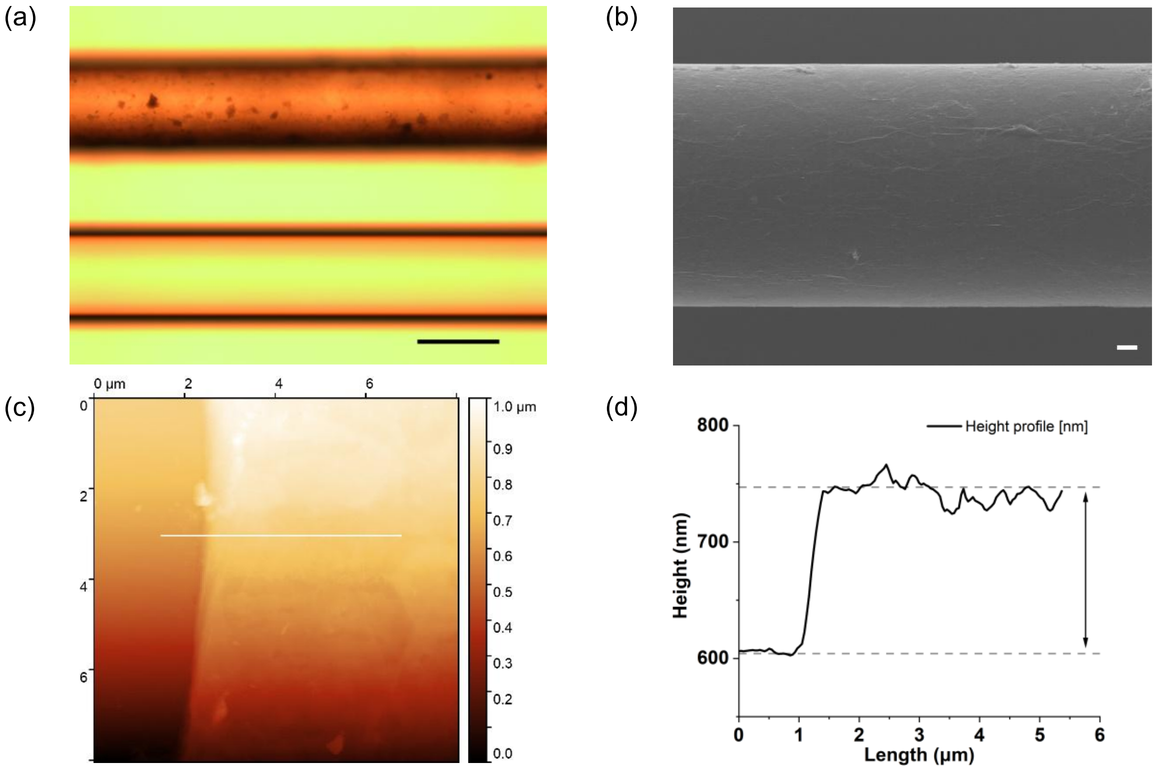

Figure 1. Surface morphology of GO-coated fiber. (a) Optical microscope image (scale bar: 100 µm, up: GO-coated fiber, down: bare fiber), (b) SEM image with magnification of 500× (bar: 10 µm), (c) AFM image and (d) Height profile of GO overlay.

As shown in the optical microscope images (Figure 1a), a brown overlay was successfully coated on the fiber surface after four coating cycles (up image) compared to a super clear surface of the bare fiber (down image). Further morphology was characterized by SEM with magnification of 500× (Figure 1b) showing a wavy and slightly wrinkled texture of GO overlay upon the fiber surface. The AFM image (Figure 1c) shows a clear step boundary between bare and GO-coated sections, in

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which the thickness of GO overlay was measured (Figure 1d), demonstrating a homogeneous overlay deposited upon the entire cylindrical fiber surface.

3. RESULTS AND DISCUSSION

3.1 Optical characterization

A SLD light source was used to launch the light to the fiber grating, whose transmission spectra were monitored by an optical spectrum analyzer. The GO-LPG was placed straightly on a home-made container where the external medium was applied (Figure 2a). To avoid the temperature-introduced fluctuation, the experiment was operated in a temperature-controlled room at 21°C. The optical properties of sensor device were determined by monitoring the transmission spectra. Figure 2b plots the transmission spectra of LPG (in the air) before and after GO deposition, showing that the GO deposition induces an increase of 4.1 dB in intensity and a slight blue-shift of 0.1 nm in wavelength.

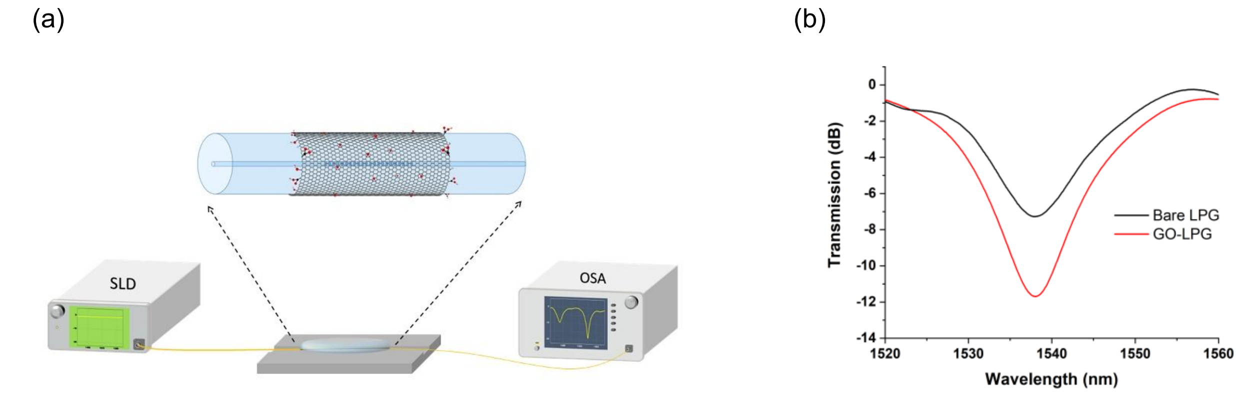

Figure 2. (a) Schematic of experimental setup. (b) Transmission spectra of bare LPG and GO-coated LPG.

3.2 Detection of breast cancer cell medium

The proposed GO-LPG was implemented to detect human breast cancer cell medium. MCF7 human breast cancer cells were set up in a 6-well plate ranging from 0, 1000, 10000, 100000, and 500000 cells per well in 5 mL DMEM complete media total per well. After 72 h normal growth, a set of cell media were collected in sterile Eppendorf tubes. For the sensing experiment, the cell media were added into the sucrose solution (RI=1.4602). The GO-LPG was submerged in these solutions in turn and the sensor spectra were monitored.

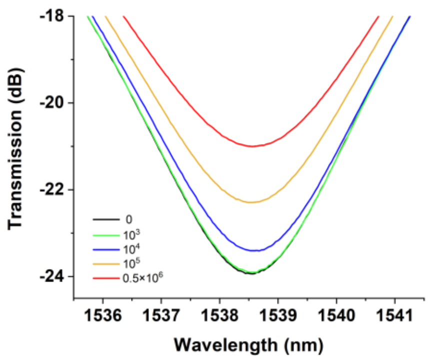

Figure 3. Transmission spectra of GO-LPG against different concentrations of cancer cell media.

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Figure 3 shows the transmission spectra of GO-LPG under different cell concentrations. The intensity of the attenuation band increases of 0.04 dB, 0.57 dB, 1.62 dB, and 3.32 dB for the cancer cell media with cell number of 10^3, 10^4, 10^5, and 5×10^5, respectively. By integrating GO nanosheets with optical device, the light-matter interaction has been enhanced when the evanescent light field penetrates from sensor boundary to the external cell medium.

4. CONCLUSIONS

In conclusion, we reported a graphene oxide integrated optical biosensor for the detection of breast cancer cell media. The GO nanosheets were deposited on LPG by using a chemical bonding associated with physical adsorption technique. The surface morphologies and optical properties of the device were investigated by the optical microscope, AFM, SEM and optical measurement system. The GO-LPG was used as biosensor to detect cancer cell medium exhibiting ultrahigh sensitivity.

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