

Nano-plasmonic graphene-quantum dots integrated photoelectronic biosensor

Jiaxing Sun

Department of Physics

School of Science and Technology

Nottingham Trent University

Nottingham, United Kingdom

jiaxing.sun2021@my.ntu.ac.uk

Lin Zhou

State Key Lab of Transducer Tech.

Shanghai Institute of Microsystem and

Information Technology, Chinese

Academy of Sciences, China

zhoulinzlw@mail.sim.ac.cn

Hongju Mao

State Key Lab of Transducer Tech.

Shanghai Institute of Microsystem and

Information Technology, Chinese

Academy of Sciences, China

hjmao@mail.sim.ac.uk

Jianlong Zhao

State Key Lab of Transducer Tech.

Shanghai Institute of Microsystem and

Information Technology, Chinese

Academy of Sciences, China

jlzhao@mail.sim.ac.cn

Xianfeng Chen*

Department of Physics

School of Science and Technology

Nottingham Trent University

Nottingham, United Kingdom

xianfeng.chen@ntu.ac.uk

Abstract—We report a nano-plasmonic biosensor with integrated optoelectronic architecture developed on a miniaturized chip. With simple means, the nano-plasmonic sensor demonstrated the capability to record the selective and specific binding of proteins to the bioreceptors immobilized on gold nanoparticles arrays placed directly on a photoconductive graphene-Perovskite quantum dots hybrid channel. The distinct combination of the nano-plasmonic structure, proteins and hybrid two-dimensional materials endowed the photoelectronic detection of biotin with advantages of label-free, ultrahigh sensitivity and rapid speed.

Keywords—graphene, quantum dots, nano-plasmonic, biosensor, label-free

I. INTRODUCTION

Protein-protein interactions are crucial in multiple biological processes. These interactions vary from being permanent to transient [1,2]. Some protein-protein interactions are particular for a pair of proteins, while some proteins interact with numerous ligands. Being able to detect protein interactions, is a key to the fundamental understanding of cellular processes and mitigating the progression of disease, thus being a driver of innovation for drug discovery, clinical diagnostics, and protein engineering [3]. Different electronic biosensors have been verified to possess the capacity to detect protein–protein interactions [4–7]. Atomically layered two-dimensional materials (such as graphene, molybdenum disulfide, and black phosphorus) have recently attracted great attentions due to their attractive electronic/optical properties, large abundance, and compatibility to planar nanofabrication processes. The field-effect transistor (FET) based biosensors have been demonstrated ultrasensitive capabilities for detecting antigen–antibody binding events [8]. However, purely electrical or electronic biosensors always suffer from the degradation of detection stability and sensitivity after prolonged exposure to liquid reagents, which is caused by ionic screening of electric field and unwanted short-circuit effects in an aqueous environment.

Here we propose a novel hybrid graphene-quantum dots

phototransistor biosensor for label-free detection of antigen–antibody binding events, where the nano-plasmonic resonance induces a photoconduction change in a graphene-quantum dots hybrid channel consequently alerting the sensor signal. The nano-plasmonic filter consists of Neutravidin-conjugated hemispherical gold nanoparticles on a transparent thin layer, which is placed above a graphene-Perovskite quantum dots hybrid photoconductive channel. By the use of the developed nano-plasmonic biosensor, we have implemented label-free detection of biotin, a prototype protein, achieving a limit of detection of femtogram per milliliter level for biotin modified Bovine Serum Albumin (biotin-BSA). The proposed nano-plasmonic biosensor could be further developed for point-of-care diagnosis and portable biochemical sensing with advantages of label-free, ultrahigh sensitivity and rapid speed.

II. METHODS AND EXPERIMENTS

A. Materials

Gold nanoparticle (AuNPs, d = 50nm) were purchased from JCNANO Tech Co., Ltd (Nanjing, China). (3-Aminopropyl) triethoxysilane (APTES), Trichloro(octadecyl)silane (ODTS), were purchased from Sigma-Aldrich. Chemical vapor deposition graphene film on Cu was acquired from 2D Carbon (Changzhou, China). CsPbI₃ perovskite was purchased from Mesolight. Phosphate buffered saline (PBS) and Neutravidin were purchased from Thermo Fisher Scientific. Biotin-BSA was purchased from Sangon Biotech (Shanghai, China). Pure deionized (DI) water (18.1 MΩ·cm) was produced by Milipore-Q purification system.

B. Fabrication of graphene-perovskite photoelectronic transistor

Photolithography, metal sputtering and lift-off processes were utilized to fabricate the Ti (5 nm)/Au (50 nm) electrodes as the drain and source contacts on silicon oxide substrate. The pattern of these electrodes was achieved by laser direct writing lithography (MicroWriter ML3, Durham Magneto Optics). Single layer graphene with polymethylmethacrylate (PMMA) was transferred to the surface of the gold electrodes via a PMMA-assisted wet transfer method. Finally, the CsPbI₃ perovskite film was spin-coated onto the device (3000 rpm, 30 s) and crystallized by soft annealing at 80 °C.

C. Preparation of nano-plasmonic filter

To prepare the nano-plasmonic structure, the thin glass layer (100μm) was used as the substrate. Thin glass substrate was washed with DI water carefully. After drying, the surface of the glass substrate was treated by O₂ plasma for 2 min and subsequently incubated in a 2% APTES solution for 12h. The AuNP solution was then loaded on the APTES-modified glass and incubated overnight. After the incubation, the AuNPs-glass substrate was washed with DI water followed by strong air blowing.

D. Integration of nano-plasmonic graphene-quantum dots photoelectronic biosensor

The AuNPs-glass substrate was immersed into Neutravidin solution for overnight at 4°C. The nano-plasmonic filter consisted of Neutravidin-conjugated hemispherical gold nanoparticles on a transparent thin layer, which was placed above a graphene-perovskite quantum dots hybrid photoconductive channel. All electrical and photo-response characteristics of the perovskite-graphene hybrid photodetectors were monitored using a Keithley 4200 semiconductor parameter analyzer under dark and illuminated conditions. The Coherent Compass 115M-5 laser was used as the incident light source. The intensity of the incident light (with 532 nm) on the device surface was adjusted from 1 μW to 0.5 mW using an optical attenuator (Thorlabs NDC-50C-4M) and was measured using a laser power meter (ADVANTEST, Q8230).

III. RESULTS AND DISCUSSIONS

A. Design of nano-plasmonic graphene-perovskite hybrid photoelectronic biosensor

Fig. 1 illustrates the structure of the integrated graphene-perovskite hybrid photoelectronic biosensor. Medical double-sided adhesive was utilized to fix the nano-plasmonic filter on the top of a graphene-perovskite quantum dots hybrid photoconductive channel. The nano-plasmonic filter consists of Neutravidin-conjugated hemispherical gold nanoparticles on a transparent thin layer.

The principle of the biosensor operation is based on tuning the delivery of incident light to the graphene-quantum dots hybrid photoconductive channel pass through the nano-plasmonic filter by means of nano-plasmonic resonance shifts induced by biomolecular surface binding. The tuning is dependent on biotin-BSA concentration on the nano-plasmonic filter and detected by the optoelectronic graphene-quantum dots hybrid channel.

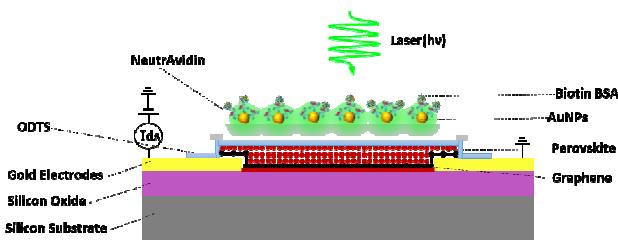


Fig. 1. Schematic illustration of the integrated nano-plasmonic graphene-quantum dots photoelectronic biosensor.

B. Characterization of integrated photoelectronic nanostructure

After the graphene-perovskite hybrid conductive channel was formed on the substrate, the surface topography of the graphene-perovskite hybrid film was verified by scanning electron microscopy (SEM) (Fig. 2a). The AuNPs were successfully immobilized onto the thin glass layer (Fig. 2b). The effect of the drain bias on the photo-response of the device was shown in Fig. 3a. The photocurrent (drain current as a function of the illuminated laser power) was proportional to the drain voltage under the illumination at 532 nm. Then the temporal photo-response of the graphene-perovskite hybrid photodetector was measured under 500 μW illumination at 532 nm, photo-switching characteristics of the graphene-perovskite hybrid photodetector hybrid photodetector exposing to the air for different days were shown in Fig. 3b, where the experimental results indicated the photoelectric response performance of this device decreased gradually with the time of exposure to the air.

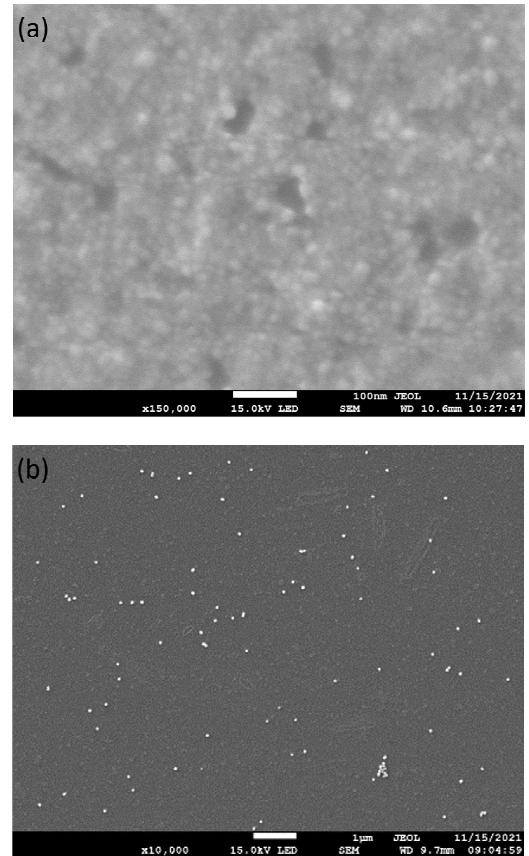


Fig. 2. (a) SEM morphology of graphene-perovskite hybrid film; (b) The distribution of gold nanoparticles on onto a thin glass layer.

C. Biomarker Detection of Photoelectronic Biosensor

The avidin-biotin complex is the strongest known noncovalent interaction between a protein and ligand [9]. Compared with streptavidin, the neutral isoelectric point of NeutrAvidin could minimize nonspecific binding caused by electrostatic interaction. NeutrAvidin could offer a powerful and universal tool as biotin binding surfaces (Antibodies, DNA etc.) and are suitable to set up different kind of immune-molecular biosensor. Our study employed biotin-BSA in an aqueous phase as our model analyte.

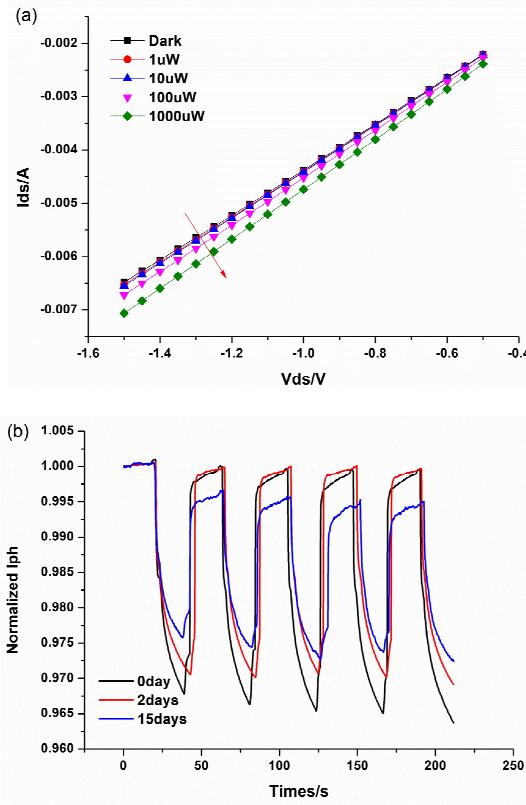


Fig. 3. Drain voltage dependence and photo-switching characteristics of the perovskite-graphene hybrid photodetector. (a) Drain current – drain voltage plot under various illumination powers; (b) Photo-switching characteristics of the perovskite-graphene hybrid photodetector under alternating dark and light illumination (500 μ W, 532 nm). The gate and drain voltages were 0 and 0.1 V, respectively.

We further performed the NeutrAvidin-biotin interaction measurement with different concentrations of Biotin-BSA from 0.1 pg/mL to 1 ng/mL (Fig. 4). Varying the concentration of Biotin-BSA was expected to change the optical throughput of the nano-plasmonic filter. Increasing the Biotin-BSA concentration resulted in lower optical transmission, leading to a decrease in the photocurrent of the device. Measuring the photocurrent changes allowed us to quantify the Biotin-BSA concentration of a sample. Our biosensor device incorporating the high-sensitivity graphene-perovskite hybrid photoconductive thin layer enabled the recognition of a very low light intensity change at the presence of low concentration biomarker.

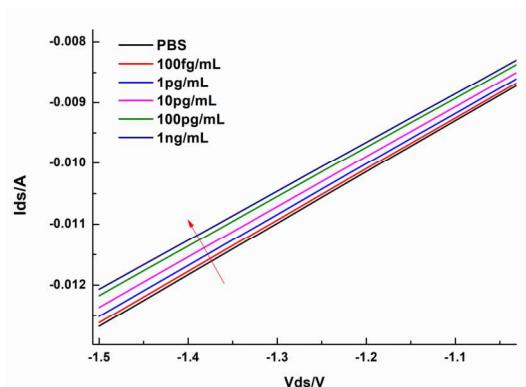


Fig. 4. Drain current – drain voltage plot with different concentrations of Biotin-BSA under 1000 μ W illumination powers.

IV. CONCLUSIONS

In this work, we proposed a nano-plasmonic biosensor with an integrated optoelectronic architecture in a miniaturized chip. With simple means, it was demonstrated the capability of recording the selective and specific binding of protein to receptors immobilized on gold nanoparticles arrays placed directly on a photoactive graphene-quantum dots hybrid channel. The distinct combination of the nano-plasmonic structure, immobilized protein and hybrid two-dimensional materials endowed the independent photoelectronic detection of biotin-BSA with advantages of label-free, ultrahigh sensitivity and rapid speed.

ACKNOWLEDGMENT

This work has received fundings from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 872049, The Science and Technology Commission of Shanghai Municipality (No. 21JM0010402, No. 22ZR1473500), and National Natural Science Foundation of China (grant No. 62231025).

REFERENCES

- [1] Keskin, O., Gursoy, A., Ma, B. and Nussinov, R., “Principles of protein-protein interactions: What are the preferred ways for proteins to interact?”, *Chem. Rev.*, vol. 108, pp. 1225–1244, 2008.
- [2] Bryant, P., Pozzati, G., Elofsson, A., “Improved prediction of protein-protein interactions using AlphaFold2”, *Nat. Commun.*, vol. 13, pp. 1694, 2022.
- [3] Rego, N. B., Xi, E. T. and Patel, A. J., “Identifying hydrophobic protein patches to inform protein interaction interfaces”, *Proc. Natl. Acad. Sci. U. S. A.*, vol. 118, e2018234118, 2021.
- [4] Bhattacharyya, I. M., Cohen, S., Shalabny, A., Bashouti, M., Akabayov, B. and Shalev, G., “Specific and label-free immunosensing of protein-protein interactions with silicon-based immunoFETs”, *Biosens. Bioelectron.*, vol. 132, pp. 143-161, 2019.
- [5] Yousefi, N., Caba, C., Hu, A., Mooney, M., Zhang, S., Agostinis, A. D., Mirhassani, M., Ahamed, M.J., Tong, Y. F. and Rondeau-Gagne, S., “Building a Versatile Platform for the Detection of Protein-Protein Interactions Based on Organic Field-Effect Transistors”, *ACS Appl. Electron. Mater.*, vol. 4, pp. 4972–4981, 2022.
- [6] Hine, A. V., Chen, X., Hughes, M. D., Zhou, K., Davies, E., Sugden, K., Bennion, I., Zhang, L., “Optical fibre-based detection of DNA hybridization”, *Biochem. Soc. Trans.*, vol. 37, pp. 445-449, 2009.
- [7] Chen, X., Liu, C., Hughes, M. D., Hine, A., Zhang, L., “EDC-mediated oligonucleotide immobilization on a long period grating optical biosensor”, *Journal of Biosensors and Bioelectronics*, vol. 6, 1000173, 2015.
- [8] Sedki, M., Shen, Y., Mulchandani, A., “Nano-FET-enabled biosensors: Materials perspective and recent advances in North America”, *Biosens. Bioelectron.*, vol. 176, 112941, 2021.
- [9] Thermo Fisher Scientific, “Thermo Scientific Avidin-Biotin Technical Handbook”, 2009.