

## Article

# Ultrasensitive Leaky Surface Acoustic Wave Immunosensor for Real-Time Detection of Alpha-Fetoprotein in Biological Fluids

Sana Rauf <sup>1</sup>, Hafiz Imran Ahmad Qazi <sup>2</sup>, Jingting Luo <sup>1,\*</sup>, Chen Fu <sup>1</sup>, Ran Tao <sup>1</sup>, Sajid Rauf <sup>3</sup>, Lei Yang <sup>1</sup>, Honglang Li <sup>4,5,6</sup> and Yongqing Fu <sup>7</sup>

- <sup>1</sup> Key Laboratory of Optoelectronic Devices and Systems of Education Ministry and Guangdong Province, College of Physics and Optoelectronic Engineering, Shenzhen University, Shenzhen 518060, China; sanichms@gmail.com (S.R.); chenfu@szu.edu.cn (C.F.); ran.tao@szu.edu.cn (R.T.); yangleigas@foxmail.com (L.Y.)
  - <sup>2</sup> SZU-CASIPP Joint Laboratory for Applied Plasma, College of Physics and Optoelectronic Engineering, Shenzhen University, Shenzhen 518060, China; emranphy@gmail.com
  - <sup>3</sup> College of Electronics and Information Engineering, Shenzhen University, Shenzhen 518086, China; sajidrauf.physics@gmail.com
  - <sup>4</sup> National Center for Nanoscience and Technology, Beijing 100000, China; lhl@nanoctr.cn
  - <sup>5</sup> GBA Research Innovation Institute for Nanotechnology, Guangzhou 510000, China
  - <sup>6</sup> Guangdong Guangnaxin Technology Co., Ltd., Guangzhou 510000, China
  - <sup>7</sup> Faculty of Engineering and Environment, Northumbria University, Newcastle upon Tyne NE1 8ST, UK; Richard.fu@northumbria.ac.uk
- \* Correspondence: luojt@szu.edu.cn

**Citation:** Rauf, S.; Qazi, H.I.A.; Luo, J.; Fu, C.; Tao, R.; Rauf, S.; Yang, L.; Li, H.; Fu, Y. Ultrasensitive Leaky Surface Acoustic Wave Immunosensor for Real-Time Detection of Alpha-Fetoprotein in Biological Fluids. *Chemosensors* **2021**, *9*, 311. <https://doi.org/10.3390/chemosensors9110311>

Academic Editor: Nicole Jaffrezic-Renault

Received: 14 October 2021

Accepted: 31 October 2021

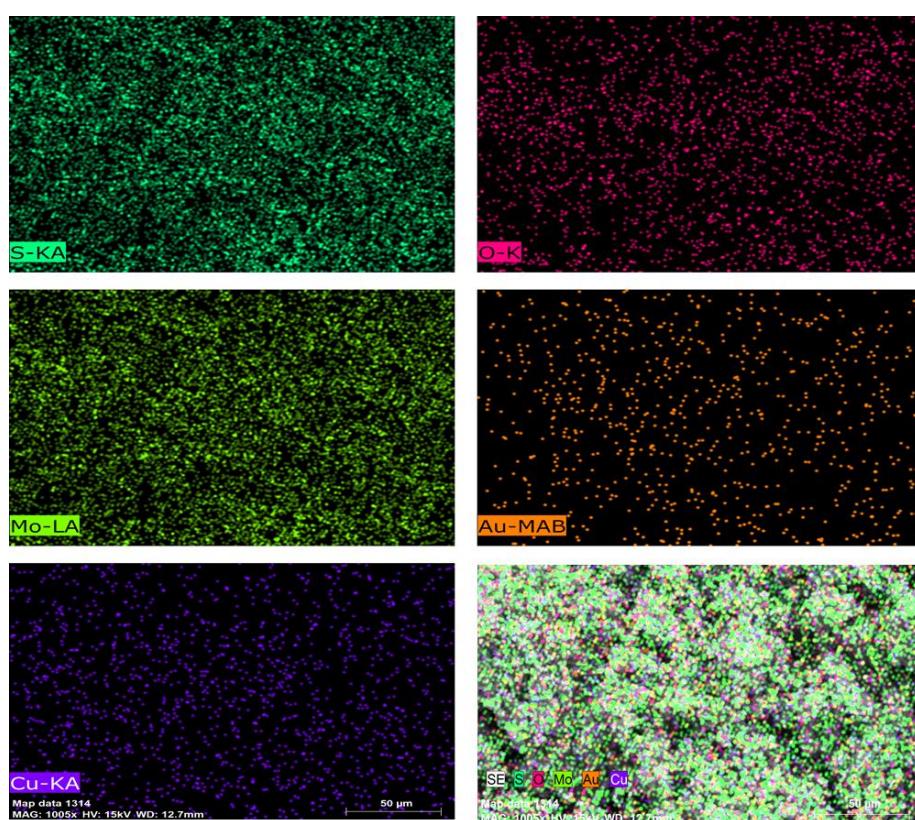
Published: 4 November 2021

**Publisher's Note:** MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

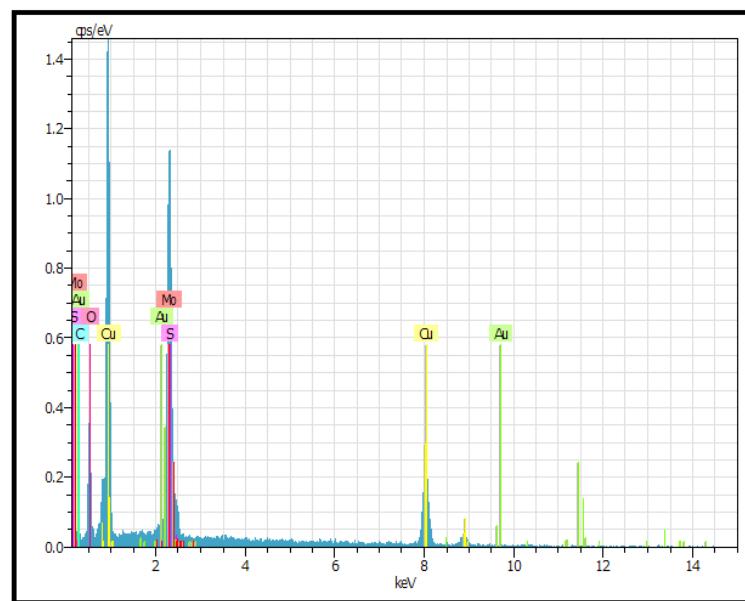


**Copyright:** © 2021 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

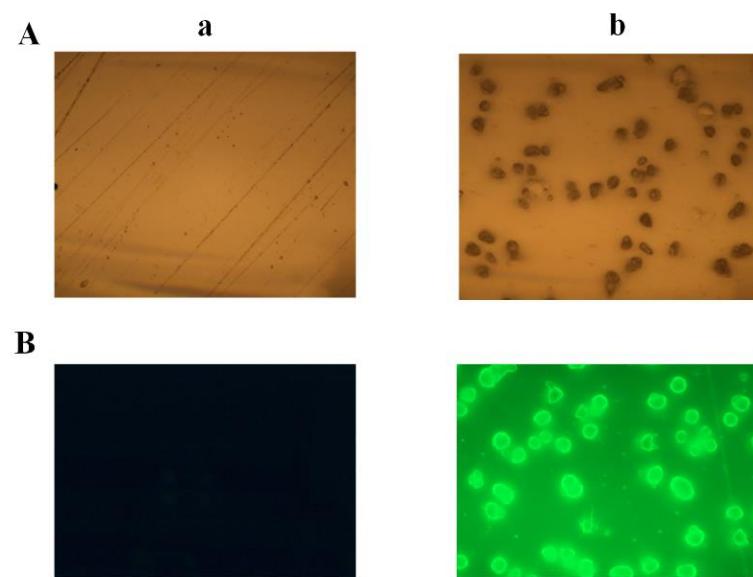
## Supplementary Material



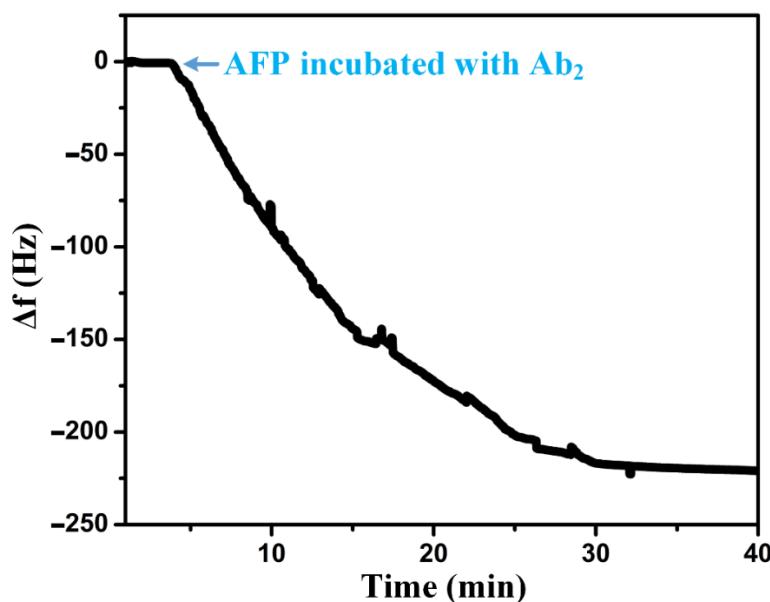
**Figure S1.** Elemental mapping of MoS<sub>2</sub>@Cu<sub>2</sub>O-Au using SEM.



**Figure S2.** EDX spectra of  $\text{MoS}_2@\text{Cu}_2\text{O}-\text{Au}$  nanoparticles.



**Figure S3.** Optical microscopic images (A) of the delay line before (a), and after immobilization of  $\text{Ab}_1$  (b); Optical microscopic images (B) of the delay line before (a), and after immobilization of FITC- $\text{Ab}_1$  (b).



**Figure S4.** Frequency shift observed upon injection of AFP solution incubated with  $Ab_2$  (secondary anti-AFP antibody).

**Table S1.** Comparison of other methods for detection of AFP with SAW based immunosensor.

Technique	Detection limit <sup>1</sup>	Biological sample used	References
Ultrasensitive label-free electrochemical immunosensor based on multifunctionalized graphene nanocomposites for the detection of alpha-fetoprotein	2.7 fg/ml	Human serum sample	[1]
Detection of AFP with an ultra-sensitive giant magnetoimpedance biosensor	100 fg/ml	NA	[2]
Sandwich-type electrochemical immunoassay based on $Co_3O_4@MnO_2$ -thionine and pseudo-ELISA method toward sensitive detection of alpha-fetoprotein	0.33 pg/ml	Human serum sample	[3]
A graphene oxide-based label-free electrochemical aptasensor for the detection of alpha-fetoprotein	3 pg/ml	Human serum sample	[4]
Micro-piezoelectric immunoassay chip for simultaneous detection of Hepatitis B virus and $\alpha$ -fetoprotein	0.1 ng/ml	NA	[5]
GTP as a peroxidase-mimic to mediate enzymatic cascade reaction for alkaline phosphatase detection and alkaline phosphatase-linked immunoassay	0.5 ng/ml	Serum sample	[6]
A piezoelectric immunosensor for the detection of $\alpha$ -fetoprotein using an interface of gold/hydroxyapatite hybrid nanomaterial	15.3 ng/ml	Human serum sample	[7]
Label-free electrochemical aptasensor for detection of alpha-fetoprotein based on AFP-aptamer and thionin/reduced graphene oxide/gold nanoparticles	50 ng/ml	Human serum sample	[8]
Development of a piezoelectric immunosensor for the detection of alpha-fetoprotein	50 ng/ml	Human serum sample	[9]
Ultrasensitive leaky surface acoustic wave immunosensor for real time detection of alpha-fetoprotein in biological fluids	5.5 pg/ml	Serum and saliva	This work

<sup>1</sup> All the LOD values are determined in the PBS buffer

## References

1. Wang, Y.; Zhang, Y.; Wu, D.; Ma, H.; Pang, X.; Fan, D.; Wei, Q.; Du, B., Ultrasensitive label-free electrochemical immunosensor based on multifunctionalized graphene nanocomposites for the detection of alpha fetoprotein. *Sci. Rep.* **2017**, *7*, 42361.
2. Zhu, Y.; Zhang, Q.; Li, X.; Pan, H.; Wang, J.; Zhao, Z., Detection of AFP with an ultra-sensitive giant magnetoimpedance biosensor. *Sens. Actuators B: Chem.* **2019**, *293*, 53–58.
3. Wang, Y.; Zhao, G.; Wang, H.; Cao, W.; Du, B.; Wei, Q., Sandwich-type electrochemical immunoassay based on Co<sub>3</sub>O<sub>4</sub>@MnO<sub>2</sub>-thionine and pseudo-ELISA method toward sensitive detection of alpha fetoprotein. *Biosens. Bioelectron.* **2018**, *106*, 179–185.
4. Yang, S.; Zhang, F.; Wang, Z.; Liang, Q., A graphene oxide-based label-free electrochemical aptasensor for the detection of alpha-fetoprotein. *Biosens. Bioelectron.* **2018**, *112*, 186–192.
5. Xu, T.; Miao, J.; Wang, Z.; Yu, L.; Li, C. M., Micro-piezoelectric immunoassay chip for simultaneous detection of Hepatitis B virus and  $\alpha$ -fetoprotein. *Sens. Actuators B: Chem.* **2011**, *151*, 370–376.
6. Shi, Y.; Yang, M.; Liu, L.; Pang, Y.; Long, Y.; Zheng, H., GTP as a peroxidase-mimic to mediate enzymatic cascade reaction for alkaline phosphatase detection and alkaline phosphatase-linked immunoassay. *Sens. Actuators B: Chem.* **2018**, *275*, 43–49.
7. Ding, Y.; Liu, J.; Wang, H.; Shen, G.; Yu, R., A piezoelectric immunosensor for the detection of  $\alpha$ -fetoprotein using an interface of gold/hydroxyapatite hybrid nanomaterial. *Biomaterials* **2007**, *28*, 2147–2154.
8. Li, G.; Li, S.; Wang, Z.; Xue, Y.; Dong, C.; Zeng, J.; Huang, Y.; Liang, J.; Zhou, Z., Label-free electrochemical aptasensor for detection of alpha-fetoprotein based on AFP-aptamer and thionin/reduced graphene oxide/gold nanoparticles. *Anal. Biochem.* **2018**, *547*, 37–44.
9. Tsai, W.-C.; Lin, I. C., Development of a piezoelectric immunosensor for the detection of alpha-fetoprotein. *Sens. Actuators B: Chem.* **2005**, *106*, 455–460.