RGC Ref.: N_PolyU506/13
NSFC Ref. : 21361162002

The Research Grants Council of Hong Kong
NSFC/RGC Joint Research Scheme
Joint Completion Report

(Please attach a copy of the completion report submitted to the NSFC by the Mainland researcher)

Part A: The Project and Investigator(s)

1. Project Title

The Application of Organic Electrochemical Transistors as a State-of-the-art Platform for Label-free, Ultrasensitive, High Throughput and Portable Nucleic Acid Detection

2. Investigator(s) and Academic Department/Units Involved

	Hong Kong Team	Mainland Team
Name of Principal Investigator *(with title)*	Prof. Feng YAN	Prof. Huangxian Ju
Post	Professor	Professor
Unit / Department / Institution	Department of Applied Physics / The Hong Kong Polytechnic University	State Key Laboratory of Analytical Chemistry and Life Science / Department of Chemistry / Nanjing University
Contact Information	+852 2766 4054	+86 25 83593593
Co-investigator(s) *(with title and institution)*	N.A.	Dr. Jie Wu Department of Chemistry, Nanjing University

3. Project Duration

	Original	Revised	Date of RGC/ Institution Approval *(must be quoted)*
Project Start date	01-Jan-2014		
Project Completion date	31-Dec-2017		
Duration *(in month)*	48		
Deadline for Submission of Completion Report	09-Feb-2018		

Part B: The Completion Report

5. Project Objectives

5.1 Objectives as per original application

1. *OECT-based ultrasensitive detection of nucleic acid to attomolar level*
2. *Ultrasensitive real-time detection of MicroRNA*
3. *Fabrication of OECT arrays for high throughput label-free nucleic acid sensing*

5.2 Revised Objectives
N . A .

6. Research Outcome

Major findings and research outcome
(maximum 1 page; please make reference to Part C where necessary)

1. We find that OECT is an excellent transducer for the detection of biomolecules with high sensitivity. The device can be easily prepared by solution process with low cost. By modifying the devices with different biomaterials, the OECT-based biosensors show high sensitivity as well as high selectivity (**Adv. Mater.** 27, 676-681 (2015).).
2. The device is successfully used to detect various biomarkers with ultrahigh sensitivity. In the devices, we proposed a new sending mechanism of the devices based on the modulation of the electrochemical activity of the gate electrode (**Adv. Mater.** 29, 1703787 (2017)). The concentration of the analyte can influence the concentration of the nano-probes modified on the gate electrode and induce a different device response (**ACS Appl. Mater. Interface** (submitted)). Based on this principle, highly sensitive miRNA sensors have been realized and an ultralow detection limit down to 10^{-15} M was obtained (Paper in preparation).
3. We found the interaction between biomolecules and the organic channel of an OECT for the first time (**Adv. Mater.** 27, 7493-7527 (2015); One paper is in preparation). The bulk capacitance of the organic semiconductor layer in aqueous solution was changed when negatively charged miRNA was immobilized on the surface, which leads to the change of the channel current of an OECT. So the device can be conveniently used to detect miRNA and other biomolecules without labeling.

Potential for further development of the research and the proposed course of action
(maximum half a page)

OECTs can be developed as low-cost and highly sensitive biosensors for many medical applications. The possible practical applications include: (1) The devices for the detection of miRNA can be used for the diagnosis of diseases such as cancer. (2)Due to the low cost and portable characters, the devices can also be used for healthcare purposes, such as the monitoring of glucose and uric acid levels for elderly. (3) The devices can be further developed for the detection of many other biomarkers based on the same principle and thus multifunctional sensing arrays can be prepared for many real applications. (4) The mechanism of the interaction between biomolecules and organic semiconductors is still not

very clear. Fundamental study is needed to provide a better understanding of the observed results.

7. The Layman's Summary

(describe in layman's language the nature, significance and value of the research project, in no more than 200 words)

Micro RNAs (miRNAs) are small RNA molecules that regulate gene expression post-transcriptionally. They play an important role in cancer development and therefore have become next-generation biomarkers for the diagnosis and prognosis of cancers. We have fabricated organic electrochemical transistors and used a dual-functionalized nanoprobe for ultra-sensitive analysis of cancer inhibitor miRNA. A dual-functionalized nanoprobe was also prepared for generating electrochemical signal and as amplification section. The device combined with this nanoprobe could specifically detect miRNA level down to 10^{-15} M, which is about three orders magnitude lower than conventional electrochemical methods using the same functionalized working electrode. Moreover, this device has been used for the practical sensing of miRNA expression levels in cancer cells, normal cells and anticancer drug treated cancer cells and can differentiate them easily. Microarrays of the OECTs were successfully prepared and used for multifunctional biological detections. Therefore, the OECT devices functionalized with labeled nanoprobes demonstrate great potential for the real detection of human mRNA in cancer cells in physiological environments. The success of the research project leads to a cost-effective approach to detecting various biomarkers with ultrahigh sensitivity and pave a way of using novel organic semiconductor devices with low cost in biological systems.

Part C: Research Output

8. Peer-reviewed journal publication(s) arising directly from this research project

(Please attach a copy of each publication and/or the letter of acceptance if not yet submitted in the previous progress report(s). All listed publications must acknowledge RGC's funding support by quoting the specific grant reference.)

The Latest Status of Publications				Author(s) ***(bold** the authors belonging to the project teams and denote the correspondin g author with an asterisk*)*	Title and Journal/ Book *(with the volume, pages and other necessary publishing details specified)*	Submitted to RGC *(indicate the year ending of the relevant progress report)*	Attached to this report *(Yes or No)*	Acknowledged the support of this Joint Research Scheme *(Yes or No)*	Accessible from the institutional repository *(Yes or No)*
Year of publication	Year of Acceptance *(For paper accepted but not yet published)*	Under Review	Under Preparation *(optional)*						
2015				**Caizhi Liao**, **Chunhin Mak**, **Meng Zhang**, Helen L.W. Chan and **Feng Yan***	Flexible Organic Electrochemical Transistors for Highly Selective Enzyme Biosensors and Used for Saliva Testing, **Advanced Materials.** 27, 676-681 (2015).		Yes	Yes	Yes
2015				**Caizhi Liao, Meng Zhang,** Mei Yu Yao, Tao Hua, Li Li*, **Feng Yan*,**	Flexible Organic Electronics in Biology: Materials and Devices, ***Advanced Materials.*** 27, 7493-7527 (2015).		Yes	Yes	Yes
2015				**Meng Zhang, Caizhi Liao,** Chun Hin Mak, Peng You, Chee Leung Mak & **Feng Yan*,**	Highly sensitive glucose sensors based on enzyme-modified whole-graphene solution-gated transistors, **Scientific Reports.** 5, 8311, 1-6 (2015).		Yes	Yes	Yes

2015				**Chun Hin Mak, Caizhi Liao, Ying Fu, Meng Zhang,** Chun Yin Tang, Y. H. Tsang, H.L.W. Chan and **Feng Yan***	Highly-sensitive epinephrine sensors based on organic electrochemical transistors with carbon nanomaterials modified gate electrodes**, Journal of Materials Chemistry C.** 3, 6532-6538 (2015).		Yes	Yes	Yes
2017				**Ying Fu, Naixiang Wang, Anneng Yang**, Helen Ka-wai LAW, Li Li, **Feng Yan***,	Highly Sensitive Detection of Protein Biomarkers with Organic Electrochemical Transistors, ***Advanced Materials.*** 29, 1703787 (2017)		Yes	Yes	Yes
2018		Under review		**Lizhen Chen, Ying Fu, Naixiang Wang, Anneng Yang, Yuanzhe Li, Jie Wu, Huangxian Ju, Feng Yan**	Organic electrochemical transistors for the detection of cell surfaces glycans, ***ACS Applied Materials & Interfaces*** (Submitted on 31 Jan 2018)		Yes	Yes	Yes
2018			In preparation	**Ying Fu, Naixiang Wang, Anneng Yang, Yuanzhe Li, Feng YAN**	Organic electrochemical transistors for miRNA analysis and cancer cell detection		Abstract only	Yes	Yes

2018			In preparation	Kai Xie, **Naixiang Wang**, Xudong Lin, Peiling Fang, **Feng Yan*,** Peng Shi*	Heterogeneous regulation along the dopaminergic circuits revealed by in vivo real-time mapping of neurotransmitter release using organic electrochemical transistor arrays		Abstract only	Yes	Yes

9. Recognized international conference(s) in which paper(s) related to this research project was/were delivered *(Please attach a copy of each delivered paper. All listed papers must acknowledge RGC's funding support by quoting the specific grant reference.)*

Month/Year/ Place	Title	Conference Name	Submitted to RGC *(indicate the year ending of the relevant progress report)*	Attached to this report *(Yes or No)*	Acknowledged the support of this Joint Research Scheme *(Yes or No)*	Accessible from the institutional repository *(Yes or No)*
12/2015 /Boston, USA	Highly sensitive biosensors based on organic electrochemical transistors	2015 MRS Fall Meeting & Exhibit		Yes	Yes	Yes
07/2015 /	High performance biosensors based on solution-gated flexible transistors with functionalized gate electrodes	8th International Symposium on Flexible Organic Electronics (ISFOE15), Greece		Yes	Yes	Yes
2/2017	Organic thin film transistors for high-performan ce biosensors	International Conference on Display Technology (ICDT) 2017, Feb 18-20, 2017, Fuzhou, China.		Yes	Yes	Yes
4/2017	Solution-Gated Organic Thin-Film Transistors for High-Performan ce Biosensors	2017 MRS Spring Meeting, April 17-21, 2017, Phoenix, Arizona, USA.		Yes	Yes	Yes

10. Student(s) trained *(Please attach a copy of the title page of the thesis.)*

Name	Degree registered for	Date of registration	Date of thesis submission/ graduation
Caizhi Liao	MPhil	03-JUL-2012	24-JUL-2014/ graduation
Chun Hin Mak	MPhil	02-JUL-2013	19-NOV-2015/ graduation
Naixiang Wang	PhD	1-Sep-2015	31-Aug-2018

11. Other impact *(e.g. award of patents or prizes, collaboration with other research institutions, technology transfer, etc.)*

We have successful collaboration with Prof. Huangxian Ju's group in Nanjing University and have developed some novel biosensors (Submitted to *ACS Appl. Mater. Interfaces.*).