Taylor & Francis
Taylor & Francis Group

Expert Review of Molecular Diagnostics

ISSN: 1473-7159 (Print) 1744-8352 (Online) Journal homepage: informahealthcare.com/journals/iero20

Application of thin-film transistors in label-free DNA biosensors

Feng Yan & Hao Tang

Application of thin-film transistors in label-free DNA biosensors

Expert Rev. Mol. Diagn. 10(5), 547–549 (2010)

Feng Yan

Author for correspondence
Department of Applied Physics, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong, China
Tel.: +852 2766 4054
Fax: +852 2333 7629
apafyan@poly.edu.hk

Hao Tang

Department of Applied Physics, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong, China

"DNA microarray (DNA chip) technology has been developed to offer unprecedented simultaneous and multiplexed analysis in a high-throughput screening format."

DNA sensors are the most important biosensors that have been popularly studied. The detection of nucleic acid is of great scientific and economic importance. Applications of DNA sensors include gene-expression monitoring, pharmacogenomic research and drug discovery, clinical diagnostics, and viral and bacterial identification. It is also important for the detection of biowarfare and bioterrorism agents, and for forensic and genetic identification. It has been recognized that the DNA sensors for the above applications should be highly sensitive, selective, integrated, portable and disposable. Therefore, DNA microarray (DNA chip) technology has been developed to offer unprecedented simultaneous and multiplexed analysis in a high-throughput screening format.

Today, the confocal fluorescence microscope is the standard detection platform for the analysis of DNA microarrays [1]. However, fluorescent scanning and imaging technology is not portable and has a limited spatial resolution and sensitivity. More importantly, this technique requires labeling of targets, which is time-consuming, more complex and expensive. Therefore, various technologies, such as electrochemical detection [2], surface vibration spectroscopy [3], atomic force microscopy [4], scanning Kelvin probe microscopy [5], genetic field effect transistor (FET) [6–9] and microcantilever [10] have been developed recently to realize highly sensitive and label-free DNA microarrays.

Genetic FET has many advantages over other label-free techniques. First, the fabrication of high-density FET arrays is a mature technology; it has been developed for more than half a century. For example, random access memory based on FETs is one of the highest density integrated circuits, and has billions of devices in a small chip. Second, a sensor based on a FET is the combination of a sensor and an amplifier: a small variation of gate voltage may change the channel current of the device by several orders of magnitude. Third, the device can be miniaturized without losing signal-to-noise ratio because the channel current of a FET is proportional to the ratio of the channel width to the channel length and not related to the area of the device [11]. Therefore, FET is ideal for use in small-sized, high-density and multifunctional microarray sensors. In addition, biosensors based on FETs can be easily integrated with circuitry to form self-supported and portable DNA detection platforms since FET is the key component of an integrated circuit.

"...field effect transistor is ideal for use in small-sized, high-density and multifunctional microarray sensors."

DNA sensors have been developed based on various FETs, including single crystal silicon FETs, polycrystalline or amorphous silicon thin-film transistors (TFT), silicon nanowire transistors [12], carbon nanotube transistors [13,14], graphene transistors [15,16], organic TFTs (OTFT) [8,9,17] and so on. TFT is a FET fabricated on an insulating substrate, especially a low-cost or flexible one. Therefore, TFTs show great advantages over devices based on silicon wafers in disposable applications. Here, transistors based on carbon nanotubes, silicon nanowires and graphene can also

Expert Reviews

10.1586/ERM.10.50

ISSN 1473-7159

be regarded as different types of TFTs. It is worth noting that polysilicon or amorphous silicon TFTs have been popularly used in flat-panel displays and thus they are mature technologies that can be directly transferred to sensing applications, including high-density DNA sensors. OTFT is another promising device for application in disposable DNA sensors, because it is much cheaper than any other FETs. OTFT will be discussed in more detail later in this article.

Although many types of TFTs have been used as DNA sensors, the operation principles of these devices are somewhat different. They can be classified by where the DNA molecules are immobilized on the transistor. The first type of TFT-based DNA sensor is normally modified with DNA molecules on gate dielectric, and similarly to other TFT-based biosensors, the DNA layer is exposed to an electrolyte during the measurement [18]. In this case, the applied gate voltage is modulated by the potential drop near the DNA layer due to the intrinsic charge of the DNA molecules. Bendriaa *et al.* reported a type of DNA sensor based on a suspended gate polysilicon TFT [19]. The hybridization of probe DNA with complementary target DNA is evidenced by a positive shift of the gate voltage as large as 0.35 V. Goncalves *et al.* used amorphous silicon TFTs for a pH and label-free DNA sensor [20]. A shift of the gate voltage by approximately 100 mV has been observed after the immobilization of DNA molecules on the gate insulator. Estrela *et al.* have developed DNA sensors based on extended gate polysilicon TFTs [7]. A parallel shift of transfer characteristics (drain current versus gate voltage) of 355 mV has been observed after the hybridization of single-strand DNA probes with its complementary strands. It is worth noting that, for DNA sensors based on single-crystal silicon FETs, the shift of gate voltage owing to DNA hybridization is normally tens of millivolts [6], which is much lower than that of the TFT-based DNA sensors. Since the DNA molecules in electrolytes are screened by mobile counter ions during a measurement, the induced interface potential drop is influenced by various factors, including the concentration of ions in the electrolyte, DNA concentration in the surface and the length of DNA strand, which may be the main reasons for the different shift of gate voltage in different reports.

> "Organic thin-film transistor is another promising device for application in disposable DNA sensors, because it is much cheaper than any other field effect transistors."

The second type of TFT-based DNA sensor is a device modified with DNA probes on the active layer of the transistor. Since DNA molecules have a negative charge and can interact with the active layer directly, this type of device is much more sensitive than the first type described above. Most of the DNA sensors based on carbon nanotube transistors, graphene transistors, silicon nanowire transistors and OTFTs can be regarded as the second type. Wu *et al.* reported a highly sensitive DNA sensor based on a silicon nanowire transistor, which showed the detection limit of subfemtomolar level [12]. This sensor distinguished 1-bp mismatched DNA strands. Star *et al.* reported DNA sensors based on carbon nanotube network FET for label-free DNA detection at picomolar to micromolar concentrations [13]. Although in another paper Tang *et al.* mentioned that DNA hybridization could not occur near carbon nanotubes, their carbon nanotube FET was still a successful DNA sensor because the contact resistances of the transistor were changed by DNA hybridization [14]. Dong *et al.* reported a DNA sensor that used a graphene transistor [15]. The device shows a high sensitivity to DNA with a concentration as low as 0.01 nM, which was attributed to electronic n-doping to the device. Mohanty *et al.* reported a DNA sensor based on a graphene transistor, whose sensing ability was attributed to the electrostatic interaction between DNA molecules and the graphene layer [16]. Although all of the DNA sensors based on the novel transistors use different sensing mechanisms, the gate voltages of the transfer characteristics of the devices corresponding to DNA hybridization normally shift for hundreds of millivolts to several volts, which are much larger than that of the first type of DNA sensor. The detection limit to DNA concentration has also been extended down to a much lower level.

> "The fabrication of uniform devices based on carbon nanotubes or graphene remains a significant technological challenge."

However, it is not easy to use the above transistors based on nanomaterials in disposable sensing arrays. The fabrication of uniform devices based on carbon nanotubes or graphene remains a significant technological challenge. Silicon nanowire transistors require access to advanced clean-room facilities similar to those used for microelectronics and thus are not suitable for low-cost and disposable sensors. In this aspect, OTFTs are excellent candidates for disposable DNA sensors for their easy and cheap fabrication compared with their inorganic counterparts. OTFT has been studied extensively for various applications, including flexible displays, organic circuits, memories and sensors. Organic materials can be dissolved in various solvents, so that transistors can be coated or printed on many different substrates by various technologies. In addition, some organic semiconductors are biocompatible and flexible, and thus they can be integrated with biological systems. Until now, there are several types of OTFT-based DNA sensors that have been reported.

One type of OTFT-based DNA sensor was reported by Zhang *et al.*, in which DNA molecules were immobilized on the surface of semiconductor layer (pentacene) and an unambiguous doping-induced threshold voltage shift up to 20 V has been observed [8]. A drawback of this technique is that pentacene is not stable when it is exposed to DNA solution. In addition, it is not convenient to firmly bind biomolecules to the surface of pentacene. Another type of DNA sensor based on OTFT was suggested by Yan *et al.*, in which DNA molecules were immobilized on a gold source with drain electrodes before coating with an organic semiconductor layer (poly[3-hexylthiophe]) [9]. The DNA layer changed the work function of the source/drain electrodes and increased the contact resistances of the transistor. Single- and double-stranded DNA have been differentiated successfully in these experiments. Although this technique cannot be used for *in situ* DNA sensing because the transistor is fabricated after the hybridization of DNA, it is expected to be suitable for application in high-density DNA arrays because the whole fabrication process is very convenient and low cost.

Another important OTFT is organic electrochemical transistor (OECT), which has attracted much attention recently because the device can be used in electrolyte with very stable performance and can provide *in situ* DNA detection [21]. Second, the device has a very low operating voltage, which is normally less than 1 V. Krishnamoorthy *et al.* fabricated OECTs based on poly(3,4-ethylenedioxythiophene) (PEDOT) by electropolymerization from 3,4-ethylenedioxythiophene solution in the presence of probe single-stranded DNA [17]. The expected conductivity changes were observed when the PEDOT-based TFT sensors were exposed to complementary single-stranded DNA solution and, as predicted, no response was observed when the device was exposed to a non-complementary target sequence. However, the fabrication process is not suitable for high-density DNA arrays.

Therefore, OTFTs have already shown promising application in DNA sensors; however, several important issues, including the stability, reproducibility and specificity, of the devices must be further optimized.

Financial & competing interests disclosure
The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

References

1 DeRisi JL, Iyer VR, Brown PO. Exploring the metabolic and genetic control of gene expression on a genomic scale. *Science* 278 (5338), 680–686 (1997).

2 Boon EM, Salas JE, Barton JK. An electrical probe of protein–DNA interactions on DNA-modified surfaces. *Nat. Biotechnol.* 20(3), 282–286 (2002).

3 Miyamoto KI, Ishibashi KI, Hiroi K, Kimura Y, Ishii H, Niwano M. Label-free detection and classification of DNA by surface vibration spectroscopy in conjugation with electrophoresis. *Appl. Phys. Lett.* 86(5), 1–3 (2005).

4 Wang J, Bard, AJ. Monitoring DNA immobilization and hybridization on surfaces by atomic force microscopy force measurements. *Anal. Chem.* 73(10), 2207–2212 (2001).

5 Thompson M, Cheran LE, Zhang MQ, Chacko M, Huo H, Sadeghi S. Label-free detection of nucleic acid and protein microarrays by scanning Kelvin nanoprobe. *Biosens. Bioelectron.* 20(8), 1471–1481 (2005).

6 Pouthas F, Gentil C, Côte D, Bockelmann U. DNA detection on transistor arrays following mutation-specific enzymatic amplification. *Appl. Phys. Lett.* 84(9), 1594–1596 (2004).

7 Estrela P, Stewart A G, Yan F, Migliorato P. Field effect detection of biomolecular interactions. *Electrochim. Acta* 50(25), 4995–5000 (2005).

8 Zhang QT, Subramanian V. DNA hybridization detection with organic thin film transistors: toward fast and disposable DNA microarray chips. *Biosens. Bioelectron.* 22(12), 3182–3187 (2007).

9 Yan F, Mok SM, Yu JJ, Chan HLW, Yang M. Label-free DNA sensor based on organic thin film transistors. *Biosens. Bioelectron.* 24(5), 1241–1245 (2009).

10 Shekhawat G, Tark SH, Dravid VP. MOSFET-embedded microcantilevers for measuring deflection in biomolecular sensors. *Science* 311(5767), 1592–1595 (2006).

11 Sze SM. *Physics of Semiconductor Devices* John Wiley & Sons, NY, USA 440 (1981).

12 Wu CC, Ko FH, Yang YS, Hsia DL, Lee BS, Su TS. Label-free biosensing of gene mutation using a silicon nanowire field-effect transistor. *Biosens. Bioelectron.* 25(4), 820–825 (2009).

13 Star A, Tu E, Niemann J, Gabriel JCP, Joiner CS, Valcke C. Label-free detection of DNA hybridization using carbon nanotube network field-effect transistors. *Proc. Natl Acad. Sci. USA* 103(3), 921–926 (2006).

14 Tang X, Bansaruntip S, Nakayama N, Yenilmez E, Chang YL, Wang Q. Carbon nanotube DNA sensor and sensing mechanism. *Nano. Lett.* 6(8), 1632–1636 (2006).

15 Mohanty N, Berry V, Graphene-based single-bacterium resolution biodevice and DNA transistor: interfacing graphene derivatives with nanoscale and microscale biocomponents. *Nano. Lett.* 8(12), 4469–4476 (2008).

16 Dong XC, Shi Y, Huang W, Chen P, Li LJ. Electrical detection of DNA hybridization with single-base specificity using transistors based on CVD-grown graphene sheets. *Adv. Mater.* 22(14), 1649–1653 (2010).

17 Krishnamoorthy K, Gokhale RS, Contractor AQ, Kumar A. Novel label-free DNA sensors based on poly(3,4-ethylenedioxythiophene). *Chem. Commun. (Camb.)* 7, 820–821 (2004).

18 Yan F, Estrela P, Mo Y, Migliorato P, Maeda H, Inoue S, Shimoda T. Polycrystalline silicon ion sensitive field effect transistors. *Appl. Phys. Lett.* 86(5), 053901 1–3 (2005).

19 Bendriaa F, Le-Bihan F, Salaun AC *et al.* DNA detection by suspended gate polysilicon thin film transistor. *2005 IEEE Sensors* 1, 412–415 (2005).

20 Goncalves D, Prazeres DMF, Chu V, Conde JP. Label-free electronic detection of biomolecules using a-Si:H field-effect devices. *J. Non-Cryst. Solids* 352(9–20), 2007–2010 (2006).

21 Berggren M, Richter-Dahlfors A. Organic bioelectronics. *Adv. Mater.* 19(20), 3201–3213 (2007).