



## MoS<sub>2</sub>-DNA and MoS<sub>2</sub> based sensors

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MoS<sub>2</sub>, a family member of transition-metal dichalcogenides, has shown highly attractive superiority for detection arising from its unique physical and chemical properties. Coupling MoS<sub>2</sub> with DNA recognition events leads to novel sensing platforms. Therefore, it has attracted increasing interest for MoS<sub>2</sub> based sensors in the increasing demands of biomedical applications. This has led to its rapid development in field of sensor. This paper summarizes the key issues in the development of MoS<sub>2</sub>-DNA and MoS<sub>2</sub> based sensors related to fluorescence resonance energy transfer (FRET), electrochemical biosensing, and field effect transistors (FET) biosensing for use in the detection of DNA, proteins, metal ions, and others. The detection mechanisms and the advantages of MoS<sub>2</sub> are revealed. Future directions in which the field is likely to thrive and some critical challenges are also discussed.

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### 1. Introduction

MoS<sub>2</sub> emerging two-dimensional-layered material analogous to graphene has been attracting much attention because of its unique physical and chemical properties, such as extraordinary thermal conductivity, robust mechanical properties, excellent nanoelectronics, unusual optical properties, and energy harvesting properties.<sup>1</sup> MoS<sub>2</sub> is a family member of transition-metal dichalcogenides. Each Mo is coordinated in a trigonal prismatic geometry to six S atoms; it is constructed by stacking covalently bound S–Mo–S through weak van der Waals interactions,<sup>2</sup> which aids in enhancing planar electric transportation properties.<sup>3</sup> MoS<sub>2</sub> nanosheets are able to adsorb single-stranded DNA by the van der Waals force between nucleobases and the basal plane of MoS<sub>2</sub> nanosheets.<sup>1</sup> Furthermore, MoS<sub>2</sub> nanosheets could be synthesized on a large scale and display strong fluorescence quenching properties in aqueous solution for sensing without further processing comparing with other nanomaterials such as graphene oxide.<sup>4</sup> MoS<sub>2</sub> shows the similar property and application with graphene oxide.<sup>2,5,6</sup> Therefore, MoS<sub>2</sub> has been widely applied in sensors that can detect DNA, proteins, metal ions, and other compounds. This paper provides an overview of the current approaches for sensors using DNA as recognition elements and their applications based on MoS<sub>2</sub>. Future perspectives and some challenges are also discussed.

### 2. Synthesis of MoS<sub>2</sub>

#### 2.1. Exfoliation

Various methods have been reported about the synthesis of MoS<sub>2</sub> nanosheets, including scotch tape based micro-mechanical exfoliation,<sup>7</sup> spontaneous exfoliation,<sup>8</sup> chemical exfoliation,<sup>9</sup> ultrasound exfoliation,<sup>10</sup> liquid exfoliation,<sup>11</sup> and electrochemical exfoliation.<sup>12</sup> However, scotch tape based micromechanical exfoliation was limited to the fabrication of a small amount of single-layer nanosheet materials with low reproducibility.<sup>13</sup> Chemical exfoliation easily results in loss of the pristine semiconducting properties of MoS<sub>2</sub> due to structural changes that occur during Li intercalation.<sup>9</sup> Ultrasound exfoliation was possible to prepare MoS<sub>2</sub> nanosheets maintaining the semiconducting properties comparing with exfoliation using Li intercalation.<sup>10</sup> The liquid exfoliation was also easier to transfer the exfoliated products to arbitrary substrates avoiding complex transfer processes. The lateral size in electrochemical exfoliation of MoS<sub>2</sub> nanosheets was in the 5–50 μm range, which was much larger than that of chemically or liquid-phase exfoliated MoS<sub>2</sub> nanosheets.<sup>12</sup> Some improved methods have been reported, for example, the ethanol water mix-solvent sonication combined with grinding<sup>14</sup> and high power tip sonication.<sup>15</sup> Yao *et al.* also reported an effective grinding-assisted liquid exfoliation technique to achieve MoS<sub>2</sub> nanoflakes. However, this method was not scalable and the size and thickness of exfoliated flakes cannot be controlled.<sup>16</sup>

#### 2.2. Chemical vapor deposition (CVD)

Ultrathin MoS<sub>2</sub> nanosheets were prepared by using exfoliation methods. With rapid development of study on MoS<sub>2</sub>, the chemical vapor deposition (CVD) method generating large-area continuous MoS<sub>2</sub> films was in great demand. Kong proposed

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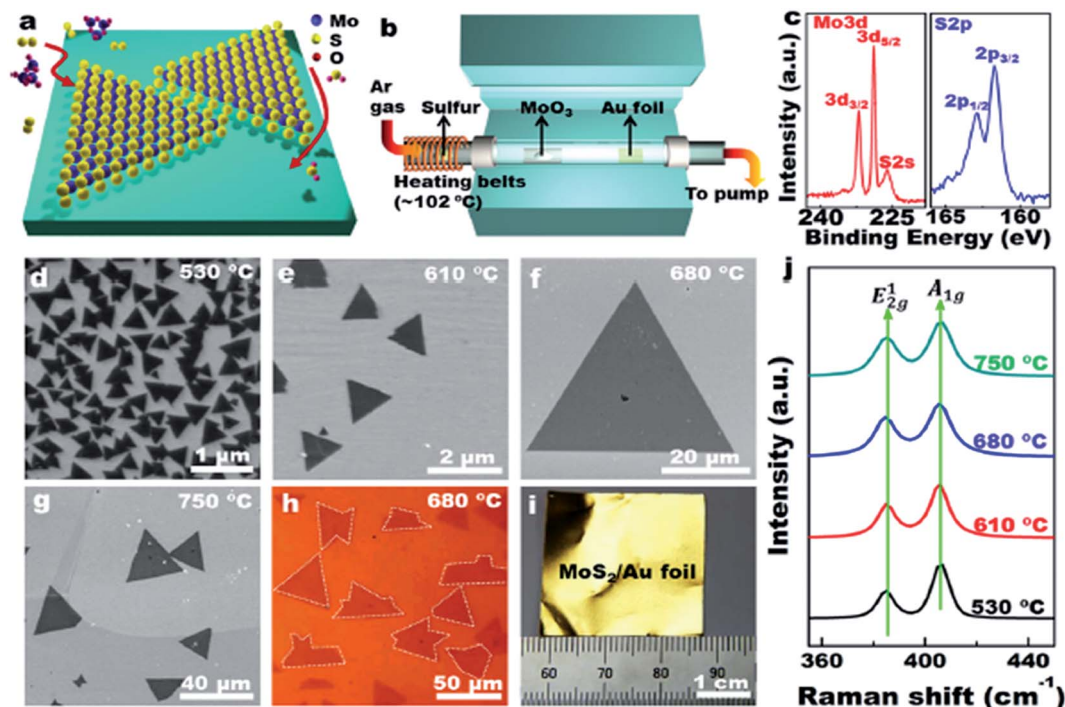


Fig. 1 LPCVD synthesis of monolayer MoS<sub>2</sub> on Au foils. Reprinted from Shi *et al.* (2014) with permission from American Chemical Society.

a novel chemical vapor deposition method to synthesize MoS<sub>2</sub> films with vertically aligned layers.<sup>17</sup> Wu *et al.* designed MoS<sub>2</sub> nanosheets with a high active site density by a microdomain method, and a high edge/basal ratio was obtained.<sup>18</sup>

Shi *et al.* demonstrated, for the first time, the scalable synthesis of monolayer MoS<sub>2</sub> on commercially available Au foils via a facile low-pressure CVD/(LPCVD) method (Fig. 1).<sup>19</sup> Wang

*et al.* present an approach for synthesizing MoS<sub>2</sub> atomic layers with controlled shape and number of layers by the layer-by-layer surface sulfurization of MoO<sub>2</sub> microplates. The obtained MoS<sub>2</sub> flakes exhibited rhomboidal shape with lengths up to tens of micrometers that was larger than irregular flakes exfoliated from MoS<sub>2</sub> crystals.<sup>20</sup> It was a challenge to obtain crystalline MoS<sub>2</sub> thin film with controlled number of layers by CVD than

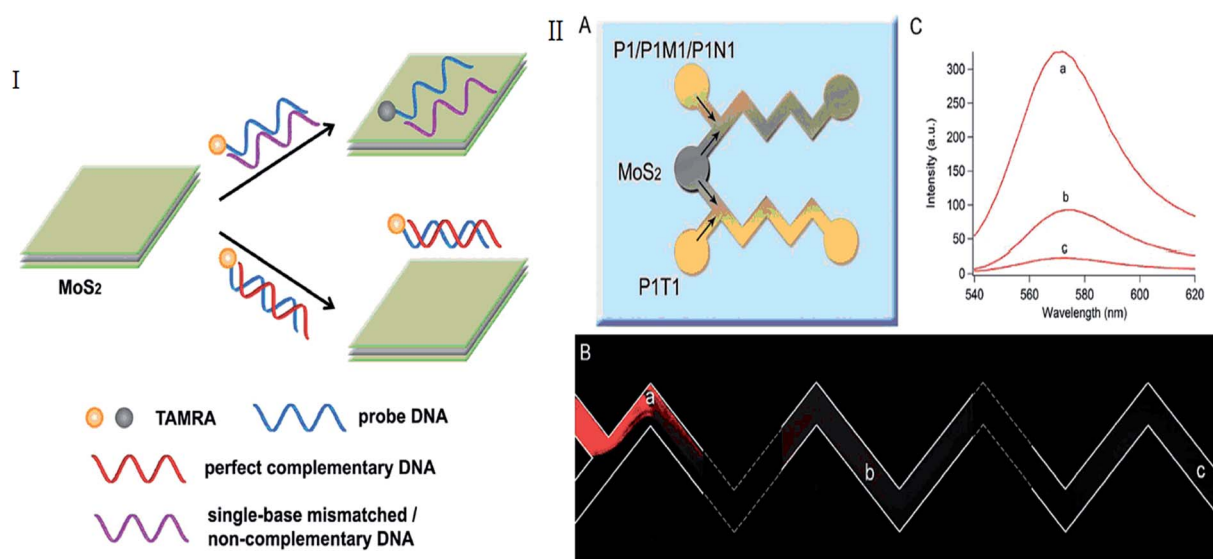


Fig. 2 (I) Schematic illustration of the MoS<sub>2</sub> nanosheet-based fluorometric DNA sensing assay. (II) (A) Design of a microfluidic detection scheme. Typical fluorescence image (B) and related fluorescence spectra (C) of P1 (100 nM) mixed with MoS<sub>2</sub> at the (a) start, (b) middle and (c) end of the microchannel. Reproduced from Huang *et al.* (2015) with permission from Royal Society of Chemistry.



graphene because no catalyst was involved in the growth of MoS<sub>2</sub>. CVD has an advantage of growing uniform MoS<sub>2</sub> on a large scale. However, it is an expensive method and employs complicated procedures.<sup>21</sup> The synthesis of islands on the order of tens of nanometers grown by physical vapor deposition (PVD). It was difficult for achieving coverages in excess of 0.3 ML (monolayer) without compromising the structural quality of the MoS<sub>2</sub> that has been reported for the (111) faces of Cu<sup>22</sup> and Au.<sup>23</sup> Grønberg *et al.* present a growth method based on reactive PVD that solved this problem and permitted the growth of MoS<sub>2</sub> SL (single layer) with an almost unity coverage.<sup>24</sup>

### 2.3. Other methods

Various synthetic methods were explored in preparing MoS<sub>2</sub> nanomaterials with specific morphologies and unique properties, including gas-phase reactions or solid-gas,<sup>25</sup> thermal decomposition,<sup>26</sup> laser ablation,<sup>27</sup> sonochemical synthesis,<sup>28</sup> magnetron sputtering,<sup>29</sup> and electron beam irradiation activation.<sup>30</sup> However, the morphology and size of the products were hard to control. Compared with the other methods, hydrothermal synthesis was considered as an effective way to prepare inorganic nanomaterials in mild synthetic conditions.<sup>31</sup> Many types of MoS<sub>2</sub> micro/nano materials with various morphologies were made in the above approaches, such as nanotubes,<sup>32</sup> fullerene-like nanoparticles,<sup>33,34</sup> nanoplates,<sup>35,36</sup> nanorods,<sup>37</sup> nanowires,<sup>38</sup> nanoflowers,<sup>39</sup> and nanospheres,<sup>40</sup> nanoribbons,<sup>41</sup> nanoboxes<sup>42</sup> and hierarchical hollow cubic cages.<sup>43</sup> However, it was still a challenge to fabricate some novel structures of MoS<sub>2</sub> with the controlled morphologies in mild reaction conditions.<sup>44</sup> In addition, the scale up of current processes were limited because of expensive or corrosive precursors.

## 3. Detection using MoS<sub>2</sub>-DNA based sensors

### 3.1. Detection based on FRET

MoS<sub>2</sub> monolayer shows dramatic improvement in photoluminescence quantum efficiency because of the specific 2D confinement of electron motion and the absence of interlayer perturbation. The improvement of photoluminescence in MoS<sub>2</sub> monolayer is also due to the fact that the monolayer, differently from few layer and bulk MoS<sub>2</sub>, had a direct bandgap.<sup>45-47</sup> Compared with other nano-materials, except high fluorescent quenching efficiency, cheap bulk MoS<sub>2</sub> materials can be facilely

synthesized in large scale and directly dispersed in aqueous solution.<sup>1,48</sup> When a ssDNA probe is absorbed on the surface of MoS<sub>2</sub>, the nucleobases are buried between the densely negatively charged helical phosphate backbones. After combining with its target, this made weakly interact with the MoS<sub>2</sub> causing the dye-labeled probe is away from the surface of MoS<sub>2</sub>.<sup>2,49</sup> This results in retention of the fluorescence of the probe. Therefore, MoS<sub>2</sub> nanosheets can act as efficient dye quenchers,<sup>1,2</sup> which have been employed to develop fluorescent sensing systems using DNA as recognition units (as shown in Table 1).

Huang *et al.* reported a novel MoS<sub>2</sub>-based fluorescent biosensor for DNA detection *via* hybridization chain reactions (HCRs). The detection limit in this strategy was 15 pM.<sup>50</sup> Including DNA hybridization, Deng *et al.* described a simple signal-on fluorescence DNA methyltransferase (MTase) activity assay using a MoS<sub>2</sub> nanosheet. The Dam MTase activity can be quantified accordingly. Based on this assay, a linear range of 0.2–20 U mL<sup>-1</sup> was achieved with high sensitivity and selectivity.<sup>51</sup> Huang *et al.* combined microfluidic biosensor for fluorescent DNA detection based on single-layered MoS<sub>2</sub> nanosheets (Fig. 2).<sup>52</sup> Yang *et al.* further present a novel microfluidic biosensor for sensitive fluorescence detection of DNA based on 3D architectural MoS<sub>2</sub>/multi-walled carbon nanotube (MWCNT) nanocomposites.<sup>53</sup> Some label-free detection based on MoS<sub>2</sub>-DNA sensors were also reported. In these papers, the probes without fluorescence were used and maybe lower the cost for detection. DNA oligonucleotides induced size control of layered MoS<sub>2</sub> was considered a label-free bioassay for the detection of single-nucleotide polymorphism.<sup>54</sup> Cao *et al.* developed a simple, low-cost and sensitive DNA sequences detection biosensor based on a label-free molecular beacon (MB) whose DNA hairpin structure terminal had a guanine-rich sequence that can enhance fluorescence of silver nanoclusters (Ag NCs). Even one nucleotide mismatched target can also be distinguished using this sensor.<sup>55</sup>

Many biological processes were related with the proteins. MoS<sub>2</sub>-DNA based sensors were also developed to detect various proteins. Kong *et al.* proposed a novel aptamer-functionalized MoS<sub>2</sub> nanosheet fluorescent biosensor that detected PSA (as shown in Fig. 3). PSA was important for the early diagnosis of prostate cancer. The aptamer probe modified with FAM label at its 5'-terminal was absorbed on the surface of MoS<sub>2</sub>. The fluorescence of the FAM-labeled aptamer was largely quenched owing to transfer of energy between the dye molecules and the MoS<sub>2</sub>. In the presence of PSA, the FAM-labeled aptamer adopted a rigid structure owing to binding with the PSA. The affinity of

Table 1 Detection based on FRET<sup>a</sup>

Detected element	DNA probe	Donor, Exc/Em [nm]	MQE	Detection range or detection linear range	LOD	References
Target DNA	ssDNA	FAM, 494/520 nm	98%	0–15 nM	500 pM	Zhu <i>et al.</i> (2013) <sup>2</sup>
Target DNA	ssDNA	FAM, 490/520 nm	95%	0 to 200 pM	15 pM	Huang <i>et al.</i> (2015) <sup>50</sup>
Target DNA	ssDNA	TAMAR, 565/580 nm	90%	0 to 50 nM	0.5 fM	Huang <i>et al.</i> (2015) <sup>52</sup>
Disease-related genes	Hairpin loop DNA	AgNCs, 563/623 nm	90%	10 to 200 nmol	4.4 nmol	Cao <i>et al.</i> (2015) <sup>55</sup>
Dam activity	dsDNA	FAM, 495/518 nm	About 90%	0.2–20 U mL <sup>-1</sup>	0.14 U mL <sup>-1</sup>	Deng <i>et al.</i> (2015) <sup>51</sup>

<sup>a</sup> Exc, excitation; Em, maximum emission wavelength; MQE, maximum quenching efficiency; LOD, limit of detection.



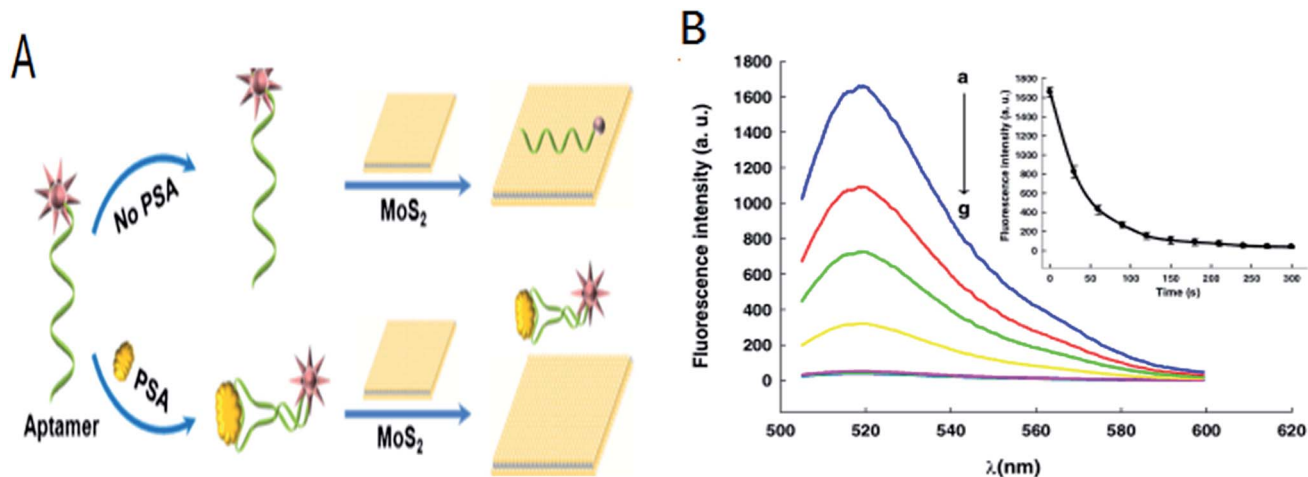


Fig. 3 (A) Schematic illustration of fluorescence sensing of PSA based on the aptamer-functionalized MoS<sub>2</sub> nanosheet biosensor, (B) fluorescence quenching of aptamer probe PA (50 nM) in the presence of an increasing amount of MoS<sub>2</sub> nanosheets (from (a) to (g) was 0, 5, 8, 10, 20, 30, and 40  $\mu\text{g mL}^{-1}$ , respectively). Inset fluorescence quenching of PA (50 nM) by MoS<sub>2</sub> nanosheet. Reproduced from Long *et al.* (2015) with permission from Springer Publishing Group.

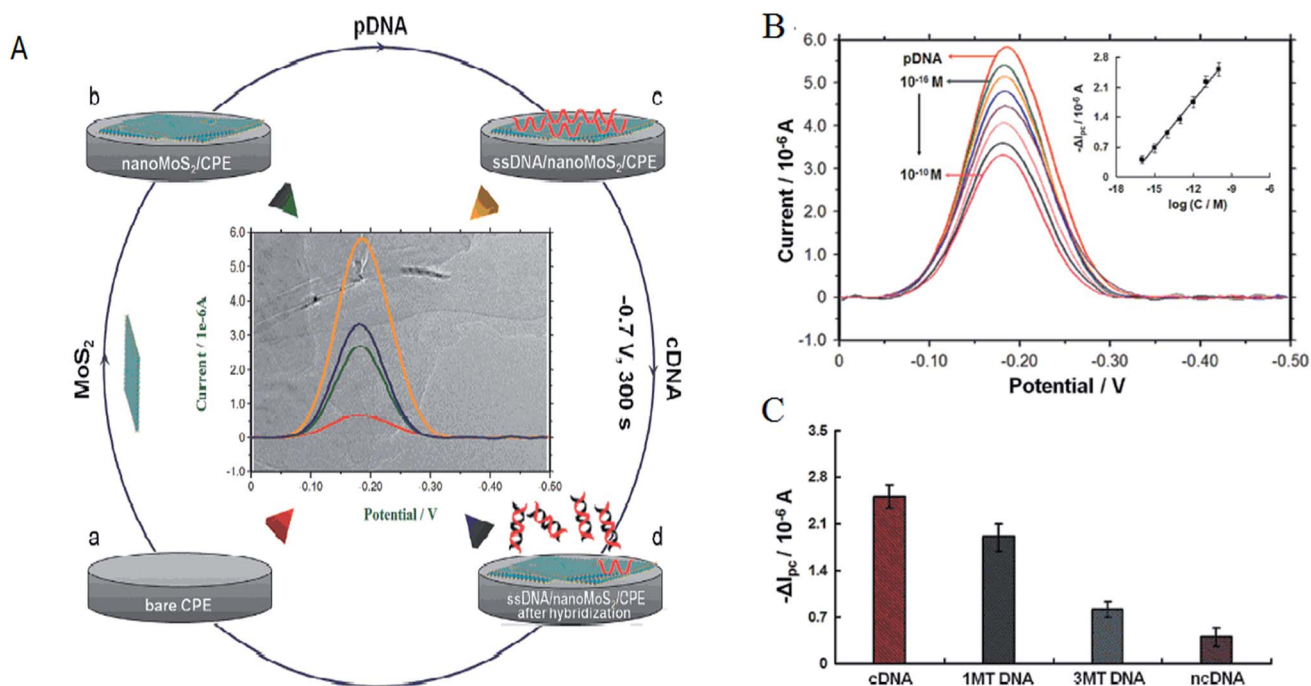


Fig. 4 (A) Schematic illustration of the label-free electrochemical DNA assay; (B) DPV plots of  $2.0 \times 10^{-5}$  M MB at pDNA ( $1.0 \times 10^{-6}$  M) modified nanoMoS<sub>2</sub>/CPE and that after hybridization with different concentrations of th gene sequence; (C) comparison with cDNA, single-base mismatched DNA, three-base mismatched DNA, and non-complementary DNA. Reproduced from Wang *et al.* (2015) with permission from Elsevier.

the aptamer with the MoS<sub>2</sub> decreased resulting in the release of the aptamer from the MoS<sub>2</sub> surface and the fluorescence signal was restored. PSA was detected with a limit of  $0.2 \text{ ng mL}^{-1}$ .<sup>48</sup> Ge *et al.* developed a novel fluorescence-activated MoS<sub>2</sub>-DNA nanosheet biosensor for detecting proteins based on the self-assembled architecture of a DNA aptamer and a MoS<sub>2</sub> nanosheet.<sup>1</sup> In order to improve the sensitivity of detection, Xiang *et al.* combined the terminal protection of small-molecule-linked DNA and exonuclease III (Exo III)-aided DNA recycling amplification to detect protein based on MoS<sub>2</sub> nanosheet. In

this method, protein was recycling used and resulted in the improvement of sensitivity for detection comparing with other methods. The detection limit was  $0.67 \text{ ng mL}^{-1}$  using the streptavidin (SA)-biotin system as a model.<sup>56</sup>

Detection of metal ions found in biological systems and in the environment was an attracted intense attention area of research. Mao *et al.* used for the first time single layer MoS<sub>2</sub> as the fluorescence quencher to design a detection method for Ag<sup>+</sup> with excellent robustness, selectivity and sensitivity. The detection limit in this assay was 1 nM for Ag<sup>+</sup>.<sup>57</sup> Zhang



developed a novel fluorescent biosensor for uranyl ion ( $\text{UO}_2^{2+}$ ) detection in aqueous environment based on the specific recognition of DNazyme and  $\text{MoS}_2$ . The detection limit in this assay was 2.14 nM.<sup>58</sup>

### 3.2. Detection based on electrochemistry

Electrochemistry was an important tool for sensing.  $\text{MoS}_2$  was quickly used to develop electrochemical DNA-based sensors. Some papers have reported electrochemical DNA-based sensors based on  $\text{MoS}_2$  possess the exceptional physical and

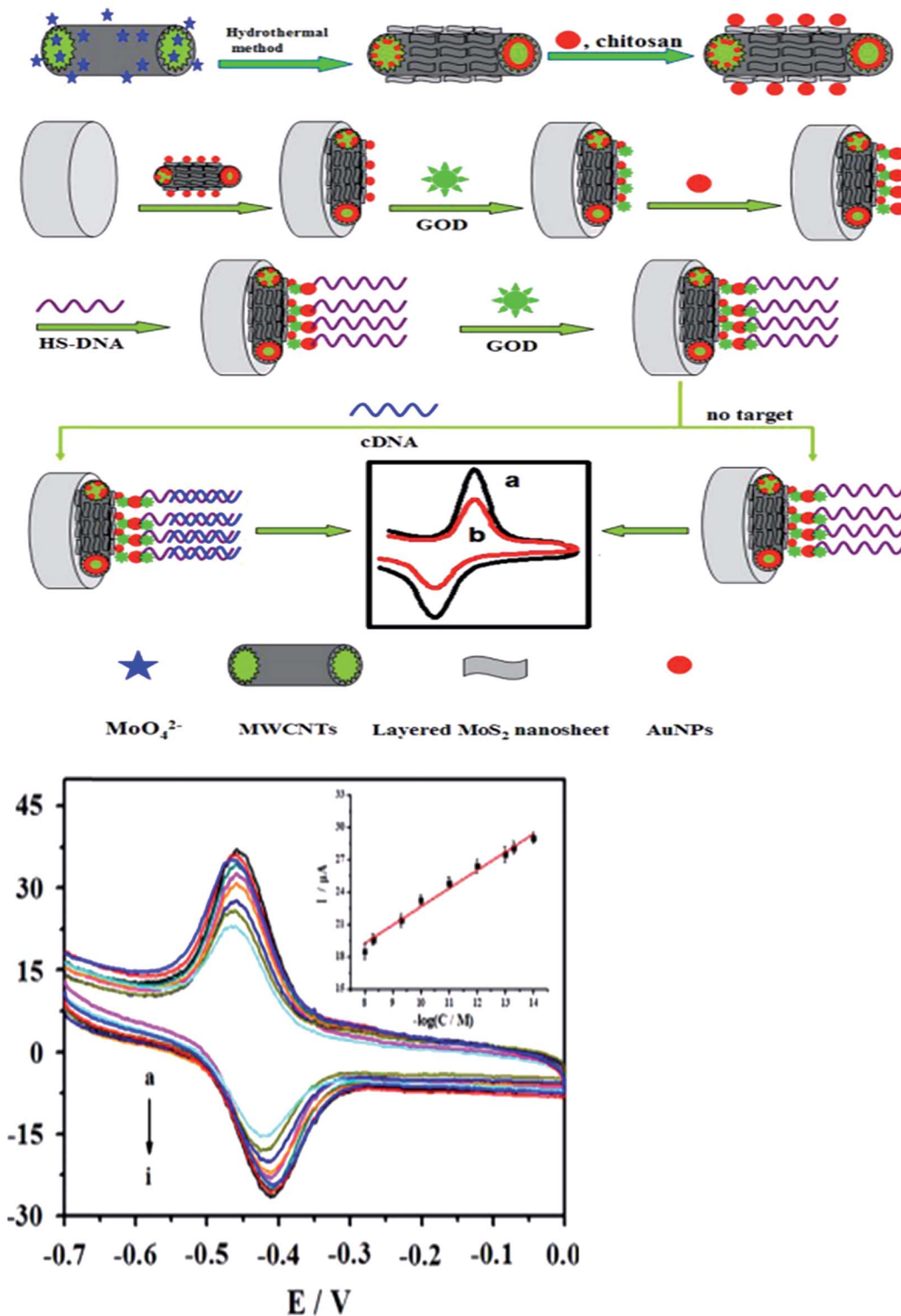


Fig. 5 (A) Schematic diagram of the electrochemical DNA biosensor; (B) the CVs of the proposed aptasensor after incubation in different concentrations of target ssDNA standard solution. Reproduced from Huang *et al.* (2014) with permission from Elsevier.



Table 2 Detection based on electrochemical sensors

Sensor materials	Detected element	Detection range or detection linear range	Detection limit	References
CdS–MoS <sub>2</sub> nanocomposites	IgE	0.001–10.0 nM	0.34 pM	Shi <i>et al.</i> (2015) <sup>65</sup>
MoS <sub>2</sub>	DNA	1.0 × 10 <sup>-16</sup> M to 1.0 × 10 <sup>-10</sup> M	1.9 × 10 <sup>-17</sup> M	Wang <i>et al.</i> (2015) <sup>60</sup>
MoS <sub>2</sub> –thionin composite	DNA	0.09 to 1.9 ng mL <sup>-1</sup>	0.17 μA mL ng <sup>-1</sup>	Wang <i>et al.</i> (2014) <sup>62</sup>
	RNA	10 ng mL <sup>-1</sup> to 200 ng mL <sup>-1</sup>	0.0022 μA mL ng <sup>-1</sup>	
MoS <sub>2</sub> /MWCNT	DNA	10 fM to 10 <sup>7</sup> fM	0.79 fM	Huang <i>et al.</i> (2014) <sup>3</sup>
CdSe/ZnS quantum dots (QDs)–MoS <sub>2</sub>	IgE	0.5 pM to 0.5 nM	0.18 pM	Liu <i>et al.</i> (2016) <sup>66</sup>
AuNPs–MoS <sub>2</sub> nanocomposites	ATP		0.74 nM	Su <i>et al.</i> (2016) <sup>67</sup>
	Thrombin		0.0012 nM	

electrochemical properties for detections. Loo *et al.* reported the principle of detection was based on the differential affinity of molybdenum disulfide nanoflakes towards single-stranded DNA and double-stranded DNA.<sup>59</sup> Based on the different affinity toward ssDNA *versus* dsDNA of the thin-layer MoS<sub>2</sub> nanosheets, Wang *et al.* performed the assay of tth gene sequence from 1.0 × 10<sup>-16</sup> M to 1.0 × 10<sup>-10</sup> M with a detection limit of 1.9 × 10<sup>-17</sup> M. The detection method described here was without labeling and the use of amplifiers, which resulted in the priority in sensitivity, simplicity, and costs. Furthermore, the proposed sensing platform could be extended to detect more targets (as shown in Fig. 4).<sup>60</sup>

Some functional materials have been decorated on MoS<sub>2</sub> to form MoS<sub>2</sub>-based composite materials in order to further enhance the properties and broaden the applications of MoS<sub>2</sub>. MoS<sub>2</sub>-based composite materials have many significant advantages comparing with MoS<sub>2</sub>. This maximized the advantages and minimized the drawbacks of the individual components. The composites can improve the sensitivity for DNA detection. Huang *et al.* constructed an ultrasensitive electrochemical DNA biosensor by assembling a thiol-tagged DNA probe on a MoS<sub>2</sub>/MWCNT and gold nanoparticle (AuNP)-modified electrode coupled with glucose oxidase (GOD). The MoS<sub>2</sub>/MWCNT composites film possessed large specific surface area and excellent biocompatibility. This increased the immobilization of GOD and enhanced the stability of the DNA probe. Moreover, the GOD membranes as tracer brought about higher current response and higher sensitivity. The detection signals were amplified (as shown in Fig. 5). The detection for DNA was down to 0.79 fM with a linear range from 10 fM to 10<sup>7</sup> fM. One-base mismatched DNA can be differentiated in this method.<sup>3</sup> Chu *et al.* made nano MoS<sub>2</sub>/graphene composites by integrating nano MoS<sub>2</sub> and graphene through hydrothermal process and ultrasonic method. They developed an electrochemical circulating tumor DNA sensing platform based on this material. The cost and simplicity of the sensor preparation was decreased.<sup>61</sup> Including MoS<sub>2</sub> and materials (MWCNT and graphene) composites, MoS<sub>2</sub> and chemicals, such as polyaniline (PANI) and thionin that have some electrical conductivity, formed the composites improving the electrical property for high sensitivity. Wang *et al.* prepared a layered MoS<sub>2</sub>–thionin composite to fabricate a double-stranded DNA (dsDNA) electrochemical biosensor. The linear range over dsDNA concentration from 0.09 ng mL<sup>-1</sup> to 1.9 ng mL<sup>-1</sup> was obtained. Moreover, single-stranded DNA (ssDNA) can be detected.<sup>62</sup> Yang *et al.* synthesized a PANI–

MoS<sub>2</sub> nanocomposite based on ANI monomer and MoS<sub>2</sub>. The PANI–MoS<sub>2</sub> nanocomposite with 0.054 g of MoS<sub>2</sub> can be considered as the optimal sensing platform for high sensitive DNA detection.<sup>63</sup> The sensitivity of detection based on MoS<sub>2</sub> and materials composites was higher comparing with MoS<sub>2</sub> and chemicals composites from publications. It maybe be electrochemical stability, more excellent electrocatalytic activity, and fast charge transfer rate.

The cooperative effects between MoS<sub>2</sub> and metal compounds paved the way to explore a variety of sensing applications. This can not only provide the couple sites with DNA but also improve the sensitivity of detection.<sup>64</sup> Proteins were also detected by using MoS<sub>2</sub> composites-based sensors. Immunoglobulin E (IgE) was one of important proteins. Shi *et al.* reported the CdS–MoS<sub>2</sub> composites immobilized on glassy carbon electrode surface as ECL emitter attached a complementary ssDNA (NH<sub>2</sub>-ssDNA) of IgE. IgE aptamer (T-Apt) with DNazyme-AuNPs hybridized with NH<sub>2</sub>-ssDNA to form dsDNA. The DNazyme with horseradish peroxidase-like activity could electrocatalyze the reduction of H<sub>2</sub>O<sub>2</sub>. The changed ECL intensity was proportional to concentration of IgE in the range of 0.001–10.0 nM with the detection limit of 0.34 pM (S/N = 3).<sup>65</sup> Liu *et al.* developed a novel competitive electrochemiluminescence (ECL) aptasensor based on CdSe/ZnS quantum dots (QDs) functionalized MoS<sub>2</sub> modified electrode for sensitive IgE detection using horseradish peroxidase (HRP) catalyzed biocatalytic precipitation (BCP) for signal quenching. This fabricated aptasensor displays a linear range from 0.5 pM to 0.5 nM with a detection limit of 0.18 pM (S/N = 3).<sup>66</sup> Liu *et al.*'s method had higher sensitivity than Shi *et al.*'s method. Other proteins were also reported by using MoS<sub>2</sub> composites-based sensors. Su *et al.* developed a MoS<sub>2</sub>-based electrochemical aptasensor for the simultaneous detection of thrombin based on gold nanoparticles-decorated MoS<sub>2</sub> nanocomposites. This aptasensor could simultaneously determine thrombin as low as 0.0012 nM.<sup>67</sup> These results showed the signal amplification can be achieved by hybridizing MoS<sub>2</sub> with other components due to synergy effect. Therefore, the multifarious sensors have attracted more attention by some researchers as a new era (Table 2).

#### 4. Detection based on MoS<sub>2</sub> sensors

The detection based on MoS<sub>2</sub> sensors were mainly using field-effect transistor (FET) that can offer a real-time and efficient



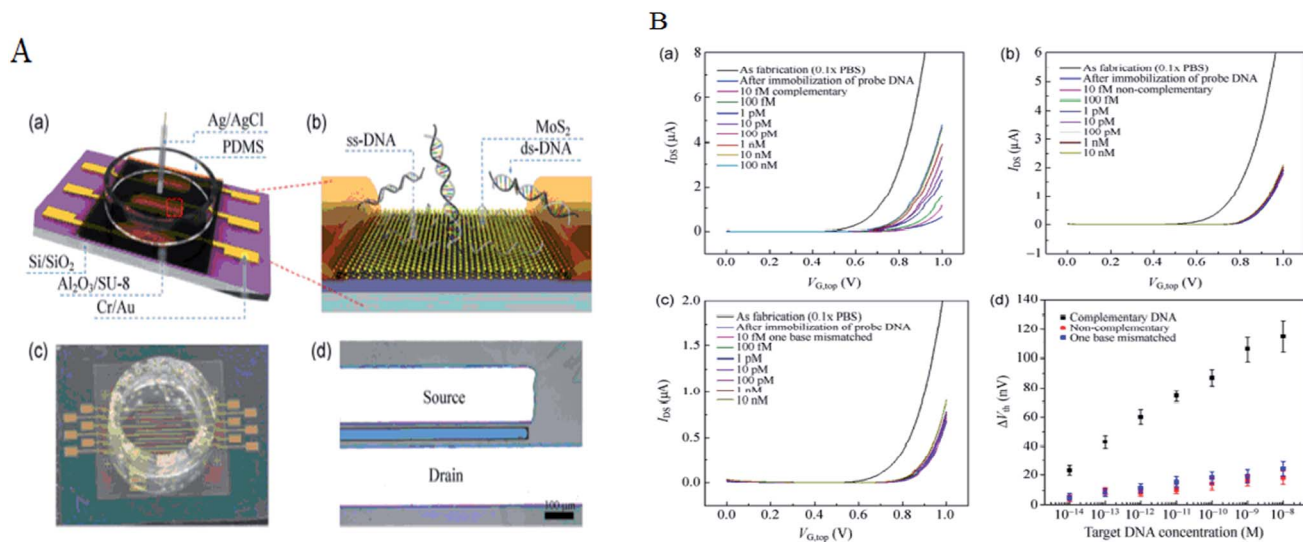


Fig. 6 (A) Schematic of MoS<sub>2</sub> FET and optical image of MoS<sub>2</sub> FETs; (B) transfer characteristics of MoS<sub>2</sub> FETs immobilized with the probe DNA molecules and hybridized with (a) complementary, (b) non-complementary, and (c) single-base mismatched DNA molecules. Reproduced from Lee *et al.* (2015) with permission from Springer Publishing Group.

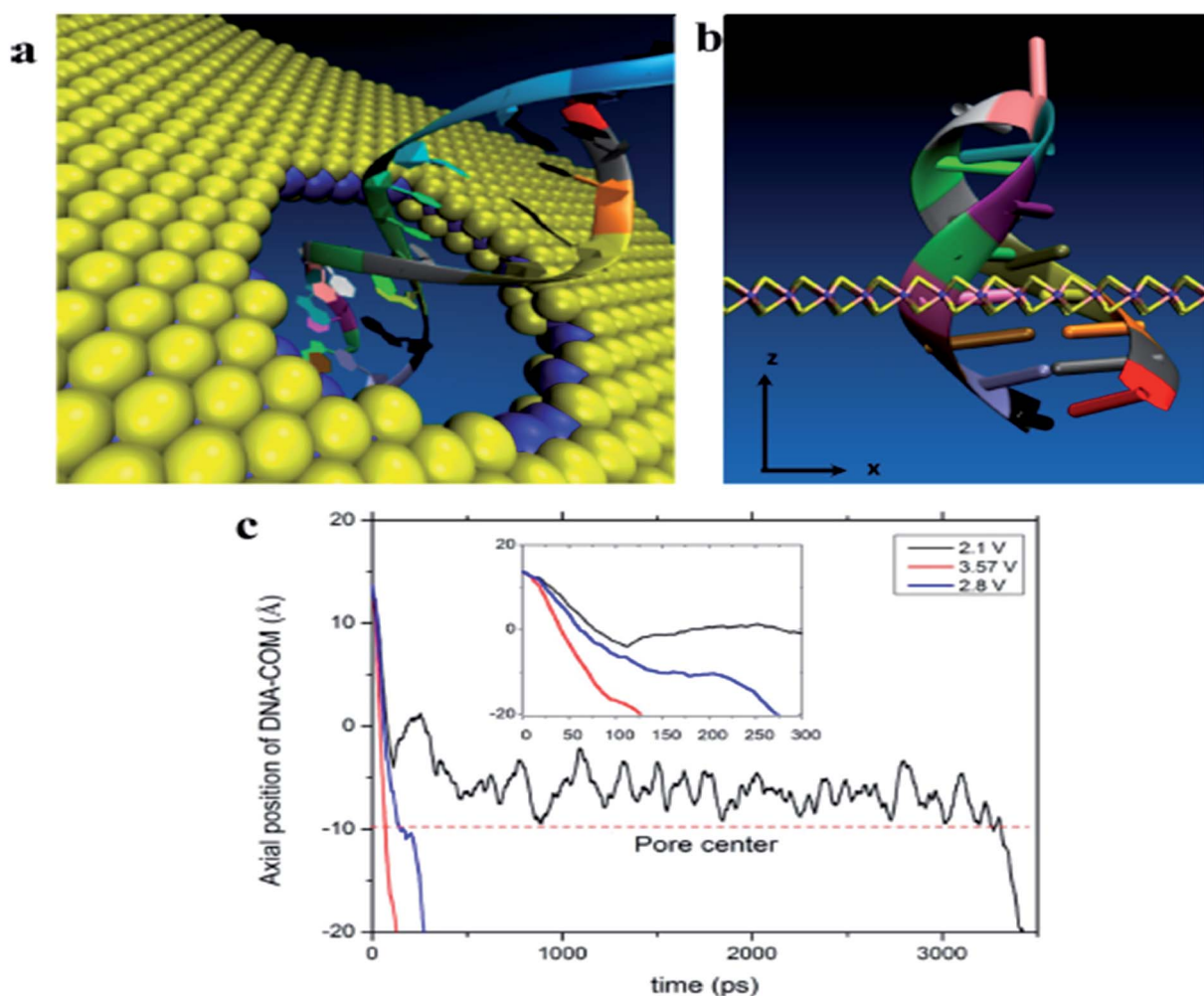


Fig. 7 (a) DNA translocation through a MoS<sub>2</sub> nanopore. (b) DNA hairpin structure with the loop at the top and the size view of MoS<sub>2</sub> fish-bone structure. (c) DNA translocation history for different biases. Reprinted from Farimani *et al.* (2014) with permission from American Chemical Society.



sensing platform for a variety of target analytes because of rapid electrical detection without fluorescence-labeling. Highly sensitive and rapid detection of biomolecules with a bioelectronic field-effect transistor was essential for clinical, military, or environmental applications.<sup>68,69</sup> FETs with two-dimensional (2D) nanomaterials attracted great attention owing to their many interesting electrical, optical, and mechanical properties.<sup>70</sup> MoS<sub>2</sub> with the bandgap is different from the pristine graphene. Single layer of MoS<sub>2</sub> has a large intrinsic bandgap of 1.8 eV.<sup>71</sup> Therefore, MoS<sub>2</sub> was applied in FET as a sensor. Lee *et al.* investigated a field-effect transistor (FET) with few-layer MoS<sub>2</sub> as a sensing-channel material for label-free detection of the hybridization of DNA molecules. Hybridization of DNA molecules adsorbed on the MoS<sub>2</sub> channel resulted in a shift of the threshold voltage in the negative direction and an increase in the drain current.<sup>72</sup> Lee *et al.* further demonstrated a non-volatile memory field-effect transistor (FET) for hybridization of single-stranded target DNA molecules with single-stranded probe DNA molecules physically adsorbed on the MoS<sub>2</sub> channel. This resulted in a shift of the threshold voltage ( $V_{th}$ ) in the negative direction and an increase in the drain current because of the change in the surface charge density of the channel. The low detection limit was 10 fM in this method (as shown in Fig. 6).<sup>73</sup> Loan *et al.* first stacked graphene on a CVD MoS<sub>2</sub> to perform the differentiation of complementary and one-base mismatched DNA with the graphene/MoS<sub>2</sub> heterostructure. The concentration as low as 1 aM ( $10^{-18}$  M) can be detected.<sup>70</sup> Metal ion was also reported for detecting by FET. Zhou *et al.* reported a DNA-functionalized MoS<sub>2</sub> nanosheet/gold nanoparticle hybrid FET sensor for the ultrasensitive detection of Hg<sup>2+</sup> in an aqueous environment. The sensor shows a rapid response (1–2 s) to Hg<sup>2+</sup> and an ultralow detection limit of 0.1 nM.<sup>74</sup>

Some researchers focused on sequencing using MoS<sub>2</sub>. The strong interaction between graphene and DNA and the high translocation velocity were the challenges for graphene nanopore on DNA sequencing. MoS<sub>2</sub> nanopore has shown promising potential for applications of DNA sequencing because MoS<sub>2</sub> is highly preferable to graphene in terms of DNA electronic base sensing. MoS<sub>2</sub> nanopore showed a distinct ionic current signal for single-nucleobase detection with a SNR of 15 using the simulation. The band gap of MoS<sub>2</sub> was significantly changed when bases are placed on the top of pristine MoS<sub>2</sub>. DNA showed a nonsticky behavior and a more distinguishable signature per base using MoS<sub>2</sub> nanopore (as shown in Fig. 7).<sup>75</sup> Aluru *et al.* found that a single-layer MoS<sub>2</sub> was an extraordinary material (with a SNR > 15) for DNA sequencing by two competing technologies using atomistic and quantum simulations. A MoS<sub>2</sub> nanopore shows four distinct ionic current signals for single-nucleobase detection with low noise.<sup>69</sup> This can solve the problem that the noise increased in the detection process because the strong adsorption of DNA on graphene surface in graphene nanopore. Feng *et al.* further introduced a viscosity gradient system based on room-temperature ionic liquids (RTILs) to control the dynamics of DNA translocation through a nanometer-size pore fabricated in a thin MoS<sub>2</sub> membrane solving the high translocation velocity (3000–50 000 nt per m per s) of DNA molecules moving across such membranes limits

their usability. This was the first time to statistically identify the DNA oligomer and the order of current of DNA oligomer was poly(A)<sub>30</sub> > poly(T)<sub>30</sub> > poly(C)<sub>30</sub> > poly(G)<sub>30</sub> when DNA oligomer translocates through the MoS<sub>2</sub> nanopore.<sup>76</sup> In addition, MoS<sub>2</sub> nanoribbon was also used for sequencing. Thomas analyzed the transmission of narrow semiconducting nanoribbons designed from MoS<sub>2</sub>.<sup>77</sup> Smolyanitsky *et al.* proposed an aqueous functionalized molybdenum disulfide nanoribbon suspended over a solid electrode as a capacitive displacement sensor aimed at determining the DNA sequence. The results suggested a realistic, inherently base-specific, high-throughput electronic DNA sequencing device as a cost-effective *de novo* alternative to the existing methods.<sup>78</sup> However, the velocity of DNA passing through the nanopore and nanoribbon was too high in these experiments. It was still a challenge for achieving single-base resolution.

## 5. Conclusions and outlook

This paper provides a short history for MoS<sub>2</sub>-DNA and MoS<sub>2</sub> based sensors. MoS<sub>2</sub>, as a star among materials and widely studied by researchers worldwide, has drawn considerable interest in many fields. In this review, recent developments in MoS<sub>2</sub>-DNA and MoS<sub>2</sub> based sensors for the detection of DNA, proteins, and heavy metal ions are described and discussed using their unique structure that contribute to their exceptional chemical and physical properties. Those properties lead to a broad range of applications in sensing. Some researchers have reported that MoS<sub>2</sub>-DNA and MoS<sub>2</sub> sensors had relatively high sensitivity when compared with other nanomaterials; for example, the detection limitation based on MoS<sub>2</sub>-DNA sensors for DNA was 0.5 fM (ref. 52) higher than 0.5 pM based on graphene oxide-DNA sensors.<sup>79</sup> MoS<sub>2</sub> is also highly preferable to graphene in terms of electronic-based sensing of DNA.<sup>75</sup> Therefore, this study helps to provide useful solutions related to some of the world's key problems, such as water and food security and the development of rapid and sensitive medical analysis methods.

Currently, the investigation of biosensing applications using MoS<sub>2</sub> is still in the early stage.

Some challenges related to sensing based MoS<sub>2</sub>-DNA and MoS<sub>2</sub> remain and need to be resolved. (1) ssDNA is adsorbed on the surface of MoS<sub>2</sub>, and not all dsDNA can detach from the surface of MoS<sub>2</sub> after the complementary ssDNA, protein or other molecules combine to ssDNA. This hinders further improvement of the sensitivity of reported DNA sensors. (2) MoS<sub>2</sub>, as a newly discovered material, faces some challenges including improving synthesis methods and extending its application in various fields. (3) MoS<sub>2</sub> properties such as the number of layers, sizes, morphology, functional groups and thickness influence the performance of DNA sensors, especially for electrochemical DNA sensors. (4) The large surface of low density MoS<sub>2</sub> in mass production may be difficult to handle, which can lead to health risks caused by inhaling and handling toxic reducing chemicals. (5) MoS<sub>2</sub> integrates with micro-fabrication techniques, such as current complementary metal oxide semiconductor (CMOS) technologies, which can increase





potential access for the development of label-free, low-cost and high-throughput detection arrays for sensing. However, the stability, selectivity and reproducibility of the devices based on MoS<sub>2</sub> should be further improved.

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