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Liquid Crystal Biosensor Based on Cd^{2+} Inducing the Bending of PS-Oligo for the Detection of Cadmium

Shixiong Deng[1*], Qifeng Jiang[1*], Tingting Zhang[1], Xingliang Xiong[1], Ping Chen[1,2#]

[1]Laboratory of Biomedical Engineering, Chongqing Medical University, Chongqing, China
[2]Experimental Teaching Management Center, Chongqing Medical University, Chongqing, China
Email: [#]chenp93@163.com

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Abstract

In this study, a novel liquid crystal (LC) biosensor was developed for the highly sensitive and selective detection of Cd^{2+} based on Cd^{2+} inducing the bending of PS-oligo. This strategy makes use of the DNA conformational change to enhance the disruption of orientation of LC leading to an amplified optical signal. DNA containing-SH was bound on the glass slide of the LC cell modified with the DMOAP/APTES. The DMOAP can effectively induce the homeotropic alignment of LC. In the presence of Cd^{2+}, Cd^{2+} can induce DNA to bend and become a 2 nm spherical structure, which can greatly disrupt the orientational arrangement of LC, resulting in the correspond changes of the optical image of LC cell birefringent under the polarizing microscope. When the Cd^{2+} concentration is low to 0.1 nM, the optical signal of LC biosensor has an obvious change. But in the absence of Cd^{2+}, there is no orientational response of LC and the optical image under the polarizing microscope is still a uniform dark background. Thus, this LC sensing method has a sensitive and clear distinction between positive and negative results and offers a highly sensitive detection of Cd^{2+} with a low detection limit down to 0.1 nM.

Keywords

Liquid Crystal (LC), Biosensor, Cd^{2+}, PS-Oligo (DNA)

1. Introduction

Cadmium (Cd) is a heavy metal environmental toxicant which is widely present in air, soil, water and food. It

[*]These authors contributed equally to this work and should be regarded as co-first authors.
[#]Corresponding author.

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can be accumulated in the human body mainly in the lungs, liver, kidney, brain, heart and testis with a biological half-life of greater than 20 - 30 years [1]-[3]. Cd^{2+} has a strong affinity with the protein containing thiol, when being binded, the structure and function of protein can be changed in the body. Meanwhile, Cd^{2+} can displace essential metal ions such as Zn^{2+} from the enzyme, which would inactivate the enzyme and result in disorder of biochemical processes. Toxicological studies have shown that cadmium poisoning can cause kidney failure, reproductive disorders, Itai-Itai disease, osteoporosis and respiratory system diseases and so on. More seriously, low doses of Cd^{2+} exposure can significantly increase the risk of cancer [4]-[8], so it is identified as Class I carcinogens by the International Union Against Cancer (IARC). Therefore, it is of great significance to develop a rapid, simple, high sensitive and high selective detection technology of Cd^{2+} for environmental protection, food safety and disease prevention, especially for pollution site screening and emergency disposal.

The instrument analysis method is a common method for Cd^{2+} detection, including electrochemical stripping analysis, atomic absorption spectroscopy (AAS) [9], inductively coupled plasma-atomic emission spectroscopy (ICP-AES) [10], inductively coupled plasma mass spectrometry (ICP-MS) [11] and so on. Although these methods provide excellent sensitivity (nM to sub nM level), there are some shortcomings, such as time-consuming, high-cost analysis, require large instruments and professional operation. Furthermore, Cd^{2+} pollution has the features of burstiness and fast-diffusion in water. Therefore such mentioned methods are not suitable for on-site analysis.

In order to improve the selectivity, recently, the nucleic acid aptamer (or oligonucleotide fragments) widely concerned is an ideal molecular recognition element on account of its some advantages including the broader universality than antibodies, specificity and affinity comparable to antibody, large-scale and low-cost production, high extremely stability, used repeatedly, etc. [12]. Therefore, it is widely used to detect proteins, nucleic acids, biological small molecules and heavy metal ions. For example, Pb^{2+} and G-rich DNA aptamer can form G-quadruplex [13]; Ag^{+} and C-C mismatchs aptamers can form C-Ag^{+}-C complexes [14]; Hg^{2+} and T-T mismatchs aptamers can form T-Hg^{2+}-T complexes [14] and so on. They have realized the high sensitive and selective detection for Pb^{2+}, Ag^{+} and Hg^{2+}, respectively. Although it has not been reported for the Cd^{2+} detection with the same approach, as we all know, Cd^{2+} has better affinity with guanine-rich DNA molecules [15] [16], and the main reason of Cd^{2+} carcinogenic is that Cd^{2+} can attack the guanine nucleotide of certain DNA molecules, leading to DNA damage. Hence, it should be a good idea to select the appropriate oligonucleotide fragment as recognition molecule of Cd^{2+}.

How to improve the detection sensitivity of Cd^{2+} (lower detection limit) is another key problem that must be solved in biological sensor. In recent years, Wu [17] group successfully developed a high-sensitivity LC biosensor for Hg^{2+} with detection limit 0.1 nM using T-T mismatch aptamers as Hg^{2+} recognition molecules and LC (Liquid Crystal, LC) molecules as signal transducer and signal amplification molecules. This sensor made skillfully the high selectivity of aptamers to combine with high sensitivity of LC molecules, which also had some advantages such as simple manufacture, no optical aids and visible results observed directly by naked eyes. Such high detection sensitivity was due to the fact that the orientation of LC molecules is extremely sensitive to the physical and chemical changes of the interface. Moreover, the long-range orientational order inherent in LC molecules can greatly amplify the alignment change induced by surface [18]. These idiosyncrasies, combined with the optical anisotropy of the LC molecules, make them well-suited to transduce directly and amplify binding events between the recognition molecule and target analyte on the surface into optical outputs. Recently, Schwartz has reported that they made use of the orientation change of LC molecules caused by the conformational change of before and after DNA hybridization to detect the target DNA, which can directly detected 50 fM concentration [19]. Although the detection of Cd^{2+} has not been reported, the liquid crystal is undoubtedly a very attractive material of signal transducer and signal amplifying from the existing results.

Therefore, combining the DNA specificity and the advantages of LC biosensors, we exploit a high specificity and sensitivity LC biosensing technique using DNA as specific recognition for Cd^{2+} detection.

2. Experimental

2.1. Materials and Apparatus

N, N-dimethyl-N-octadecyl-3-aminopropyltrimethoxysilyl chloride (DMOAP) and (3-aminopropyl) triethoxysilane (3-APTES) were purchased from Sigma-Aldrich. LC 4-cyano-4'-pentylbiphenyl (5CB) was obtained from Huajing Scientific and Technological Development Co., Ltd. (Hebei, China). Glutaraldehyde (GA) was obtained

from Sinopharm Chemical Reagent Co., Ltd. (Shanghai, China). Glass sides were provided by Xinhua Laboratory Glassware Company (Haimen, China). All metal ions were purchased from Chemical Reagent Co. WELDECH (Shanghai China). Oligonucleotides were purchased from TaKaRa Biotechnology Co., Ltd. (Dalian China). Coppers contained network were purchased from Beijing Zhongjingkeyi Technology Co., Ltd. (Beijing, China). All chemicals used in this work were analytical reagent. Ultrapure water was used throughout all experiments.

The sequence of DNA employed is as follows:

5'-G-(SH)-GGGGGGGGG-$(CH_2)_6$-NH_2-3'.

2.2. Procedures

2.2.1. Cleaning of Substrates

The glass sides were firstly cut into size of 2 cm × 2 cm square, and then the glass slides were cleaned with freshly prepared piranha solution (70% H_2SO_4, 30% H_2O_2) at 80˚C for 1 h. The glass slides were then rinsed with ultrapure water and ethanol for 5 - 6 times, dried with nitrogen, and stored in a 110˚C vacuum oven for 3 h before use.

2.2.2. Self-Assembling of Slides

1) DMOAP-decoration. Cleaned glass slides were immersed in an aqueous solution containing 0.35% (v/v) DMOAP for 30 min and then rinsed with ultrapure water. The DMOAP-coated glass slides were dried with nitrogen and heated in a 110˚C vacuum oven for 1 h.

2) DMOAP/APTES-decoration. Cleaned glass slides were immersed in ethanol solution containing 0.3% (v/v) DMOAP and 3% (v/v) APTES at 80˚C for 2 h, rinsed with ethanol and ultrapure water, respectively, dried with nitrogen, and then stored at 110˚C for 1 h. Subsequently, the sides were immersed in a 0.3 mol/L GA solution for 30 min and rinsed with ultrapur water, dried with nitrogen.

2.2.3. DNA Immobilization

All DNA employed in this work were first dissolved in a 10 mM HEPES buffer (pH 7.0) containing 0.03 M NaCl, 0.03 M trisodium citrate 200 μL 100 nM solution of capture probe was dropped to the DMOAP/APTES/GA-decorated glass slides, then incubation at room temperature for 1h, rinsed with a solution of 0.3 M sodium chloride/0.03 M trisodium citrate (2× SSC, pH 7.0) containing 0.01% (v/v) SDS and ultrapure water.

2.2.4. LC Cells

The LC cells were fabricated by spacing a DMOAP-coated glass and a DMOAP/APTES-coated glass with two thin strips of Mylar (~23 μm), and then held together with small binder clips. The DMOAP-coated glass was used to induce the homeotropic alignment of liquid crystals, while the DMOAP/APTES-coated glass was used to covalent attachment of amine-labeled capture probes. The cells were placed at 40˚C for 5 min. The LC material, 5CB, heated into its isotropic phase was spontaneously drawn into each LC cell by capillary action. The LC cells were then slowly cooled to ~28˚C.

2.2.5. Detection of Cd^{2+}

100 μL mixture solution contains different concentrations of Cd^{2+} were dropped on the DNA decorated glass slides at room temperature for 1 h. The unbounded DNA probes were rinsed with 2× SSC containing 0.01% (v/v) SDS and abundant ultrapure water. The optical appearance was examined using a polarized light microscope (Shaihai Changfang Optical Instrument, China) in transmission mode under crossed polarizer. The images were captured by a digital camera mounted on the microscope.

In selectivity experiments, Cd^{2+} ions were simply displaced substitute or mixed by other metal ions under the same conditions (*i.e.*, K^+, Ca^{2+}, Co^{2+}, Al^{3+}, Zn^{2+}, Cr^{3+}, Mn^{2+}, Cu^{2+} and Pb^{2+}).

3. Results and Discussion

3.1. Detection Mechanism

The detection mechanism of this LC biosensing technique is shown in **Figure 1**. A chemically functionalized

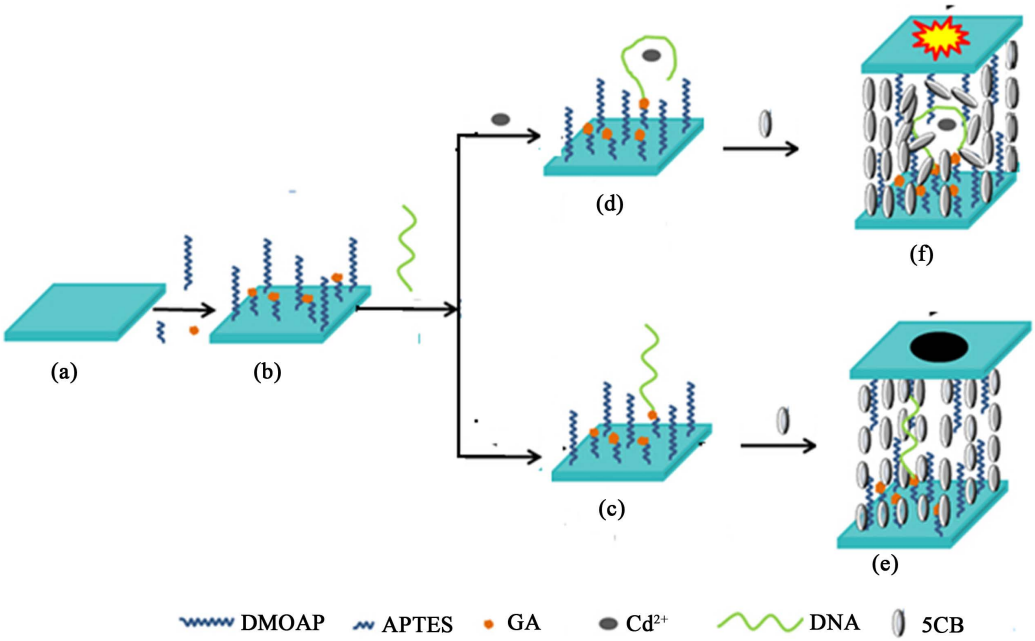


Figure 1. Illustration diagram of detection stragegy and fabrication process of LC biosensing substrate based on DNA aptamer. (1) Cleaned glass (a) and mixed self-assembled DMOAP/APTES by activation with GA (b); (2) immobilization DNA with in the absence of Cd^{2+} (c) or in the presence of Cd^{2+} (d); (3) The corresponding 5CB LC molecules ((e), (f)) fabricated with the DMOAP-coated glass slides(upper) and the modified slides ((c), (d); lower).

surface on a pretreated plane slide was firstly obtained by self-assembling the DMOAP, APTES and GA film (**Figure 1(b)**). The DMOAP, which is a long chain alkyl-rich molecules, can effectively induce the homeotropic alignment of LCs. The GA activates APTES and provides aldehyde groups to immobilize DNA (**Figure 1(c)** and **Figure 1(d)**).When the sensing interface is incubated with the solution containing Cd^{2+}, Cd^{2+} can induce DNA containing-SH to bend and become a 2 nm spherical structures [20] (**Figure 1(d)**) that can greatly change the surface topology and further obviously disrupt the orientation of LC molecules surrounding them. So the orientation of LC molecules on the surface changed from homeotropic to tilted or planar alignment. Then the birefringent texture in the optical image was observed by using the polarizing microscope (**Figure 1(f)**). In the absence of Cd^{2+}, the long alkyl chain layer of DMOAP still induces the homeotropic alignment of LC molecules and provides a uniform dark background (**Figure 1(e)**).

3.2. Optimization of the DMOAP/APTES Ratio on the Slide Surface

To improve the signal-to-background contrast, we studied the background signal affected by the self-assembling modification of DMOAP/APTES mixture with different volume ratio. As can be seen from **Figure 2**, the bright region in the optical image decreases gradually with the volume ratios of DMOAP/APTES increases and until displays a uniform dark background. When the volume ratio of DMOAP/APTES is 1:20, the images shows a obvious optical textures because a small amount of DMOAP has a weak capability in inducing the homeotropic alignment of LC molecules (**Figure 2(a)**). When the volume ratio of DMOAP/APTES is increased to 1:15 or 1:12, the image shows the mixed areas of bright and dark as the amount of DMOAP increase, which can induce amount of LC molecules arranged vertically (**Figure 2(b)** and **Figure 2(c)**). However, when the volume ratio of DMOAP/APTES is further increased to 1:10 or 1:5, the image shows a uniform dark background and appears a cross diffraction spots under the cone light mode while the bright spots in the optical images disappeare completely (**Figure 2(d)** and **Figure 2(e)**), which proves that LC molecules are uniform homeotropic alignment. Since the volume ratio of DMOAP/APTES is above 1:10, the number of APTES modified on the slide surface reduces relatively, which can reduce the immobilized efficiency of capture DNA probe. So we choose the volume ratio of DMOAP/APTES is 1:10.

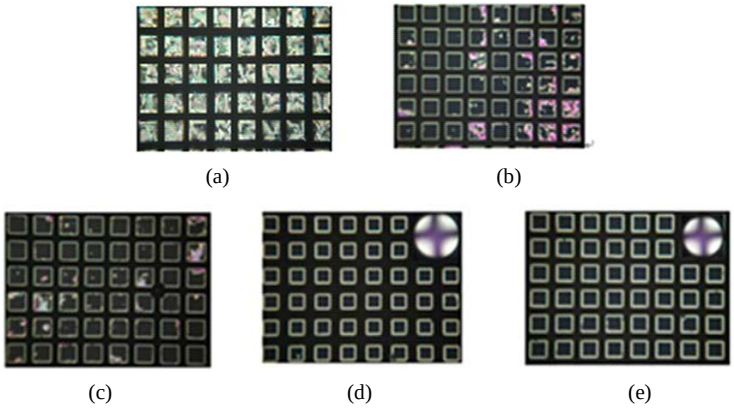


Figure 2. Optical images under cross polarizers of LC cells with 5CB in different volume ratios of DMOAP/APTES. The DMOAP/APTES ratios were (a) 1:20; (b) 1:15; (c) 1:12; (d) 1:10 and (e) 1:5. All the mixture of DMOAP / APTES were performed under the reaction conditions of 80˚C for 2 h followed by activation with 0.3 mol/L GA for 30 min.

3.3. Optimization of DNA Concentration

DNA concentrations can also affect the signal-to-background contrastl, which would affect the sensitivity of the sensor. So the concentration of DNA was optimized in this test. As can be seen from **Figure 3**, the bright region in the optical images increases gradually with the concentration of DNA increases.

When the DNA concentrations is higher than 100 nM (150 nM or 200 nM), the excessive amount of DNA immobilized on the substrate surface can greatly affect the orientation of the LC molecules, resulting in the bright spots and birefringent textures appeared in the optical images (**Figure 3(c)** and **Figure 3(d)**). When the DNA concentrations is 100 nM, the amount of DNA is relatively small immobilized on the substrate surface, which can few affect the orientation of the LC molecules. So the LC molecules remain vertical alignment and the optical image is a uniform dark background (**Figure 3(b)**). When the DNA concentrations is less than 100 nM (50 nM), although the optical image is still a uniform dark background (**Figure 3(a)**), the amount of DNA bound to the substrate surface is relatively less under the same conditions, which can reduce the sensitivity of the sensor.S o we choose the DNA concentration is 100 nM.

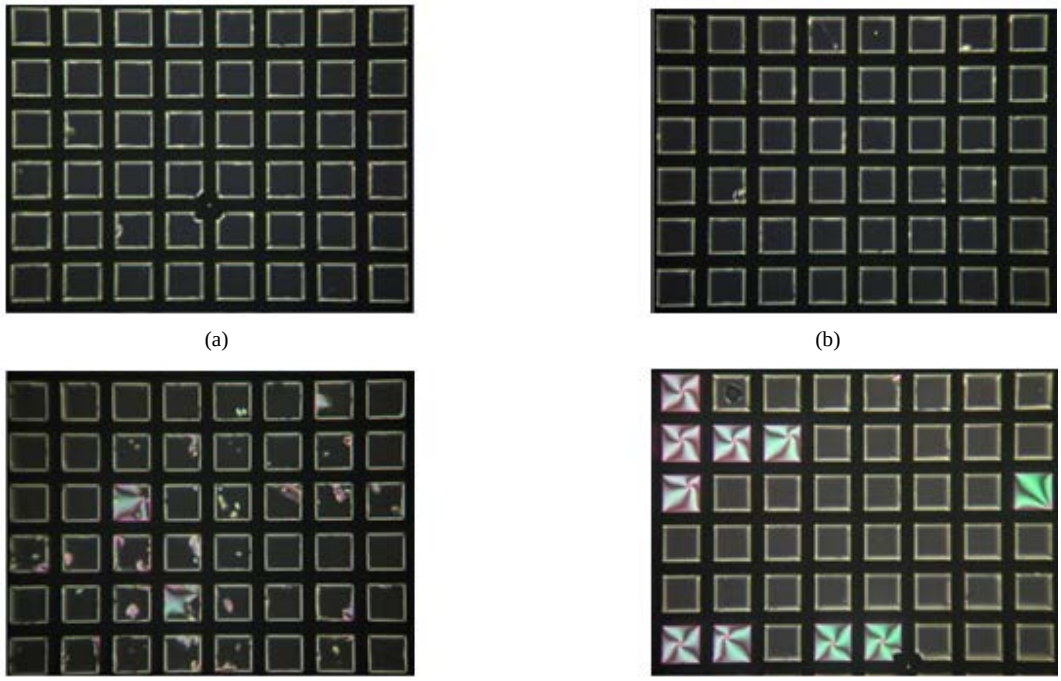
3.4. Detection of Cd^{2+}

3.4.1. Sensitivity

The solution containing different concentrations of Cd^{2+} was added onto the DNA-modified under glass slide, after being treated, the lower glass slide combined with the DMOAP-coated upper glass slide face to face and the liquid crystal cell was obtained. As shown in **Figure 4**, some distinct bright spots begin to appear in the optical image with the addition of Cd^{2+} concentration up to 0.1 nM, which can be easily distinguished from the dark background (**Figure 4(c)**). The number of bright spots and the birefringent textures in the optical images increased with the Cd^{2+} concentration from 0.1 nM to 1 nM (**Figure 4(a)** and **Figure 4(b)**), because the higher the Cd^{2+} concentration, the more the number of DNA combined with Cd^{2+}, which can greatly interfere with the orientation of LC moleculars. When Cd^{2+} concentration is less than 0.1 nM, the optical image tends to be a uniform dark background (**Figure 4(d)**), because the lower the Cd^{2+} concentration, the less the number of DNA combined with Cd^{2+}, which can few interfere with the orientation of LC moleculars. The experimental results show that the significant change of optical signal was still observed even though the Cd^{2+} concentration was reduced to 0.1 nM (**Figure 4(c)**). So the sensitivity of Cd^{2+} detection is 0.1 nM in this method, which is far less than the highest concentration (27 nM) of Cd^{2+} in the drinking water regulated by WHO. This such low detection limit dues to the optical signal amplification of LC molecules.

3.4.2. Selectivity

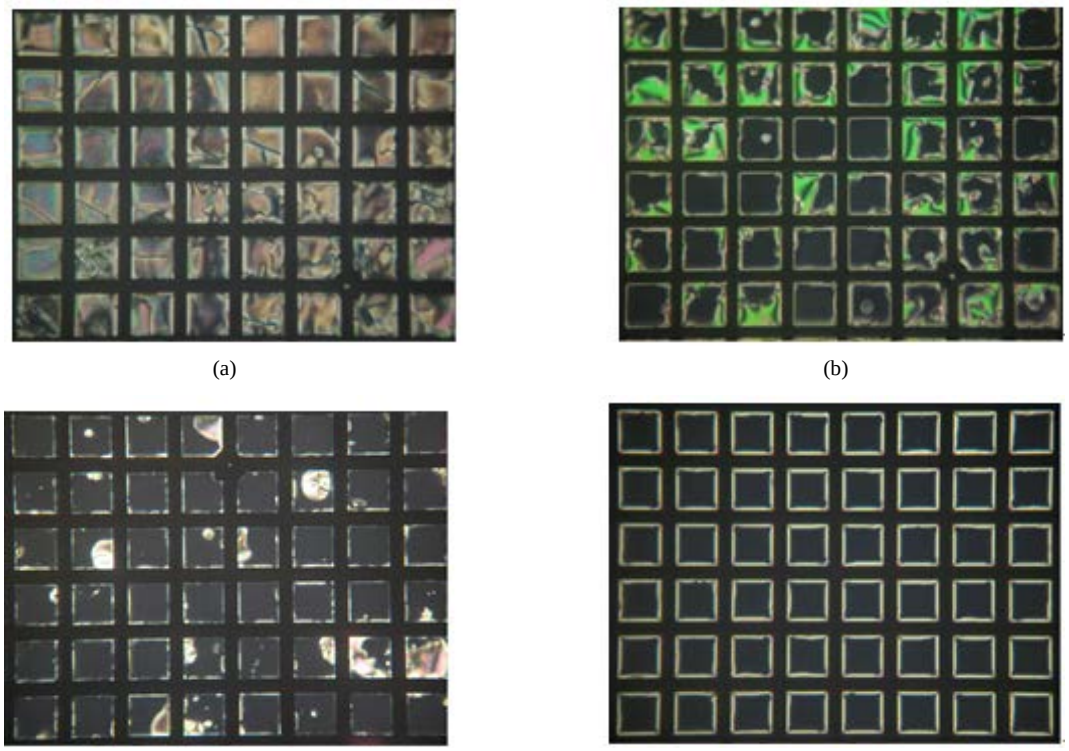
To test selectivity of Cd^{2+} , 0.1 nM Cd^{2+} and 1 nM other metal ion, including K^{+}, Ca^{2+}, Co^{2+}, Al^{3+}, Zn^{2+}, Cr^{3+}, Mn^{2+}, Cu^{2+} and Pb^{2+} were examined under the same conditions. As displayed in **Figure 5**. There is almost no



(a) (b)

(c) (d)

Figure 3. Optical images under cross ploarizers of LC cells with 5CB in different concentrations of DNA (capture probe) immobilized on the glass slide. The concentrations of DNA were (a) 50 nM; (b) 100 nM; (c) 150 nM and (d) 200 nM, respectively.



(a) (b)

(c) (d)

Figure 4. Optical images under crossed polarizer of LC cells with 5CB at different concentration of Cd^{2+}. The concentrations of Cd^{2+} were (a) 1 nM; (b) 0.5 nM; (c) 0.1 nM and (d) 0.05 nM.

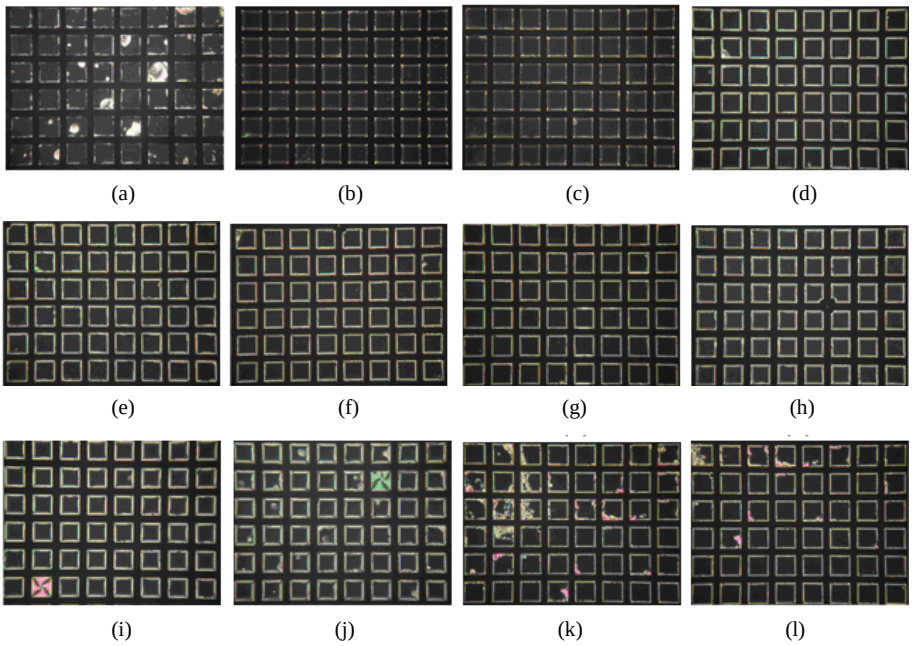


Figure 5. The response diagram of different metal ions and metal ions mixed solution (a) Cd^{2+}; (b) K^{+}; (c) Ca^{2+}; (d) Co^{2+}; (e) Al^{3+}; (f) Zn^{2+}; (g) Cr^{3+}; (h) Mn^{2+}; (i) Cu^{2+}; (j) Pb^{2+}; (k) Mixed solution containing cadmium and other metal ions; (l) Metal ions mixed solution without cadmium. (The concentration of cadmium ions is 0.1 nM, the concentration of other metal ions is 1 nM.)

signal response for other metal ions and their optical images display a uniform dark background, while the bright spots and birefringent textures in the optical images of Cd^{2+} are observed. This experimental result indicates that the LC biosensor based on DNA aptamer has a high selectivity for Cd^{2+} detection.

4. Conclusion

In summary, we have proposed a new LC biosensor to detect Cd^{2+} with high sensitivity and selectivity based on Cd^{2+} inducing DNA containing-SH to bend and become a 2 nm spherical structure. The sensitivity of this method for the detection of Cd^{2+} can achieve 0.1 nM. To our best knowledge, this is the first demonstration only using target DNA induced by Cd^{2+} to produce enhanced optical signal in the field of LC biosensors. In comparison with the previous standard methods, this proposed sensor is simple, low cost and does not require costly instrument. So this sensor is well suitable for on-site and real-time detection for Cd^{2+} and it will have great potential for practical applications.

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References

[1] Aragay, G., Pons, J. and Merkoci, A. (2011) Recent Trends in Macro-, Micro-, and Nanomaterial-Based Tools and Strategies for Heavy-Metal Detection. *Chemical Reviews*, **111**, 3433-3458. http://dx.doi.org/10.1021/cr100383r

[2] Aragay, G. and Merkoçi, A. (2012) Nanomaterials Application in Electrochemical Detection of Heavy Metals. *Electrochim Acta*, **84**, 49-61. http://dx.doi.org/10.1016/j.electacta.2012.04.044

[3] Zakir, H.S.M. and Brennan, J.D. (2011) *β*-Galactosidase-Based Colorimetric Paper Sensor for Determination of Heavy Metals. *Analytical Chemistry*, **83**, 8772-8778. http://dx.doi.org/10.1021/ac202290d

[4] Bhagure, R.G. and Mirgane, S.R. (2011) Heavy Metal Concentrations in Groundwaters and Soils of Thane Region of Maharashtra, India. *Environmental Monitoring and Assessment*, **173**, 643-652. http://dx.doi.org/10.1007/s10661-010-1412-9

[5] Khosraviani, M., *et al*. (1998) Detection of Heavy Metals by Immunoassay: Optimization and Validation of a Rapid, Portable Assay for Ionic Cadmium. *Environmental Science & Technology*, **32**, 137-142. http://dx.doi.org/10.1021/es9703943

[6] Darwish, I.A. and Blake, D.A. (2001) One-Step Competitive Immunoassay for Cadmium Ions: Development and Validation for Environmental Water Samples. *Analytical Chemistry*, **73**, 1889-1895. http://dx.doi.org/10.1021/ac0012905

[7] Darwish, I.A. and Blake, D.A. (2002) Development and Validation of a One-Step Immunoassay for Determination of Cadmium in Human Serum. *Analytical Chemistry*, **74**, 52-58. http://dx.doi.org/10.1021/ac010510r

[8] Guell, R., *et al*. (2008) Sensitive and Stable Monitoring of Lead and Cadmium in Seawater Using Screen-Printed Electrode and Electrochemical Stripping Analysis. *Analytica Chimica Acta*, **627**, 219-224. http://dx.doi.org/10.1016/j.aca.2008.08.017

[9] Malekpour, A., Hajialigol, S. and Taher, M.A. (2009) Study on Solid-Phase Extraction and Flame Atomic Absorption Spectrometry for the Selective Determination of Cadmium in Water and Plant Samples with Modified Clinoptilolite. *Journal of Hazardous Materials*, **172**, 229-233. http://dx.doi.org/10.1016/j.jhazmat.2009.06.163

[10] Matsumoto, A., *et al*. (2010) Determination of Cadmium by an Improved Double Chamber Electrothermal Vaporization Inductively Coupled Plasma Atomic Emission Spectrometry. *MicroChem*, **95**, 85-89. http://dx.doi.org/10.1016/j.microc.2009.10.012

[11] Guo, W., Hu, S.H., Xiao, Y.F., Zhang, H.F. and Xie, X.J. (2010) Direct Determination of Trace Cadmium in Environmental Samples by Dynamic Reaction Cell Inductively Coupled Plasma Mass Spectrometry. *Chemosphere*, **81**, 1463-1468. http://dx.doi.org/10.1016/j.chemosphere.2010.08.056

[12] Liu, J.W., Cao, Z.H. and Lu, Y. (2009) Functional Nucleic Acid Sensors. *Chemical Reviews*, **109**, 1948-1998. http://dx.doi.org/10.1021/cr030183i

[13] Li, T., Wang, E. and Dong, S.J. (2010) Parallel G-Quadruplex-Specific Fluorescent Probe for Monitoring DNA Structural Changes and Label-Free Detection of Potassium Ion. *Analytical Chemistry*, **82**, 7576-7580. http://dx.doi.org/10.1021/ac1019446

[14] Lin, Z.Z., Li, X.H. and Kraatz, H.B. (2011) Impedimetric Immobilized DNA-Based Sensor for Simultaneous Detection of Pb^{2+}, Ag^{+}, and Hg^{2+}. *Analytical Chemistry*, **83**, 6896-6901. http://dx.doi.org/10.1021/ac2014096

[15] Babkina, S.S. and Ulakhovich, N.A. (2005) Complexing of Heavy Metals with DNA and New Bioaffinity Method of Their Determination Based on Amperometric DNA-Based Biosensor. *Analytical Chemistry*, **77**, 5678-5685. http://dx.doi.org/10.1021/ac050727b

[16] Zhang, Q.R., Dai, P.P. and Yang, Z.S. (2011) Sensitive DNA-Hybridization Biosensors Based on Gold Nanoparticles for Testing DNA Damage by Cd(II) Ions. *Microchimica Acta*, **173**, 347-352. http://dx.doi.org/10.1007/s00604-011-0558-7

[17] Yang, S.Y., Wu, C., Tan, H., Wu, Y., Liao, S.Z., Wu, Z.Y., *et al.* (2013) Label-Free Liquid Crystal Biosensor Based on Specific Oligonucleotide Probes for Heavy Metal Ions. *Analytical Chemistry*, **85**, 14-18. http://dx.doi.org/10.1021/ac302989h

[18] Gupta, V.K., Skaife, J.J., Dubrovsky, T.B. and Abbott, N.L. (1998) Optical Amplification of Ligand-Receptor Binding Using Liquid Crystals. *Science*, **279**, 2077-2080. http://dx.doi.org/10.1126/science.279.5359.2077

[19] Noonan, P.S., Roberts, R.H. and Schwartz, D.K. (2013) Liquid Crystal Reorientation Induced by Aptamer Conformational Changes. *Journal of the American Chemical Society*, **135**, 5183-5189. http://dx.doi.org/10.1021/ja400619k

[20] Jiang, L., Yang, B.-Q., Ma, Y.-D., Yang, W.-S., Du, Z.-L. and Li, T.-J. (2003) Cadmium Ion Induced Bending of Phosphorothioate Oligonucleotide G10. *Physical Chemistry Chemical Physics*, **5**, 632-634. http://dx.doi.org/10.1039/b210058d