LANGMUIR

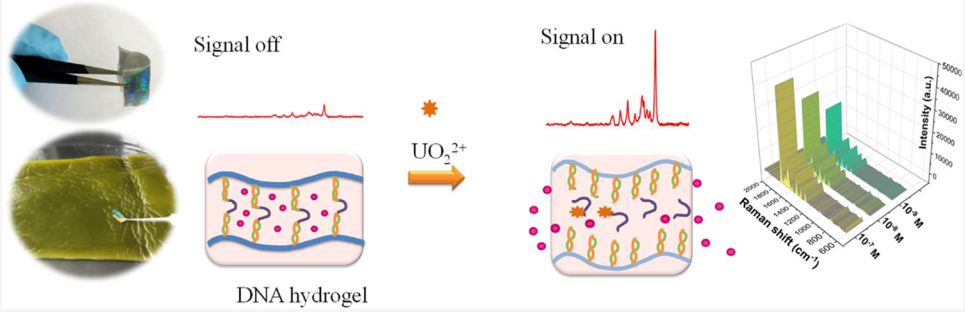
pubs.acs.org/Langmuir Article

Flexible DNA Hydrogel SERS Active Biofilms for Conformal Ultrasensitive Detection of Uranyl Ions from Aquatic Products

Xuan He, Xin Zhou, Wei Liu, Yu Liu, and Xiaolin Wang*

Cite This: *Langmuir* 2020, 36, 2930−2936 Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information



ABSTRACT: It is of great significance to sensitively and conveniently detect trace UO_2^{2+} ions in biological and environmental samples due to severe health risks. However, such suitable sensors are still scarce. In this work, DNAzyme-based hydrogels modified on Ag NP-grafted PAN nanorods array as flexible SERS biosensor have been developed for ultrasensitive UO_2^{2+} ion detection. They were first formed by the substrate strand and enzyme strand comprising the main cleavage-reaction stem-loop complex. Then, a UO_2^{2+} ions responsive smart hydrogel capsule was achieved by DNAzyme complex hybridized with DNA polyacrylamide chains. Raman reporter RhB was introduced and intentionally trapped inside the hydrogel. In the absence of UO_2^{2+} ions, a tiny Raman signal was presented because RhB was trapped inside the hydrogel and far away from SERS substrates. Conversely, the responsive hydrogel could be specifically attacked by UO_2^{2+} ions to release RhB, leading to a strong Raman signal. With the amplified signal procedure, this flexible SERS biofilm accomplished sensitive and selective detection of UO_2^{2+} ions with a wide linear range from 1 pM to 0.1 μM and a low detection limit of 0.838 pM. This result is nearly five orders below the EPA-defined maximum contaminant level (180 nM). Furthermore, this biofilm gives full play to the advantages of a flexible biosensor. It can directly detect the aquatic products (such as fish and kelp) polluted by UO_2^{2+} ions, demonstrating that this flexible SERS biofilm has promising potential for applications in a rapid environmental safety inspection.

INTRODUCTION

Stimuli-responsive smart hydrogels have undoubtedly become an attractive prospect in terms of successful performance of high degrees of mechanical flexibility, sensing capability, and user-friendly simplicity.[1−7] Among all stimuli-responsive smart hydrogels, DNA hydrogels are hybrid materials that utilize DNA-grafted polymer as a scaffold and functional DNA as a cross-linker for rapid response to specific analytes.[8−10] For example, visual sensitive detection of Cu^{2+}, Pb^{2+}, and UO_2^{2+} was reported through DNAzyme cross-linked hydrogels.[11−14] Inspired by these brilliant works, we wondered whether DNA hydrogels could be developed and applied as smart sensors for real contaminated samples detection

Surface-enhanced Raman scattering (SERS) is proposed as the most powerful ultrasensitive technique because it can be used to detect trace molecules even down to a single molecular level.[15,16] Contrast to traditional rigid SERS substrates, flexible SERS substrates showed unexceptional advantages due to the ability to conform to the underlying object. It could be easily cut into diverse sizes and shapes and also could be wrapped onto curved surfaces for practical applications, which require flexible, nonplanar, and conformal surfaces.[17,18] However, most flexible SERS substrates were disordered and rough materials, only very few types have the capability to formulate sensitive and uniform SERS signals.[19,20] Besides, the combined advantages of smart hydrogels and flexible SERS arrays substrate for ultrasensitive sensing have never been reported.

As we all know, uranium is the main fuel in nuclear reactors. Due to its high radioactivity, toxicity, and bioavailability, the environmental pollution caused by inappropriate disposal of uranium compounds raises a lot of concerns.[21−24] UO_2^{2+} ions

Received: December 17, 2019
Revised: February 29, 2020
Published: February 29, 2020

https://dx.doi.org/10.1021/acs.langmuir.9b03845
Langmuir 2020, 36, 2930−2936

Table 1. DNA Sequences Used for This Work

name	sequences (5′-3′)
A1	acrydite-TCGTCTTTTAGTGG
A2	acrydite-ATCTCAAAATGTAG
substrate strand	CCACTAAAAGACGATACTCACTATrAGGAAGA GATGGCTACATTTTGAGAT
enzyme strand	CCATCTCTTCAGTTCGGAAACGAACCTTCAGACATAGTG

are the most stable form of uranium in water and can also cause terrible harm to organs such as the liver and kidney.[25] It is of great importance to developing SERS as a sensitive method for rapid uranium contamination monitoring.[26,27] However, the small Raman cross section of UO_2^{2+} often led to a weak Raman signal.[28] Methods of signal amplification are urgently required. How to combine DNA hydrogels with SERS flexible substrates to generate a signal amplification strategy is also the key point we need to explore.

In this work, we designed and synthesized the DNA hydrogels coating to SERS substrate as a flexible biosensor for UO_2^{2+} ion detection. The large-scale flexible films of highly ordered PAN nanorods arrays, which are decorated with high-density Ag-NPs as sub-10 nm gaps, offered great SERS activity and flexibility. It is worth mentioning that this kind of flexible large-scale (2.5 × 2.5 cm^2) PAN nanorod arrays can be prepared in 20 minutes by using the Si-template.[19] Then, DNA hydrogels containing a specific response to UO_2^{2+} ion were modified under SERS films as a biosensor.[29,30] There are two signal amplification processes in our sensing principle. First, two kinds of DNA grafted on the polyacrylamide chain hybridized with the DNAzyme substrate sequence prolonged at both ends. Inside, hydrogel cross-linkers were grafted by substrate and enzyme strands and scaffolds were formed by polyacrylamide chains. Raman reporter RhB were trapped inside a 3D network of the DNA hydrogel. Once UO_2^{2+} ions triggered the cleavage of the substrate strand from the enzyme strand, Raman reporter RhB were released from the DNA hydrogel encapsulated because the cleavage reaction decreases the cross-linking density and destabilizes the hydrogel structure. This is the first signal amplification.[31] Then, the RhB molecules were captured by polyacrylonitrile (PAN) arrays and Raman signals were amplified again. Based on this principle, this DNA hydrogel flexible biosensor has an excellent performance with the limit of detection (LOD) of 8.38×10^{-13} M for UO_2^{2+} ions. The hydrogel responded specifically to UO_2^{2+} ions over 15 other metal ions, which represented excellent selectivity. Because flexible PAN films are easy to curve or roll under any other surface for practical SERS-based applications,[32,33] very interestingly, this flexible SERS biofilm was driven to wipe and detect aquatic products (like fish and kelp) contaminated by UO_2^{2+} ions directly. A comparison of calibration curves proved that our DNA hydrogel flexible biofilm has promising potential as a reliable platform for the sensitive SERS detection of toxic pollutants in the environment.

EXPERIMENTAL SECTION

Materials and Reagents. All DNA probes were purchased from Takara Biotechnology Company Ltd. (Dalian, China). Also, the DNA sequences used for this work are listed in Table 1. Uranyl(VI) acetate was purchased from ICM. *p*-Aminothiophenol (PATP, 98%), NaCl (≥99%), and rhodamine B (RhB) were obtained from Aladdin-Reagent Co., Ltd. (Shanghai, China). Other reagents were of analytical grade and used without further purification. Ultrapure water with a conductivity of 18 MΩ·cm^{-1} was used in all experiments.

Preparation of UO_2^{2+} Ion Responsive Hydrogel and SERS Biofilms. First, enzyme strand, substrate strand, and strands A1 and A2 grafted polyacrylamide chains (PA1 and PA2, respectively) were mixed at concentrations of 100 μM: 50 μM: 100 μM: 100 μM. The 0.1 mM Raman reporter RhB was encapsulated in the formed hydrogel. All mixtures were revolved alternately and violently and then incubated at 65 °C for 1 min and 3 times. After that, a homogeneous hydrogel was formed and slowly cooled to room temperature. Buffer solution in this procedure was the MES buffer containing 250 mM NaCl (50 mM, pH 5.5).

Methods for large-area flexible Ag-NPs@PAN films with highly ordered nanorod arrays were performed following our previous work.[19] Freshly prepared hydrogels were spun into flexible Ag-NPs@PAN films and the DNA hydrogel SERS test biofilms were obtained.

Detection of UO_2^{2+} Ions by DNA Hydrogel SERS Test Biofilms. Different concentrations of UO_2^{2+} ions were dropped on the DNA hydrogel SERS test biofilms and allowed to incubate at 25 °C for 2 h. They were then detected by a Raman microscope equipped spectrum with a 532 nm laser. The laser power and acquisition time were 0.4 mW and 10 s, respectively.

Prepared Aquatic Products (Fish and Kelps) and Detected by SERS Test Biofilms. To simulate the detection in real contaminated samples, clean fish and kelps were contaminated with different concentrations of uranyl ions (10^{-7}, 10^{-8}, 10^{-9} M), respectively. The contaminated samples were obtained by dropping 200 μL of UO_2^{2+} ion solutions directly on the circled position in Figure 5; the procedure was repeated three times. After drying for 3 min, the samples were wiped with SERS test biofilm and detected by Raman spectrometer.

RESULTS AND DISCUSSION

The highly ordered arrays flexible polyacrylonitrile (PAN) nanorod SERS substrates were prepared according to our previous work.[19] As shown in Figure S1, high-quality PAN nanorods were obtained as a template by nanoimprinting technology.

After decorated Ag-NPs under PAN films (Figures 1 and S2), the Ag-NPs@PAN-nanorod arrays could be efficiently regulated. The good flexibility of the film is shown in Figure 1a,

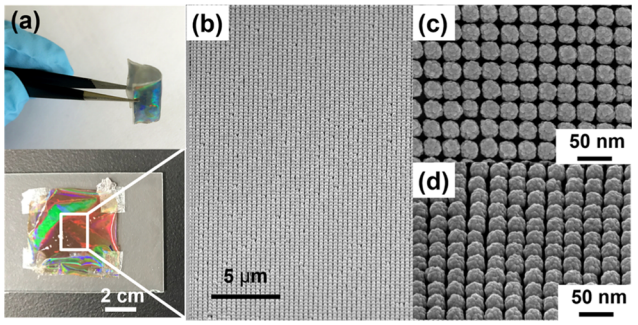
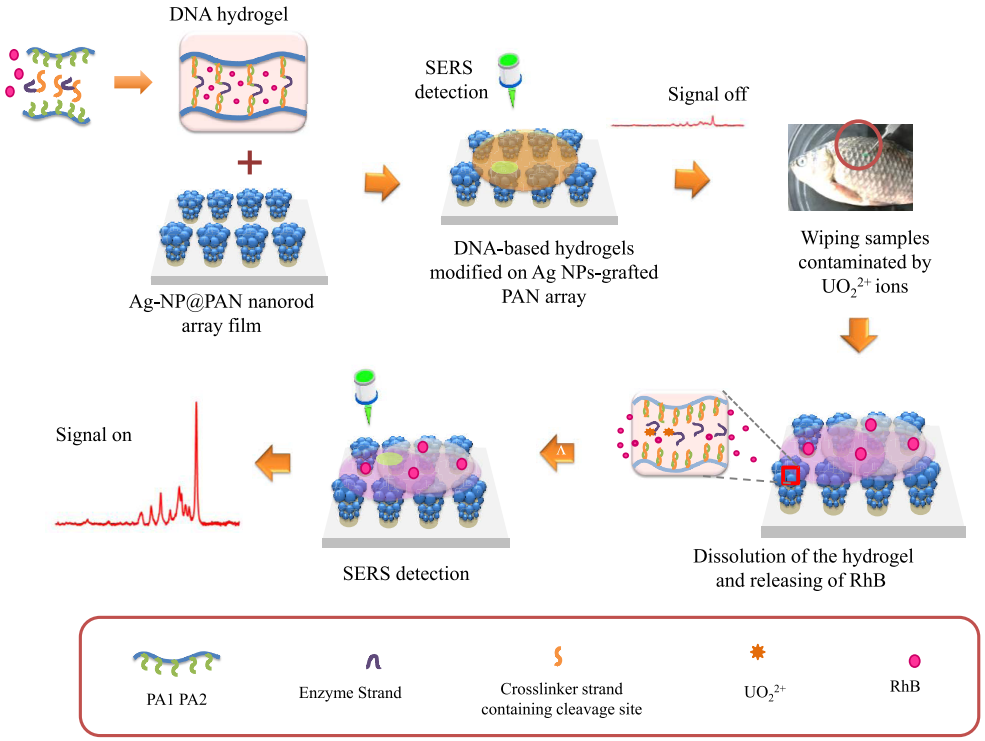


Figure 1. (a) Photograph of flexible films: (b) FE-SEM image of Ag-NPs@PAN-nanorod arrays and (c) enlarged view of (b) and (d) side view of (c).

https://dx.doi.org/10.1021/acs.langmuir.9b03845
Langmuir 2020, 36, 2930−2936

Scheme 1. Working Principle of the DNA Hydrogel-Based SERS Biofilms[a]



[a]Other 15 interfering ions (Pb^{2+}, Th^{4+}, Ag^{+}, Mg^{2+}, Ca^{2+}, Ba^{2+}, Mn^{2+}, Fe^{2+}, Fe^{3+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+}) were also detected using the DNA hydrogel SERS test biofilm.

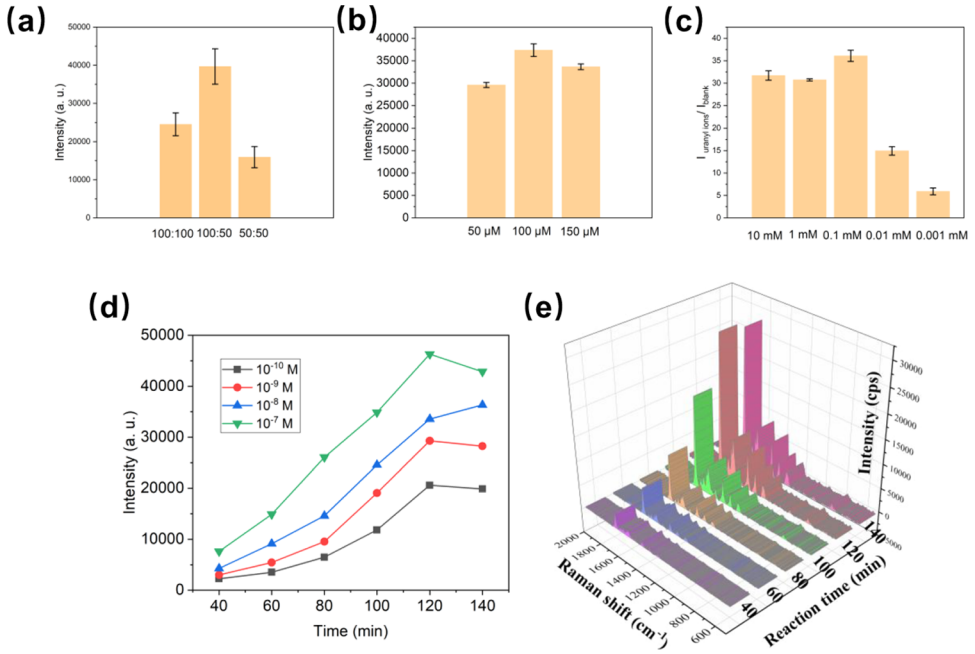


Figure 2. Optimization of assay conditions: (a) effect of substrate and enzyme strand ratio; (b) concentration of DNA hydrogel; (c) concentration of Raman reporter RhB; (d) corresponding Raman intensities of 1650 cm^{-1} were collected at 20 min intervals in the presence of UO_2^{2+} ions at different concentrations; and (e) reaction time of DNA hydrogel between UO_2^{2+} ions at concentration of 10^{-9} M.

and we also could recognize the highly ordered arrays from top and side views (Figure 1b–d). The XRD experiment showed the situation of Ag (Figure S3). Also, the SERS activity of Ag-NPs@PAN-nanorod arrays was evaluated by probe 4-ATP. Then, the calculated EF data of 1.98×10^7 showed high sensitivity toward our flexible substrates (see Supporting Information Figure S4 and page S4).

Working Principle of DNA Hydrogel-Based SERS Platform. As shown in Scheme 1 and Figure S5 in the Supporting Information, linear DNA polyacrylamide conjugates (PA1 and PA2) were formed by two short DNA strands

https://dx.doi.org/10.1021/acs.langmuir.9b03845
Langmuir 2020, 36, 2930−2936

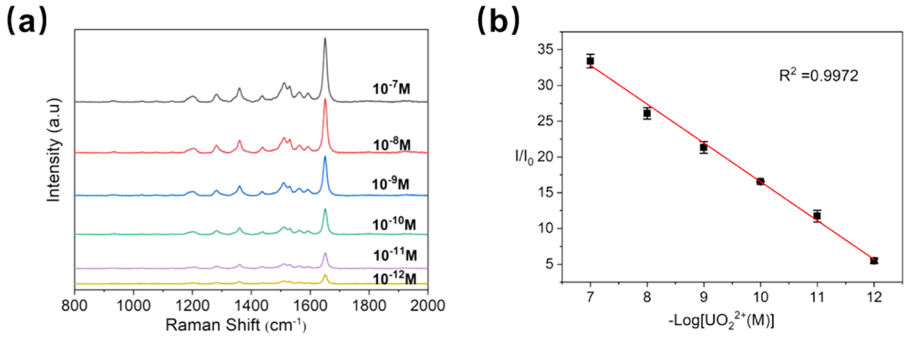


Figure 3. (a) SERS responses of RhB collected from DNA hydrogel SERS biofilm with increasing concentrations of UO_2^{2+} ions from 10^{-12} to 10^{-7} M. (b) Inset provided the dynamic range of DNA hydrogel SERS biofilm for UO_2^{2+} ion detection.

(A1 and A2) copolymerized with acrylamide, respectively. Two ends of DNAzyme sequence containing specific response of UO_2^{2+} were hybridized with A1 and A2 respectively. It was first formed by the substrate strand and the enzyme strand constituted the main cleavage reaction stem-loop complex,[34] and then hybridized with DNA polyacrylamide chains to achieve a DNA hydrogel capsule. In the absence of UO_2^{2+} ions, an enormous amount of Raman reporter RhB were tapped into the DNA hydrogel capsule. Weak Raman peaks (1650 cm^{-1}) belonging to RhB appeared due to long distance from the SERS substrate's surface, resulting in the "off" status. After triggering of the cleavage reaction by UO_2^{2+} ions, the enzyme strand of the stem-loop complex began to break from the substrate strand, inducing the dissociation of the double-strand structure. Then, the hydrogel's cross-linking ratio was gradually decreased, which led to the breakdown of the whole hydrogel capsule and the leakage of the reporter molecule RhB to the SERS substrate directly, switching to the "on" status with a strong Raman signal. During this signal amplification process, an only small amount of UO_2^{2+} ions induced the leaking of a large amount of RhB. Because UO_2^{2+} ions attacking the original stem-loop complex could separate and bind to another preformed stem-loop complex to light up another cycle of cleavage reaction, by utilizing of the DNA gel to transform and amplify Raman signal, the weak signal from Raman scattering cross section of UO_2^{2+} ions can be solved and ultrasensitive detection can be achieved.[35]

Optimization of Assay Conditions. To develop the SERS platform with high sensitivity, several parameters, such as the optimization of the cross-linker density of hydrogel, the concentration of DNA hydrogel, and the incubation time of UO_2^{2+} ion detection, the concentration of Raman reporter RhB was also investigated carefully. First, the effect of substrate and enzyme strand ratio and concentration of DNA hydrogel on the sensitive response of UO_2^{2+} ions by SERS method is shown in Figure 2a,b. It was proved that the best ratio for the substrate strand and enzyme strand was 1:2 under the concentration of 100 μM. Also, from the blank signal, at these concentrations, the DNA hydrogel was formed and remained stable enough to lock the Raman reporter RhB tightly inside. Then, the kinetics of the hydrogel decomposition upon activation by different concentrations of UO_2^{2+} ions indicated that 120 min was the optimum time when the Raman intensity was the strongest (Figure 2c,d). The last factor to be considered was the concentration of Raman reporter RhB. As shown in Supporting Information Figure S2, with the increase in concentration, it was easier to perform fluorescent interfering, which led to a decrease in Raman intensity. As a result, the best concentration of RhB was fixed at 0.1 mM.

Sensitive and Selective Detection of UO_2^{2+} Ions Using the DNA Hydrogel-Based SERS Platform. With optimal conditions at hand, the next goal was to investigate the sensitive and selective DNA hydrogel SERS platform for the application. In Figure 3, different concentrations of UO_2^{2+} ions were detected, which indicated that the intensity of the Raman signals enhanced with the increasing concentrations (1 pM–0.1 μM) of UO_2^{2+} ions. The corresponding linear relationship between the logarithm of UO_2^{2+} ions and Raman intensity at 1650 cm^{-1} is shown in Figure 3b. The regression equation was $y = -5.43 \log c + 70.8$ (where y is the Raman peak intensity of $I_{\text{uranyl ions}}/I_{\text{blank}}$ at 1650 cm^{-1} and c is the concentration of UO_2^{2+} ions) with a correlation coefficient square of 0.9972. The estimated limit of detection (LOD) was 0.838 pM, which was estimated by

the process listed in Supporting Information page S6.[36−39] Also, the error bar was calculated from each concentration of UO_2^{2+} ion tested three times. The whole calculation process is presented in the Supporting Information. Compared with other reports that focused on the detection of UO_2^{2+} ions (Table S1), this DNA hydrogel SERS platform showed higher sensitivity and a wider linear range, which illustrated that it would have a wider application in UO_2^{2+} ion sensing.

Taking advantage of the high specific responsive UO_2^{2+} ions DNA cross-linked hydrogel, high selectivity against other cations was displayed. In the presence of high concentrations of other 15 kinds of interfering metal ions (Pb^{2+}, Th^{4+}, Ag^{+}, Mg^{2+}, Ca^{2+}, Ba^{2+}, Mn^{2+}, Fe^{2+}, Fe^{3+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+}) at two different concentrations (10 and 100 μM), very weak Raman intensities were observed (Figure 4). Relatively, the concentrations of UO_2^{2+} ions were only 1 and 10 nM, which could show an obvious Raman intensity. The results confirmed the superior fidelity of the DNA hydrogel flexible SERS biofilm in selective detection of UO_2^{2+} ions. The good performance of the DNA hydrogel SERS platform may be due to the following reasons: (1) this DNA hydrogel switch controlled by UO_2^{2+} ion-specific cleavage reaction can release large amount of RhB to obviously amplify the Raman signal and (2) the highly ordered morphological features of the Ag-NPs@PAN-nanorod array biofilms as sensitive and uniform SERS substrates further ensured the ultrasensitive performance for UO_2^{2+} ion detection.

Application of the DNA Hydrogel SERS Biofilm for Real Aquatic Products (Fish and Kelps) Contaminated by UO_2^{2+} Ion Detection. To monitor the reliability of the proposed DNA hydrogel-based SERS flexible biofilm, recovery

https://dx.doi.org/10.1021/acs.langmuir.9b03845
Langmuir 2020, 36, 2930−2936

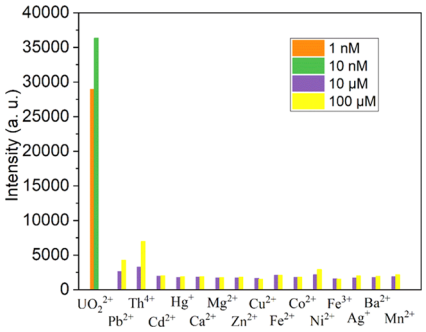


Figure 4. Selective UO_2^{2+} ion detection experiments by using DNA hydrogel SERS biofilms. Other comparison metal ions were listed on the *x*-axis and their corresponding RhB 1650 cm^{-1} band intensities were shown on the *y*-axis. Different concentrations were shown by different color bars.

experiments were carried by dipping various concentrations of UO_2^{2+} ions into the flesh of the fish's clean surface. Also, similar experiments also implemented on kelp as samples. All the Raman peaks of RhB are clearly shown in Figure 5, which demonstrated that the DNA hydrogel SERS biofilm had advantages in sample collection and potential for analytical application in real samples.

CONCLUSIONS

A novel responsive DNA hydrogel SERS flexible biofilm was proposed for the ultrasensitive detection of UO_2^{2+} ions via DNAzyme cleavage amplification strategy. In the beginning, the Raman reporter RhB were deliberately trapped inside the DNA hydrogel cross-linked structure with the "off" status. The presence of UO_2^{2+} ions, which initiated the DNAzyme's activity to cleave the substrate strand, caused the substrate strand to break and the enzyme strand to dissociate. Then, the DNA hydrogel structure was destroyed, leaking a large amount of RhB to produce a strong Raman signal ("on"). Moreover, the free released UO_2^{2+} ions can specifically cleave another substrate strand and lead to new DNAzyme cleave-reaction, inducing the next cycle and amplifying the Raman signal of RhB. The continuous signal amplification made this platform ultrasensitive to UO_2^{2+} ion detection and achieve the limit of detection (LOD) of as low as 0.838 pM. This elaborate design could circumvent the problem of the small Raman cross section of UO_2^{2+} ions. The application of DNA hydrogel SERS biofilm in real aquatic sample detection showed excellent potential for in-field monitoring of UO_2^{2+} ion contamination in the field.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.langmuir.9b03845.

Instruments; experiments; estimation of enhancement factor; calculation of limit of detection refers to the literature; references; Figure S1: FE-SEM image of large-area flexible PAN films with uniform nanorod arrays; Figure S2: FE-SEM image of large-area Ag-NPs@PAN-nanorod arrays; Figure S3: XRD patterns of the Ag-NPs@PAN-nanorod arrays flexible film; Figure S4: SERS spectra of 4-ATP collected on the Ag-NPs@PAN-nanorod arrays flexible film with Ag sputtering for 180 s after being exposed to different concentrations of 4-ATP in an alcohol solution; Figure S5: (a) Schematic for the principle of the DNAzyme cleavage reaction and (b) DNAzyme hydrogel sensing strategy; Table S1: Typical proposed comparison of an analytical method for UO_2^{2+} ion detection from 2015 to present (PDF)

AUTHOR INFORMATION

Corresponding Author

Xiaolin Wang − *College of Chemistry, Sichuan University, Chengdu 610064, China; China Academy of Engineering Physics, Mianyang 621900, China;* orcid.org/0000-0002-3463-1535; Email: xlwang@caep.cn

Authors

Xuan He − *College of Chemistry, Sichuan University, Chengdu 610064, China; Institute of Chemical Materials, China Academy of Engineering Physics, Mianyang 621900, China*

Xin Zhou − *Institute of Chemical Materials, China Academy of Engineering Physics, Mianyang 621900, China*

Wei Liu − *Institute of Chemical Materials, China Academy of Engineering Physics, Mianyang 621900, China*

Yu Liu − *Institute of Chemical Materials, China Academy of Engineering Physics, Mianyang 621900, China*

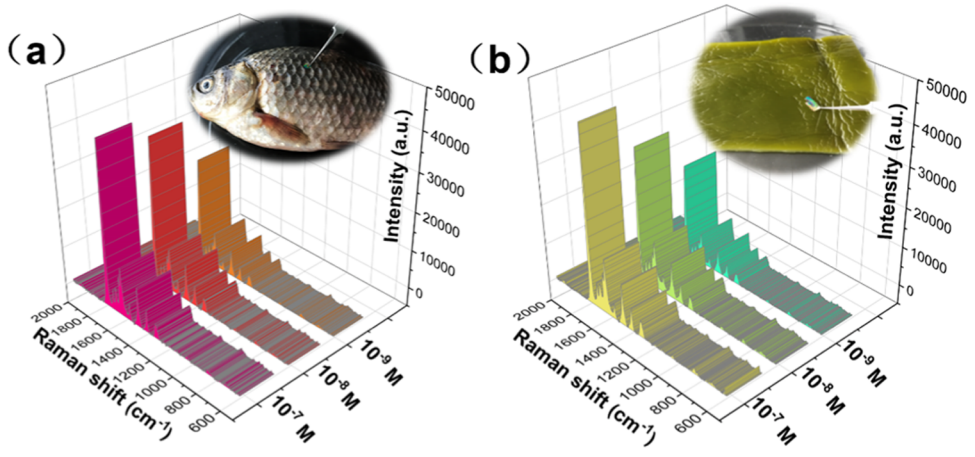


Figure 5. Application of DNA hydrogel SERS biofilm for detecting real aquatic products: (a) fishes contaminated with UO_2^{2+} ions and (b) kelps contaminated with UO_2^{2+} ions.

https://dx.doi.org/10.1021/acs.langmuir.9b03845
Langmuir 2020, 36, 2930−2936

Complete contact information is available at:
https://pubs.acs.org/10.1021/acs.langmuir.9b03845

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

X.H. appreciated Pu Huang for his discussion and help. This work was supported by the Science Challenge Project (TZ201804), and the National Natural Science Foundation of China (21502179).

■ REFERENCES

(1) Yang, H. H.; Liu, H. P.; Kang, H. Z.; Tan, W. H. Engineering Target-Responsive Hydrogels Based on Aptamer−Target Interactions. *J. Am. Chem. Soc.* **2008**, *130*, 6320−6321.
(2) Yan, L.; Zhu, Z.; Zou, Y.; Huang, Y.; Liu, D.; Jia, S.; Xu, D.; Wu, M.; Zhou, Y.; Zhou, S.; Yang, C. J. Target-Responsive "Sweet" Hydrogel with Glucometer Readout for Portable and Quantitative Detection of Non-Glucose Targets. *J. Am. Chem. Soc.* **2013**, *135*, 3748−3751.
(3) Zhu, Z.; Wu, C.; Liu, H.; Zou, Y.; Zhang, X.; Kang, H.; Yang, C. J.; Tan, W. An Aptamer Cross-Linked Hydrogel as a Colorimetric Platform for Visual Detection. *Angew. Chem., Int. Ed.* **2010**, *49*, 1052−1056.
(4) Dave, N.; Chan, M. Y.; Huang, P.-J. J.; Smith, B. D.; Liu, J. Regenerable DNA-Functionalized Hydrogels for Ultrasensitive, Instrument-Free Mercury(II) Detection and Removal in Water. *J. Am. Chem. Soc.* **2010**, *132*, 12668−12673.
(5) Lin, H.; Zou, Y.; Huang, Y.; Chen, J.; Zhang, W. Y.; Zhuang, Z.; Jenkins, G.; Yang, C. Y. DNAzyme crosslinked hydrogel: a new platform for visual detection of metal ions. *Chem. Commun.* **2011**, *47*, 9312−9314.
(6) Guo, W.; Qi, X.-J.; Orbach, R.; Lu, C.-H.; Freage, L.; Mironi-Harpaz, I.; Seliktar, D.; Yang, H.-H.; Willner, I. Reversible Ag^{+}-crosslinked DNA hydrogels. *Chem. Commun.* **2014**, *50*, 4065−4068.
(7) Gong, L.; Zhao, Z.; Lv, Y.-F.; Huan, S.-Y.; Fu, T.; Zhang, X.-B.; Shen, G.-L.; Yu, R.-Q. DNAzyme-based biosensors and nanodevices. *Chem. Commun.* **2015**, *51*, 979−995.
(8) Zhang, L.; Lei, J.; Liu, L.; Li, C.; Ju, H. Self-Assembled DNA Hydrogel as Switchable Material for Aptamer-Based Fluorescent Detection of Protein. *Anal. Chem.* **2013**, *85*, 11077−11082.
(9) Guo, W.; Orbach, R.; Mironi-Harpaz, I.; Seliktar, D.; Willner, I. Fluorescent DNA hydrogels composed of nucleic acid-stabilized silver nanoclusters. *Small* **2013**, *9*, 3748−3752.
(10) Lee, J. H.; Wang, Z.; Liu, J.; Lu, Y. Highly Sensitive and Selective Colorimetric Sensors for Uranyl (UO_2^{2+}): Development and Comparison of Labeled and Label-Free DNAzyme-Gold Nanoparticle Systems. *J. Am. Chem. Soc.* **2008**, *130*, 14217−14226.
(11) Huang, Y.; Fang, L.; Zhu, Z.; Ma, Y.; Zhou, L.; Chen, X.; Xu, D.; Yang, C. Design and synthesis of target-responsive hydrogel for portable visual quantitative detection of uranium with a microfluidic distance-based readout device. *Biosens. Bioelectron.* **2016**, *85*, 496−502.
(12) Luo, Y.; Zhang, Y.; Xu, L.; Wang, L.; Wen, G.; Liang, A.; Jiang, Z. Colorimetric sensing of trace UO_2^{2+} by using nanogold-seeded nucleation amplification and label-free DNAzyme cleavage reaction. *Analyst* **2012**, *137*, 1866−1871.
(13) Verma, I.; Devi, M.; Sharma, D.; Nandi, R.; Pal, S. K. Correction to Liquid Crystal based Detection of Pb(II) Ions Using Spinach RNA as Recognition Probe. *Langmuir* **2019**, *35*, 9994.
(14) Wu, P.; Hwang, K.; Lan, T.; Lu, Y. A DNAzyme-Gold Nanoparticle Probe for Uranyl Ion in Living Cells. *J. Am. Chem. Soc.* **2013**, *135*, 5254−5257.
(15) Huang, Y.; Wu, X.; Tian, T.; Zhu, Z.; Lin, H.; Yang, C. Target-responsive DNAzyme hydrogel for portable colorimetric detection of lanthanide(III) ions. *Sci. China: Chem.* **2017**, *60*, 293−298.
(16) Huang, Z. C.; Zhang, A. M.; Zhang, Q.; Cui, D. X. Nanomaterial-based SERS sensing technology for biomedical application. *J. Mater. Chem. B* **2019**, *7*, 3755−3774.
(17) He, Y.; Yang, X.; Yuan, R.; Chai, Y. Q. A novel ratiometric SERS biosensor with one Raman probe for ultrasensitive microRNA detection based on DNA hydrogel amplification. *J. Mater. Chem. B* **2019**, *7*, 2643−2647.
(18) Verma, I.; Devi, M.; Sharma, D.; Nandi, R.; Pal, S. K. Liquid Crystal based Detection of Pb(II) Ions Using Spinach RNA as Recognition Probe. *Langmuir* **2019**, 7816−7823.
(19) Li, Z. B.; Meng, G. W.; Huang, Q.; Hu, X. Y.; He, X.; Tang, H. B.; Wang, Z. W.; Li, F. D. Ag Nanoparticle-Grafted PAN-Nanohump Array Films with 3D High-Density Hot Spots as Flexible and Reliable SERS Substrates. *Small* **2015**, *11*, 5452−5459.
(20) Yang, N.; You, T. T.; Gao, Y. K.; Lu, S. C.; Yin, P. G. One-Step Preparation Method of Flexible Metafilms on the Water−Oil Interface: Self-Assembly Surface Plasmon Structures for Surface-Enhanced Raman Scattering Detection. *Langmuir* **2019**, 4626−4633.
(21) Xu, K. C.; Zhou, R.; Takei, K.; Hong, M. H. Toward Flexible Surface-Enhanced Raman Scattering (SERS) Sensors for Point-of-Care Diagnostics. *Adv. Sci.* **2019**, *6*, No. 1900925.
(22) Lin, S.; Lin, X.; Song, X. Y.; Han, S.; Wang, L.; Hasi, W. Fabrication of flexible paper-based Surface-enhanced Raman scattering substrate from Au nanocubes monolayer for trace detection of crystal violet on shell. *J. Raman Spectrosc.* **2019**, *50*, 1074−1084.
(23) Briner, W. The Toxicity of Depleted Uranium. *Int. J. Environ. Res. Public Health* **2010**, *7*, 303−313.
(24) Bleise, A.; Danesi, P. R.; Burkart, W. Properties, use and health effects of depleted uranium (DU): a general overview. *J. Environ. Radioact.* **2003**, *64*, 93−112.
(25) Burns, P. C. U^{6+} minerals and inorganic compounds: Insights into an expanded structural hierarchy of crystal structures. *Can. Mineral.* **2005**, *43*, 1839−1894.
(26) Burns, P. C.; Ewing, R. C.; Hawthorne, F. C. The crystal chemistry of hexavalent uranium: Polyhedron geometries, bond-valence parameters, and polymerization of polyhedra. *Can. Mineral.* **1997**, *35*, 1551−1570.
(27) Burns, P. C.; Miller, M. L.; Ewing, R. C. U^{6+} minerals and inorganic phases: A comparison and hierarchy of crystal structures. *Can. Mineral.* **1996**, *34*, 845−880.
(28) Domingo, J. L. Reproductive and developmental toxicity of natural and depleted uranium: a review. *Reprod. Toxicol.* **2001**, *15*, 603−609.
(29) Xin, W.; Yang, J. M.; Li, C.; Goorsky, M. S.; Carlson, L.; De Rosa, I. M. Novel Strategy for One-Pot Synthesis of Gold Nanoplates on Carbon Nanotube Sheet as an Effective Flexible SERS Substrate. *ACS Appl. Mater. Interfaces* **2017**, *9*, 6246−6254.
(30) Aysun, K.; Maya, K.; Gulsen, A.; Mehmet, K.; Sebastian, W. H. Inexpensive and Flexible SERS Substrates on Adhesive Tape Based on Biosilica Plasmonic Nanocomposites. *ACS Appl. Nano Mater.* **2018**, *9*, 5316−5326.
(31) Brugge, D.; Buchner, V. Health effects of uranium: new research findings. *Rev. Environ. Health* **2011**, *26*, 231−249.
(32) Wang, G. L.; Yi, R. H.; Zhai, X. T.; Bian, R. J.; Gao, Y. Q.; Cai, D. Y.; Liu, J. Q.; Huang, X.; Lu, G.; Li, H.; Huang, W. A flexible SERS-active film for studying the effect of non-metallic nanostructures on Raman enhancement. *Nanoscale* **2018**, *10*, 16895−16901.
(33) Brugge, D.; Buchner, V. Health effects of uranium: new research findings. *Rev. Environ. Health* **2011**, *26*, 231−249.
(34) Liu, J. W.; Brown, A. K.; Meng, X. L.; Cropek, D. M.; Istok, J. D.; Watson, D. B.; Lu, Y. A catalytic beacon sensor for uranium with parts-pertrillion sensitivity and millionfold selectivity. *Proc. Natl. Acad. Sci. U.S.A.* **2007**, *104*, 2056−2061.
(35) Feng, M. L.; Gu, C. M.; Sun, Y. P.; Zhang, S. Y.; Tong, A. J.; Xiang, Y. Enhancing Catalytic Activity of Uranyl-Dependent DNAzyme by Flexible Linker Insertion for More Sensitive Detection of Uranyl Ion. *Anal. Chem.* **2019**, *91*, 6608−6615.
(36) Panich, S.; Wilson, K. A.; Nuttall, P.; Wood, C. K.; Albrecht, T.; Edel, J. B. Label-Free Pb(II) Whispering Gallery Mode Sensing Using

Self-Assembled Glutathione-Modified Gold Nanoparticles on an Optical Microcavity. *Anal. Chem.* **2014**, *86*, 6299−6306.
(37) He, Y.; Yang, X.; Yuan, R.; Chai, Y. Q. "Off" to "On" Surface-Enhanced Raman Spectroscopy Platform with Padlock Probe-Based Exponential Rolling Circle Amplification for Ultrasensitive Detection of MicroRNA 155. *Anal. Chem.* **2017**, *89*, 2866−2872.
(38) Radi, A. E.; Sanchez, J. L. A.; Baldrich, E.; O'Sullivan, C. K. Reagentless, Reusable, Ultrasensitive Electrochemical Molecular Beacon Aptasensor. *J. Am. Chem. Soc.* **2006**, *128*, 117−124.
(39) Huang, Y. S.; Ma, Y. L.; Chen, Y. H.; Wu, X. M.; Fang, L. T.; Zhu, Z.; Yang, C. Y. Target-Responsive DNAzyme Cross-Linked Hydrogel for Visual Quantitative Detection of Lead. *Anal. Chem.* **2014**, *86*, 11434−11439.

https://dx.doi.org/10.1021/acs.langmuir.9b03845
Langmuir 2020, 36, 2930−2936