Journal of Colloid and Interface Science 493 (2017) 249–256

Contents lists available at ScienceDirect

Journal of Colloid and Interface Science

journal homepage: www.elsevier.com/locate/jcis

Tuning DNA adsorption affinity and density on metal oxide and phosphate for improved arsenate detection

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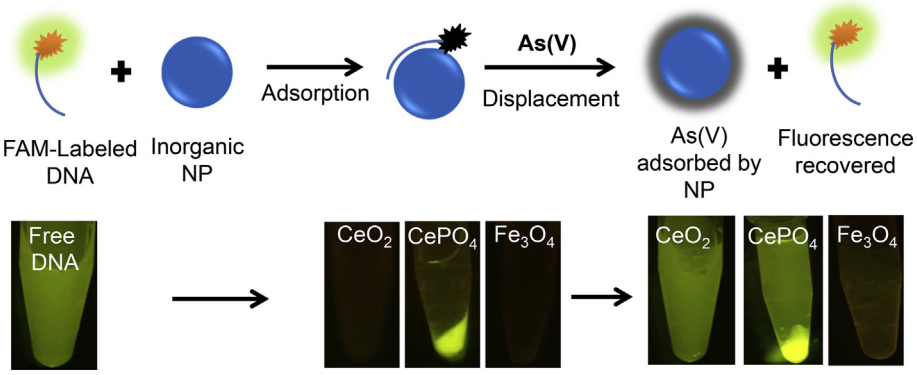
GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 7 November 2016
Revised 9 January 2017
Accepted 10 January 2017
Available online 11 January 2017

Keywords:
Adsorption
Oxides
DNA
Arsenic
Nanoceria

ABSTRACT

Arsenic (As) contamination in groundwater presents a major health and environmental concern in developing countries. Typically, As is found in two oxidation states. Most chemical tests for inorganic arsenic are focused on As(III), and few have been developed for As(V). We are interested in developing biosensors for As(V) based on its similarity with phosphate. Building upon previous work involving DNA-capped Fe_3O_4 nanoparticles for As(V) detection, we investigated two other nanomaterials: CeO_2 and $CePO_4$ in terms of DNA adsorption and As(V) induced DNA desorption. Fluorescently labeled DNA is physically adsorbed to the surface sites on the nanoparticle surface *via* its phosphate backbone. In the cases of CeO_2 and Fe_3O_4, the fluorescence was quenched due to electron transfer, whereas for the insulating $CePO_4$, no quenching was observed. Arsenate, being similar to phosphate, can also bind to the surface of the nanoparticles and displace the DNA, increasing the fluorescence signal. The length and sequence of DNA were systematically studied. Using this method, CeO_2 performed significantly better than Fe_3O_4, lowering the detection limit by almost 10-fold. In addition, for CeO_2 and $CePO_4$, using shorter DNA was more effective for As(V) detection than using the longer DNA since they both adsorb DNA more tightly than Fe_3O_4 does. Overall, CeO_2 has the best performance since it has an intermediate adsorption affinity of DNA, while $CePO_4$ adsorbs DNA too strongly.

1. Introduction

Inorganic arsenic (As) has two common oxidation states: arsenate (As(V)) and arsenite (As(III)). Arsenate is similar to phosphate

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http://dx.doi.org/10.1016/j.jcis.2017.01.037
0021-9797/

(PO_4^{3-}) in terms of size, pK_a, and especially metal binding affinity as indicated by the similar solubility products of their metal salts [1,2]. Unlike PO_4^{3-}, however, As(V) (as well as As(III)) is very toxic [3–6], leading to cancer, heart disease, and diabetes. The World Health Organization (WHO) has stipulated that the maximum allowed concentration of arsenic in a public drinking water supply is 10 μg/L or ca. 135 nM. Typically, As(V) detection is carried out using instrumental analysis, such as mass spectrometry and high performance liquid chromatography (HPLC) [7–10]. These methods often require expensive equipment and a long turnaround time. Therefore, they are not suited for low-income areas or for on-site and real-time detection.

Many chemical and biological sensors have been developed to detect As(III) based on its redox properties and strong thiophilicity [11–16]. While it is more challenging to detect As(V), a few sensors have also been developed, including those based on polymer hydrogels [17], small molecules [18], gold nanoparticles [19–21], and bimetallic NPs [22,23]. A few kits are commercially available for arsenic and they rely on the reduction of As(III) species in solution by zinc to form arsine gas (AsH_3). Typically, arsine would react with the test strip to produce a color. Studies have shown that these kits are quite unreliable [24,25]. Therefore, there is still a need to develop better arsenic sensors.

Recently, there has been significant interest in using nanomaterials for analytical applications. Nanomaterials in general have a high specific surface area and may offer high sensitivity [26,27]. At the same time, using DNA as probes offers the advantage of high programmability [28–32]. Our group reported fluorescent-DNA-loaded Fe_3O_4 NPs for As(V) detection [33,34]. Due to the small sample volume needed for detection, the cost of DNA is well below 10 cent per assay. DNA adsorbs on Fe_3O_4 NPs mainly via its phosphate backbone. Arsenate was detected based on its displacement of the adsorbed DNA. Since each DNA molecule carries one fluorophore, in theory, shorter DNA should offer higher sensitivity as they might be adsorbed with a higher density and should be more easily desorbed. However, longer DNA was required to achieve a sufficient affinity with the Fe_3O_4 surface for a stable background. Under optimized conditions, the detection limit using this method was 300 nM As(V), which was still higher than the WHO guideline.

We reason that the sensor performance might be improved by increasing DNA adsorption affinity and thus shorter DNA can be used to. At the same time, adsorption cannot be too strong so that displacement by As(V) can still take place. Thus, the arsenic detection system might provide an ideal platform for studying adsorption affinity and sensor signaling. One idea to increase the adsorption affinity is to test other nanomaterials. To still rely on DNA phosphate binding, we reason that metal oxides or phosphates containing hard Lewis acids such as cerium might be used [35]. In this study, we compare three types of nanomaterials by exploring also CeO_2 and $CePO_4$, in addition to Fe_3O_4, for DNA adsorption and ultimately As(V) detection. CeO_2 has been previously used to adsorb DNA [34–36] and for other bio-related applications [37,38], while $CePO_4$ has not been studied on this front. We herein quantitatively demonstrate the interplay between DNA adsorption affinity and arsenate detection sensitivity using these three materials.

2. Experimental methods

2.1. Chemicals

CeO_2 NPs were from Sigma-Aldrich as a 20 wt.% dispersion in 2.5% acetic acid. Fe_3O_4 NPs (purity: 97%, average particle size 50–100 nm), cerium(III) chloride heptahydrate (purity: ⩾98%), sodium arsenate dibasic heptahydrate (purity: ⩾98%), sodium (meta) arsenite (purity: ⩾90%), technical grade humic acid were also from Sigma-Aldrich. Sodium phosphate dibasic anhydrous (purity: 100%) was purchased from VWR Canada. All the DNA samples were from Integrated DNA Technologies (Coralville, Iowa) and diluted to a 10 μM stock solution. Mass spectrometry shows only labeled DNA peaks, suggesting a nearly 100% labeling efficiency. These included FAM-C_5 (FAM-CCCCC), FAM-C_{15}, FAM-A_5, and FAM-A_{15}.

2.2. Preparation of $CePO_4$ NPs

In a typical synthesis, 5 mL of 100 mM $CeCl_3$ (final concentration: 50 mM) was mixed with 1 mL of 50 mM Na_2HPO_4 (final concentration: 10 mM) in a vial while stirring. The volume was adjusted to 10 mL followed by the addition of HCl to adjust to pH 3. After incubation for 20 min, the sample was washed *via* centrifugation several times with Milli-Q water before being dispersed in buffer (10 mM HEPES, pH 7.6).

2.3. Dynamic light scattering (DLS)

DLS for size and ζ-potential measurements were performed on a Malvern Zetasizer Nano 90 at 25 °C with a NP concentration of 10 μg/mL and a scattering angle of 90°. ζ-potential measurements were performed in 10 mM pH 7.6 HEPES buffer.

2.4. Transmission electron microscopy (TEM)

Transmission electron microscopy (TEM) was performed using a Phillips CM-10 microscope at 100 kV. One drop of diluted sample (10 μg/mL) was placed on a holey-carbon grid and allowed to dry overnight before imaging.

2.5. Fluorescence spectroscopy

Fluorescence spectroscopy was performed on a Varian fluorimeter. The excitation wavelength of the FAM dye was set at 495 nm and emission spectra were scanned from 505 nm to 600 nm. Typically, 1 mL of solution was placed in a quartz cuvette before the measurement. For CeO_2 and Fe_3O_4, As(V) was added directly to the DNA loaded NPs in the cuvette, and mixed before measurement. For $CePO_4$, As(V) was added to the sample in a microcentrifuge tube and centrifuged at 6000 rpm for 30 s before measuring the fluorescence of the supernatant.

3. Results and discussion

3.1. Sensing arsenate by competitive adsorption

The signaling principle of our sensors exploits the tendency of DNA to adsorb to metal oxides (Fig. 1). A carboxyfluorescein (FAM)-labeled DNA probe is first incubated with a NP, and the fluorescence might be quenched. For CeO_2 and Fe_3O_4 NPs, we previously already demonstrated that they interact with the backbone phosphate of DNA for adsorption (Fig. 1B) [33–35]. These materials contain hard Lewis acids such as iron and cerium, and they prefer the hard phosphate ligand. Like DNA, arsenate has a strong affinity to their surfaces and would displace the adsorbed DNA from the NPs, resulting in increased fluorescence signal (Fig. 1C) [35]. In this work, we want to quantitatively compare the adsorption affinity of a few related materials to optimize sensing and understand the fundamental surface reactions.