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Label-free sensing of pH and silver nanoparticles using an "OR" logic gate

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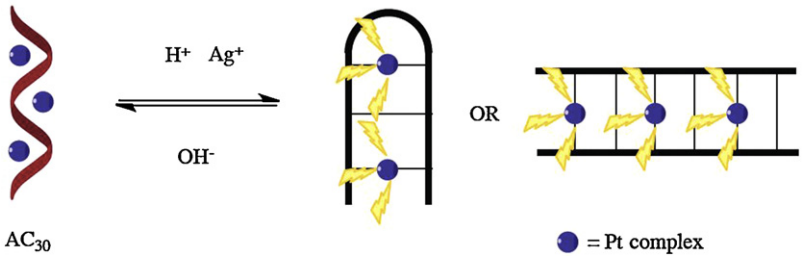
HIGHLIGHTS

- A DNA logic gate for silver nanoparticles and pH has been constructed.
- A platinum(II) complex produces a luminescence response to the analyte.
- The logic gate performs "OR" operations with a switch-on luminescent output.
- The system selectively detects nanomolar silver nanoparticles in aqueous solution.

GRAPHICAL ABSTRACT



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ABSTRACT

Many natural phenomena are associated with the presence of two or more separate variables. We report here an "OR" DNA logic gate based on a luminescent platinum(II) switch-on probe for silver nanoparticles and pH, both of which may be considered putative indicators of pollution. The modulation of metal complex/double-stranded DNA complex phosphorescence by Ag^+ and H^+ was used to construct a simple, rapid and label-free method for the label-free detection of pH and nanomolar Ag^+ ions and nanoparticles in aqueous solutions with high selectivity.

1. Introduction

Silver (Ag^+) ions and silver nanoparticles (AgNPs) have found increasing applications in consumer products such as detergents, antibacterials and wound dressings, raising concerns over their potential toxicity and bioaccumulation in our environment. Ag^+ ions are assigned to the highest toxicity class in heavy metal pollution [1], while AgNPs are known to exhibit adverse effects on prokaryotes, invertebrates and fishes in the aquatic environment [2,3]. Atomic absorption and plasma emission spectroscopy methods commonly used to detect silver are often expensive and time-consuming in practice, and are unsuitable for in-field detection of heavy metal ion contamination. Although luminescent detection methods for acutely toxic heavy metal ions such as mercury and lead have been widely reported, there have been comparatively fewer reports on the detection of Ag^+ ions and AgNPs using luminescent probes [4–6]. Meanwhile, acid rain formed from nitrogen oxide and sulfur dioxide pollutants represents a serious environmental problem due to their impacts to terrestrial and aquatic biological lifeforms [7].

Many phenomena in different fields are modulated by the presence of two or more independent variables. For example,

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intracellular H^+ and Na^+ concentrations are elevated in tissues of certain tumors compared to normal tissues [8]. Renal failure is associated with enhanced levels of urea, potassium and creatinine [9]. Chemical logic gates capable of responding to multiple sensory inputs simultaneously could form the basis of "smart" detection technologies that give single, distinct outputs depending on the presence or absence of various input signals. In particular, DNA logic gates have received wide attention due to the fascinating diversity of nucleic acid structures and functions that can be potentially harnessed to perform logic operations for molecular sensors, nanocomputers or nanomachines [10]. Willner and co-workers developed a DNAzyme logic gate capable of performing AND and OR operations with UO_2^{2+} and Mg^{2+} ion as inputs and a colorimetric output [11]. The group of Willner also developed AND and OR logic gates for Hg^{2+} and Ag^+ ions based on DNA-functionalized quantum dots [12]. Sugimoto and co-workers reported a G-quadruplex-based OR logic gate responding to H^+ and K^+ ions as inputs [13]. Wang et al. have constructed a DNAzyme-based INHIBIT logic gate for K^+ and Pb^{2+} ions that gave a colorimetric signal as the output [14]. Our group previously reported a label-free DNA based OR logic gate for H^+ and K^+ ions using crystal violet (CV) as signal transducer [15]. These examples demonstrate the application of DNA logic gates for the simultaneous detection of metal or hydrogen ions, based on the cation-induced modulation of DNA structure or activity. Encouraged by these successes, we endeavored to construct a DNA logic gate that could respond simultaneously to AgNPs and H^+ ions. To best of our knowledge, no such DNA logic gate has yet been reported. As both low pH and the presence of Ag^+ or AgNPs may be considered as indicators of pollution, such a logic gate could find potential application as a rapid sensor for in-field estimation of water or soil quality without the need for expensive sensing devices.

Ono et al. have reported that cytosine-rich oligonucleotides could be induced to form a hairpin structure stabilized by mismatched C–Ag(I)–C base pairs, and developed a probe for aqueous Ag^+ ions using a fluorescently-labelled cytosine-rich molecular beacon [16]. Our group has also reported label-free variations of the oligonucleotide-based approach for the detection of heavy metal ions by utilizing a luminescent transition metal complex [17,18]. Meanwhile, H^+ ions could induce the conversion of adenine-rich single-stranded DNA into a DNA duplex, *via* the formation of AH^+–H^+A base pairs as demonstrated previously [19]. Inspired by these works, we envisaged that a label-free OR logic gate could be constructed with high sensitivity and specificity based on the Ag^+ or H^+ ion-induced formation of duplex DNA.

Luminescent metal complexes have been widely used for the detection of DNA and other biomolecules [20–35]. In this study, a luminescent non-toxic platinum(II) metallointercalator previously developed by our group [17,18], $[Pt(C^N^N)(4\text{-appt})]^+$ (**1**, C^N^N = 6-phenyl-2,2′-bipyridine; 4-appt = 2-amino-4-phenylamino-6-(4-pyridyl)-1,3,5-triazine) platinum(II) complex

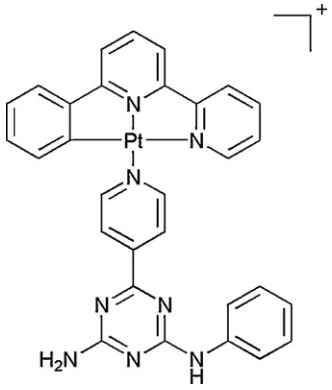
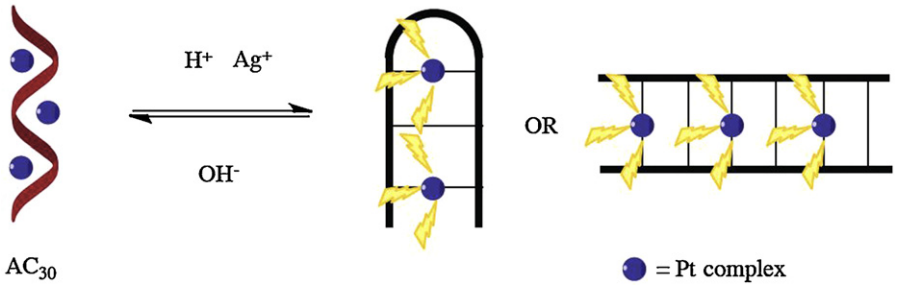


Fig. 1. Chemical structure of platinum complex **1**.

(Fig. 1) was applied for the construction of a DNA logic gate. The present luminescent DNA "OR" logic gate offers several advantages compared to other DNA-based logic gates. (1) It does not require oligonucleotide modification, such as fluorescent labeling or linking to a signal-transducing electrode, which provides simplicity and can greatly reduce the cost of the assay. (2) Luminescent metal complexes possess a long phosphorescence lifetime, allowing the luminescent readout to be easily distinguished from endogenous fluorophores using time-resolved microscopy, which allows it to be used in highly fluorescent environments. (3) The system can be easily reset by the addition of suitable chemical reagents. We present herein the construction of a luminescent DNA-based "OR" logic gate for H^+ and Ag^+ ions using a platinum(II) intercalator as a signal reporter and demostration of its application for the simultaneous detection of H^+ and Ag^+ ions in buffer solution.

The design of our "OR" logic gate operation is depicted in Scheme 1. The adenine and cytosine-rich oligonucleotide AC_{30} (5′-AAAAACCCCCAAAAACCCCCAAAAACCCCC-3′) would be expected to exist predominantly as a single-stranded conformation in solution in the absence of H^+ or Ag^+ ions. The platinum(II) complex is unable to intercalate into the single-stranded DNA, and is non-emissive due to non-radiative decay of the excited state by complex–solvent interactions [17]. The addition of either H^+ or Ag^+ will induce a single strand-to-duplex transition based on the formation of mismatched adenine or cytosine base pairs, respectively. We presume that this could take the form of a unimolecular hairpin or an intermolecular AC_{30}–AC_{30} duplex (Scheme 1). Intercalation of the metal complex **1** into the duplex structure protects the $[Pt(C^N^N)]$ moiety from the aqueous buffer environment, suppressing non-radiative decay and enhancing phosphorescence emission. Detection of AgNPs could be achieved by treatment with H_2O_2 and H_3PO_4, promoting the oxidation disintegration of the nanoparticles. The subsequent release of the Ag^+ ions stabilizes the duplex structure through formation of the cytosine–Ag–cytosine mismatch, allowing intercalation of **1** and resulting in an emission



Scheme 1. Schematic illustration of the DNA "OR" logic gate. Addition of either input (H^+ or Ag^+ ions) results in intercalation of platinum(II) complex **1** producing a switch-on phosphorescence response.