Tetrahedron 73 (2017) 4950–4954

Contents lists available at ScienceDirect

Tetrahedron

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

A modular self-assembled sensing system for heavy metal ions with tunable sensitivity and selectivity

Subhabrata Maiti, Leonard J. Prins*

Department of Chemical Sciences, University of Padova, Via Marzolo 1, 35131, Padova, Italy

ARTICLE INFO

Article history:
Received 14 March 2017
Received in revised form
2 May 2017
Accepted 8 May 2017
Available online 10 May 2017

Keywords:
Gold nanoparticles
Chemosensor
Self-selection
Self-assembly
Displacement assay
Heavy metal ions

ABSTRACT

Here we describe a self-assembled sensing system composed of three separate modules: gold nanoparticles, a reporter element, and a recognition element. The gold nanoparticles serve as a multivalent platform for the interaction with both the reporter and recognition element and the gold nucleus serves to affect the fluorescent properties of the reporter. The reporter element serves for generation of the output signal. The recognition element serves to make the assay selective. The working principle is that the interaction of the analyte with the recognition element leads to an increased affinity for the gold nanoparticle, which causes a displacement of the reporter and a turn-ON of fluorescence. It is shown that the modular nature of the system permits straightforward tuning of the dynamic detection range, the sensitivity, and the selectivity, simply by changing the recognition module. The system can detect Hg^{2+} and Ag^{+} metal ions at nanomolar concentrations in aqueous buffer.

1. Introduction

The development of innovative sensing systems for the detection of analytes plays a crucial role in, amongst others, molecular diagnostics, the detection of environmental pollution, food contamination, and counter-terrorism measures.[1–6] Intensive research over the past decades has led to the development of a wide variety of chemosensors able to convert the presence of low concentrations of analytes into a detectable and easily readable output signal (optical, electrical, thermal etc.).[7–13] To favour practical applications, these systems have often been designed based on criteria of robustness and simplicity. However, there is a current interest in developing sensing systems of higher complexity, because of features that are difficult to obtain using simple molecules.[14–17] In particular, attention is being paid to the use of self-assembly as a design principle because it enables a modular approach through which the selectivity of the systems towards different analytes can be tuned in a straightforward manner simply by changing the building blocks.[18–22]

Here we report a self-assembled fluorescence turn-ON sensing system that is able to detect the heavy metal ions Hg^{2+} and Ag^{+} at nanomolar concentrations in water. Although it is worth mentioning that the detection of toxic heavy metals is extremely important from an environmental as well as a health perspective,[23–26] it is emphasized that the main focus of this work is on demonstrating the novel features offered by a self-assembly approach to chemosensor development. It will be shown that the different modules of the sensing system can be independently changed to alter the selectivity, sensitivity and dynamic detection range of the system,[27] while maintaining the same fluorescence output signal. In addition, this work provides a relevant implementation of our recently developed protocol for dynamic combinatorial chemistry (DCC) on a multivalent nanoparticle surface.[28]

2. Results and discussion

The use of Au NP **1** for the detection of peptides, nucleotides, and small molecules has been reported by our group in recent years.[11,29–31] Au NP **1** is composed of a gold nucleus with a diameter of around 1.6 (±0.3) nm covered with a monolayer of alkyl thiols terminating with a 1,4,7-triazacyclononane (TACN)·Zn^{2+} complex (Fig. 1). Fluorescent displacement assays have been developed based on the displacement of a negatively charged fluorescent indicator from the Au NP **1** surface by analytes able to compete with binding to the surface. Recently, we have reported on a new signal transduction pathway relying on the formation of a ternary complex between two thymidine nucleotides and Hg^{2+} metal ions with an increased affinity for Au NP **1** compared to the separate nucleotides.[21,25] An interesting feature of that study was that the

* Corresponding author.
E-mail address: leonard.prins@unipd.it (L.J. Prins).

http://dx.doi.org/10.1016/j.tet.2017.05.028
0040-4020/

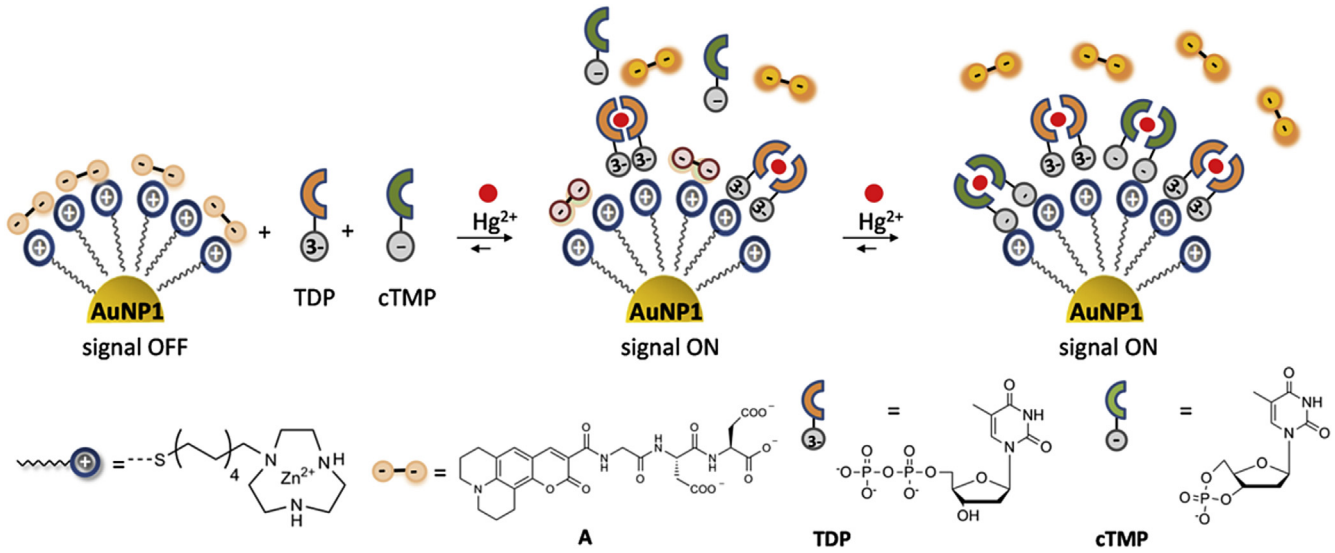

Fig. 1. Schematic representation of the signal generation process upon the addition of Hg^{2+} to the system composed of Au NP **1**, probe **A**, and both TDP and cTMP. Low concentrations of Hg^{2+} result in formation of the ternary complex TDP·Hg^{2+}·TDP. As soon as TDP is depleted, further amounts of Hg^{2+} are complexed with cTMP. This way the dynamic sensing regime of the system is enlarged covering a Hg^{2+} concentration range low nanomolar to high micromolar.

multivalent NP surface drives the equilibrium towards the more stable thermodynamic complex and self-selects the Hg^{2+} complex with the highest affinity. Indeed, it was observed that the addition of Hg^{2+} to a mixture of TMP and cTMP complex in aqueous medium in the absence of Au NP **1** led to the formation of all possible ternary complexes (TMP·Hg^{2+}·TMP, TMP·Hg^{2+}·cTMP, cTMP·Hg^{2+}·cTMP), but with an equilibrium composition shifted towards the more stable cTMP·Hg^{2+}·cTMP complex. However, the presence of Au NP **1** shifted the equilibrium entirely to the other side and exclusive formation of the TMP·Hg^{2+}·TMP complex was observed. This shift is driven by the high density of negative charges in this complex which cause a stronger interaction with the multivalent cationic surface of the Au NP **1**. This study showed that the affinity can be modulated simply by changing the signal transduction unit (the phosphates) without altering the recognition unit (the nucleobase). This stimulated us to investigate the possibility of exploiting the simultaneous use of different nucleotides to increase the dynamic detection range, which would emphasize the unique possibility offered by the signal transduction pathway that is operative in this self-assembled sensing system.

2.1. Dynamic detection range

Previous studies had shown that the sensitivity of the system is much higher when TDP is used (compared to TMP or cTMP), because of the increased number of negative charges.[21] We presumed that the combination of TDP and cTMP in the same system would enlarge the dynamic detection range with TDP operating in the nanomolar regime and cTMP in the micromolar regime. The anionic probe **A** was selected because of the following reasons: i) the high quantum yield of coumarin343 (λ_{ex} = 445 nm; λ_{em} = 493 nm) is advantageous for creating a response even at low concentrations, ii) the carboxylate-probe is readily displaced by phosphate competitors, and iii) the fluorescence properties of the probe are not affected by the analytes.[28]

The detection range for TDP and cTMP separately was determined by measuring the fluorescence intensity after the addition of increasing amounts of Hg^{2+} to a buffered aqueous solution containing Au NP **1** ([TACN·Zn^{2+}] = 20 ± 1 μM), **A** (7.3 μM) and either TDP (16 μM) or cTMP (800 μM). A much higher concentration of cTMP was used compared to TDP, because a much higher concentration of the cTMP·Hg^{2+}·cTMP complex is required to elicit a displacement of probe **A** from Au NP **1**. For TDP the fluorescence intensity started to increase already after the addition of 20 nM of Hg^{2+} and continued until a maximum intensity was reached at around 7 μM of Hg^{2+}, which corresponds roughly to the concentration at which all free TDP has been depleted (Fig. 2a). On the other

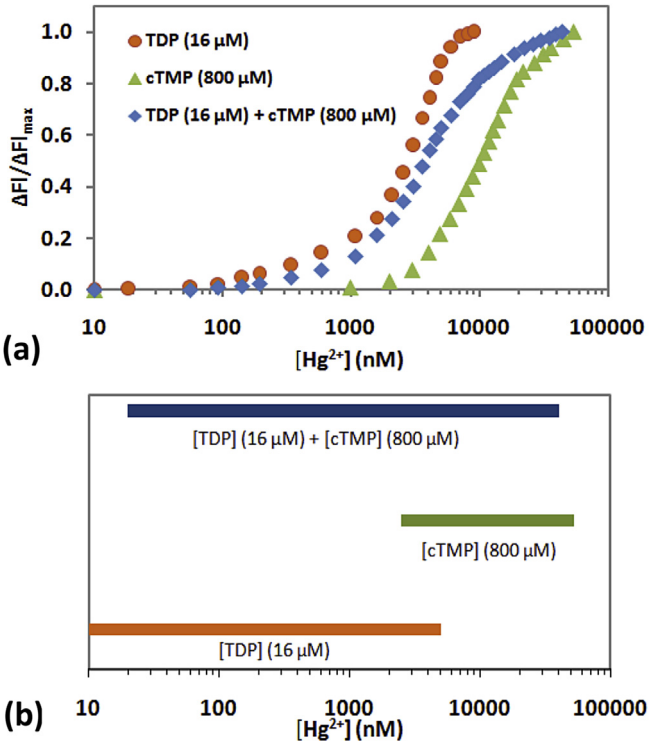

Fig. 2. (a) Normalized change in fluorescence intensity (a.u.) at 493 nm as a function of the concentration of Hg^{2+} added to a solution containing Au NP **1**, probe **A**, and TDP (orange), cTMP (green), or a mixture of TDP and cTMP (blue). Experimental conditions: [TACN·Zn^{2+}] = 20 ± 1 μM; [**A**] = 7.3 μM, [TDP] = 16 μM, [cTMP] = 800 μM, [HEPES] = 10 mM, pH 7.0, T = 37 °C, fluorescence slit width = (2.5/5) nm. (b) Hg^{2+}-detection range in the presence of TDP (orange), cTMP (green), or a mixture of TDP and cTMP (blue).