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## COMMUNICATION

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## A dual FRET based fluorescent probe as a multiple logic system

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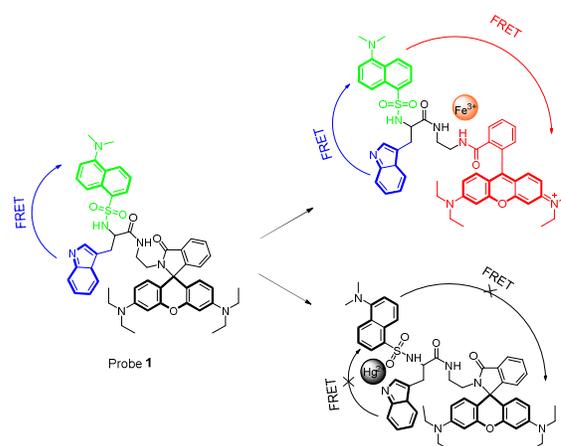
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**A new fluorescent probe with a unique sequential dual FRET process was designed and constructed. This probe showed distinguishing responses towards Fe<sup>3+</sup> and Hg<sup>2+</sup>, making it an ideal candidate for multiple logic operations at the molecular level.**

Since the first influential exploration by Silva demonstrating that fluorescent probes can serve as molecular logic gates,<sup>1</sup> the development of such molecular systems capable of performing binary arithmetic and logical operations has attracted continuous attentions from academic researchers in chemistry and biology. In the past two decades, a large number of excellent works related to this field has been achieved.<sup>2</sup> To date, there have been important advances toward finding practicality in fluorescent logic gates, such as the AND, OR, NOR, INHIBIT, XOR, YES, NOT, and XNOR logic gates. Besides their potential applications in information processing and computing at the molecular level, their novel applications in the design of smart supramolecular materials,<sup>3</sup> in drugs delivery,<sup>4</sup> and in clinical diagnostics<sup>5</sup> have also been established. However, most of the logic systems rely on only one output mode.<sup>6</sup> Recent interest has been mainly focused on the construction of molecules with multiple fluorescent output logic functions that can be modulated by multi-input combinations. This inspired us to fabricate a logic gate system that can utilize fluorescence via metal ions.<sup>2d,7</sup> Such basic logic gates, programmed at a single molecular level, have possible implications in the development of electronic and photonic devices.

Taking these factors into account, we present here our idea for the construction of a novel fluorescent probe **1**, possessing sequential dual FRET processes for multiple logic gate operations via the response signals of metal ions. The chemical structure of probe **1** is documented in Scheme 1. As described, probe **1** is composed of a dansylamide group and a rhodamine

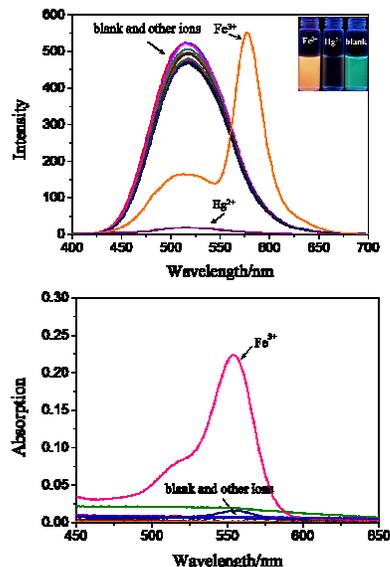
B moiety, a well known fluorophore pair for the FRET process,<sup>8</sup> which were further covalently connected by a tryptophane unit.



**Scheme 1.** Chemical structure of probe **1** and the proposed multiple sensing mechanism based on sequential dual FRET.

The design concepts of this probe are described as following. First, as shown in Fig. S1, the emission spectra of the indole group (residue of tryptophane) has significant overlap with the absorbance of the dansylamide group, which means that they are well matched as energy donor and acceptor.<sup>9</sup> As a result, a FRET process between them is possible. Meanwhile, a similar situation is also observed in the case of dansylamide and rhodamine groups, where the emission of the dansylamide group shows a large overlap with the absorbance of the rhodamine moiety. Thus, a sequential dual FRET of probe **1** from the indole group to the rhodamine moiety via the dansylamide unit is expected. Second, in the case of probe **1**, the spirolactam ring of rhodamine can be converted into its open-ring form in the presence of certain metal ions, with the

characteristic turn-on fluorescence emission and red color.<sup>8</sup> Thus, a dual FRET process of probe **1** induced by metal ions is reasonable. Moreover, as a metal ligand, the indole group could regulate the coordination behaviours of probe **1** with different metal ions, making multiple responses possible. Notably, to our knowledge, there has been no report on such a dual FRET based fluorescent probe to date.

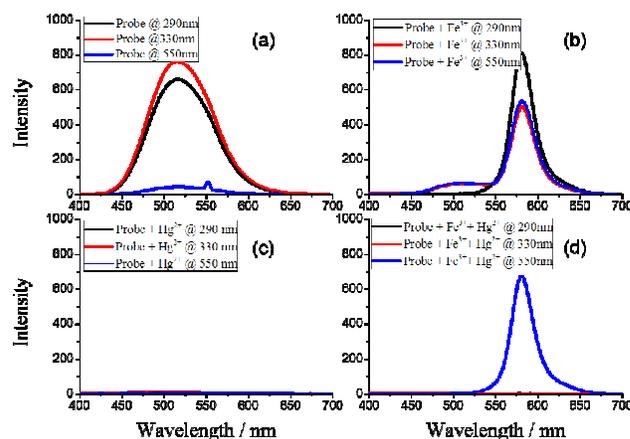


**Fig. 1.** Fluorescence and absorbance spectra of probe **1** (10  $\mu\text{M}$ ) upon addition of various metal ions (10  $\mu\text{M}$ ) in ethanol, ( $\lambda_{\text{ex}} = 290 \text{ nm}$ ). Inset: fluorescent responses of probe **1** (10  $\mu\text{M}$ ) in the presence of 1 equiv. of  $\text{Fe}^{3+}$  and  $\text{Hg}^{2+}$ , respectively, pictures were captured under 365 nm UV lamp.

To confirm these above mentioned hypotheses, probe **1** was facilely synthesized by uncomplicated reactions. Its fluorescent property was examined first. As expected, probe **1** gave a bright green fluorescent emission with a peak at 510 nm, which was attributed to the characteristic emission of the dansylamide group. No red emission corresponding to rhodamine was found, which confirmed that the rhodamine moiety of probe **1** was in its spirolactam-ring form, which is non-fluorescent and colourless. Next, the selective responses of probe **1** (10  $\mu\text{M}$ ) to various metal ions, including  $\text{Ag}^+$ ,  $\text{Al}^{3+}$ ,  $\text{Ba}^{2+}$ ,  $\text{Ca}^{2+}$ ,  $\text{Fe}^{3+}$ ,  $\text{Hg}^{2+}$ ,  $\text{K}^+$ ,  $\text{Mg}^{2+}$ ,  $\text{Ni}^{2+}$ ,  $\text{Pb}^{2+}$ ,  $\text{Zn}^{2+}$ , and  $\text{Cu}^{2+}$ , were investigated using fluorescence and absorbance spectra. As shown in Fig. 1, upon addition of  $\text{Fe}^{3+}$ , a dramatic fluorescence response was observed, in which a new emission peak at 580 nm emerged, accompanied by an obvious fluorescent color change in probe **1** from green to jacinth (Fig. 1 inset). Meanwhile, a remarkable change was also observed in the absorbance spectra, where a new peak was formed at 550 nm. The corresponding colour of probe **1** also changed from colorless to pink, which was easily distinguished by the naked eye (Fig S2). These fluorescent and colorimetric responses were attributed to a conversion from the spirolactam ring form of rhodamine to its open-ring form in the presence of  $\text{Fe}^{3+}$ .<sup>8b</sup> On the other hand, the addition of  $\text{Hg}^{2+}$  caused a complete fluorescence quenching, and no peak was observed around 550 nm in the absorbance spectra, indicating

that the open-ring reaction of the rhodamine moiety did not occur in the presence of  $\text{Hg}^{2+}$ . In contrast, other metal ions could not induce any observable fluorescent or colorimetric changes.

Subsequently, fluorescent titrations with  $\text{Fe}^{3+}$  and  $\text{Hg}^{2+}$  were examined (Fig. S3 and S4). Upon gradual addition of  $\text{Fe}^{3+}$ , the emission intensity at 510 nm decreased with simultaneous gradual appearance of a new emission peak at 580 nm (rhodamine). Notably, the emission intensity reached its maximum after the addition of one equivalent of  $\text{Fe}^{3+}$  (Fig. S3 inset). A Job plot further proves this 1:1 stoichiometry between probe **1** and  $\text{Fe}^{3+}$  (Fig. S5).  $\text{Hg}^{2+}$  titration against probe **1** was also monitored using fluorescence spectra (Fig. S4). Upon gradual addition of  $\text{Hg}^{2+}$ , the emission intensity at 510 nm decreased and this decrease saturated after adding one equivalent of  $\text{Hg}^{2+}$  (Fig. S4 inset). The association constant ( $K_a$ ) for  $\text{Fe}^{3+}$  and  $\text{Hg}^{2+}$  binding with probe **1** was determined to be  $2.66 \times 10^3 \text{ M}^{-1}$  and  $9.29 \times 10^4 \text{ M}^{-1}$ , respectively. The detection limit of fluorescent probe **1** for analysis of  $\text{Fe}^{3+}$  and  $\text{Hg}^{2+}$  was determined from the plot of fluorescence intensity as a function of the concentration of  $\text{Fe}^{3+}$  and  $\text{Hg}^{2+}$  (Fig. S6, S7).<sup>10</sup> Moreover, competition experiments indicated that the detection processes of probe **1** for  $\text{Fe}^{3+}$  and  $\text{Hg}^{2+}$  were not affected by other competitive metal ions (Fig. S8).



**Fig. 2.** Fluorescence spectra of probe **1** (10  $\mu\text{M}$ ) upon irradiation with different corresponding excitations ( $\lambda_{\text{ex}} = 290 \text{ nm}$ , 330 nm, 550 nm, respectively). (a) probe **1** only; (b) probe **1** in the presence of  $\text{Fe}^{3+}$ ; (c) probe **1** in the presence of  $\text{Hg}^{2+}$ ; (d) probe **1** in the presence of both  $\text{Fe}^{3+}$  and  $\text{Hg}^{2+}$ .

As mentioned above, probe **1** displayed a distinguishing response towards  $\text{Fe}^{3+}$  and  $\text{Hg}^{2+}$ . To further understand this mechanism, a detailed investigation was conducted, in which probe **1** was excited by using the individual excitation wavelengths of its three fluorophores. For instance, 290 nm corresponds to the excitation wavelength of the indole group, 330 nm represents the excitation wavelength of the dansylamide unit and 550 nm is the excitation wavelength of the rhodamine moiety. The results were described in Fig. 2. As shown in Fig. 2a, when probe **1** was excited at 290 nm and 330 nm respectively, strong green emission peaks at 510 nm with similar intensities were observed. This indicated that a FRET

process occurred from the indole group to the dansylamide unit. In contrast, no emission was observed after excitation at 550 nm. Upon addition of  $\text{Fe}^{3+}$ , new peaks at 580 nm corresponding to the ring-open form of the rhodamine moiety were found with the three individual excitations. The fluorescent intensities were almost equal under excitations at 290 nm and 330 nm, which demonstrated that a sequential dual FRET process occurred from the indole group to the dansylamide unit and then from the dansylamide unit to the rhodamine moiety with the excitation at 290 nm, as shown in Scheme 1. In addition, upon addition of  $\text{Hg}^{2+}$ , no emission peak was observed, which indicated that the  $\text{Hg}^{2+}$  interacted directly with the indole and dansylamide groups and suspended the initial FRET process between them, resulting in fluorescence quenching. In the presence of both  $\text{Fe}^{3+}$  and  $\text{Hg}^{2+}$ , only an emission peak was observed following excitation at 550 nm, and one peak was found after excitation at 290 nm and 330 nm. These results revealed that  $\text{Fe}^{3+}$  did induce a ring-open reaction in the rhodamine group, and  $\text{Hg}^{2+}$  suspended the initial FRET process.

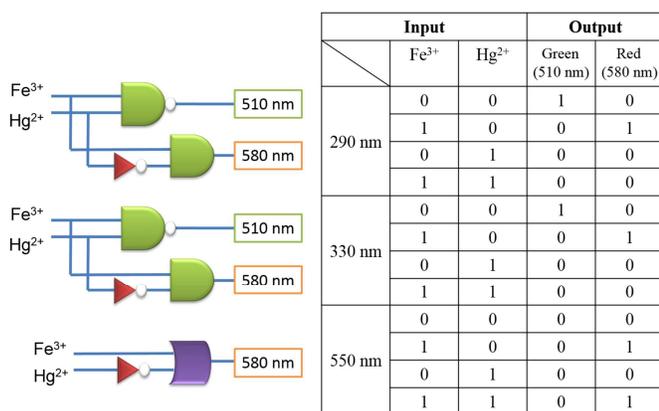


Fig. 3. Multiple logic gates schemes and their corresponding truth values table.

With these satisfactory fluorescent responses in mind, we set out to construct a multiple logic gate system using probe **1**. The corresponding truth values were collected in Fig. 3. As described, with excitation at 290 nm or 330 nm, probe **1** can mimic the INHIBIT logic gate<sup>11</sup> (integrated by combining a NOT, a YES, and an AND gate). By combining with the addition of  $\text{Hg}^{2+}$  and  $\text{Fe}^{3+}$ , two individual outputs with different emissions, i.e. at 510 nm and 580 nm, respectively, were unambiguously observed. In addition, under excitation at 550 nm, probe **1** can serve as a cascading system of NOT and an integrated OR gate with a single output at 580 nm.

In summary, we present here the design and construction of a new fluorescent probe with a unique sequential dual FRET process. This probe showed distinguishing fluorescent responses to  $\text{Fe}^{3+}$  and  $\text{Hg}^{2+}$ .  $\text{Fe}^{3+}$  activated the dual FRET process and resulted in ratiometric and colorimetric responses;  $\text{Hg}^{2+}$  blocked the initial FRET process and caused fluorescent quenching. Moreover, these responses were not affected by other competitive metal ions. Finally, after various satisfactory responses, probe **1** was employed as a multiple logic gate system for multiple tandem logic operations.

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## Notes and references

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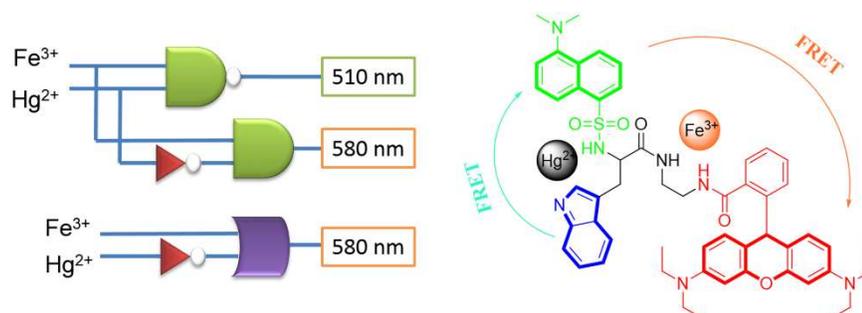
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Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/c000000x/

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## A dual FRET based fluorescent probe as a multiple logic system

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