A Dual-Emitting Two-Dimensional Nickel-Based Metal-Organic Framework Nanosheets: $\text{Eu}^{3+}/\text{Ag}^{+}$ Functionalization Synthesis and Ratiometric Sensing in Aqueous Solution

Yun Shu (✉ shuyun1008@126.com)

Yangzhou University <https://orcid.org/0000-0002-8061-5165>

Tao Dai

Yangzhou University

Qiuyu Ye

Yangzhou University

Dangqin Jin

Yangzhou Polytechnic Institute

Qin Xu

Yangzhou University

Xiaoya Hu

Yangzhou University

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Abstract

Using two-dimensional (2D) nickel-based metal organic framework (Ni-MOF) nanosheets as a matrix, Eu^{3+} and Ag^+ were incorporated to synthesize Ag/Eu@Ni-MOF with double luminescence centers of Eu^{3+} ion (615 nm) and organic ligand (524 nm). And a ratiometric luminescence sensor is constructed based on Ag/Eu@Ni-MOF for sensitive detection of biothiols in aqueous solutions. The dual-emissive fluorescence properties can be tuned by changing the amounts of Ag^+ ions doping. The results of temperature and pH effects on the fluorescence of Ag/Eu@Ni-MOF indicates that the Ag/Eu@Ni-MOF is a temperature-sensitive material and the fluorescence of Ag/Eu@Ni-MOF can keep stable over a wide pH range. Due to the binding of -SH in Cys and GSH with Ag^+ , the ligand luminescence was significantly inhibited by weakening the Ag^+ influence on the energy transfer process in the MOFs. Therefore, ratiometric fluorescent sensing of biomolecular thiols was realized based on the dual-emission Ag/Eu@Ni-MOF. More importantly, the fluorescence color change can be observed with naked eyes to realize visual detection. The ratiometric fluorescent sensor exhibits high performance for Cys and GSH detection with a wide linear range of 5-250 μM and a relatively low detection limit of 0.20 μM and 0.17 μM , respectively. Furthermore, the biothiols content in human serum was determined with satisfactory results. It proves the Ni-MOF nanosheets can be used as a stable matrix for construction luminescent MOFs for the first time, and validate the great potential of Ag/Eu@Ni-MOF as a ratiometric fluorescent probe for point-of-care testing (POCT) in disease diagnosis.

Introduction

Biological thiols such as glutathione (GSH) and cysteine (Cys) are the essential components for efficient operation of life maintenance.[1] The content of thiols at abnormal physiological levels can cause a decrease in immunity and result in diseases.[2] Cysteine is a precursor to the antioxidant glutathione, and its deficiencies can lead to edema, muscle relaxation, liver damage and skin lesions, etc.[3] Glutathione which possesses antioxidant effect can participate in biological transformation, transform harmful poisons in the body into harmless substances, and excrete them out of the body. Severe diseases such as kidney failure, liver cirrhosis, myocardial infarction and Alzheimer, which are related with the content of GSH in the body.[3] Therefore, the high-precision detection of biological thiols is very important methods for physical health assessment and disease prevention.[4, 5, 6] So far, several analytical methods for sensing biomolecular thiols have been established, such as capillary electrophoresis,[7] high performance liquid chromatography (HPLC),[8] mass spectrometry,[9] electrochemical sensing,[10, 11] etc. Above methods have various disadvantages such as high experimentation costs, cumbersome sample preparation methods, etc., making them difficult to be promoted and applied in actual sample testing. However, fluorescence-based methods have been widely considered due to their multiple advantages, including highly selective and sensitive detection, simple experimental methods, cost effectiveness, instant and fast data acquisition for real-time biological sample analysis. Many fluorescent probes have been successfully developed and used in fluorescence detection,[12] such as fluorescent dyes,[13] upconverting nanoparticles,[14] and semiconductor nanocrystals (quantum dots),[15, 16]etc. The

preparation of fluorescent materials/probes with superior fluorescence performance is very important for fluorescence detection.

Metal-organic frameworks (MOFs) are coordination polymers with a highly crystalline structure, composed of metal ions or metal clusters and organic ligands.[17] Luminescent MOFs (LMOFs) have the advantages of inherent crystallinity, adjustable pore size, clear structure, and high degree of functionalization.[18] Therefore, they have the advantages of versatility that inorganic luminescent materials and organic luminescent materials cannot match. In addition to metal ions and organic ligands, the luminescence center of LMOFs can also come from the introduction of different luminescent guests, [19] such as lanthanide ions,[20] quantum dots,[21] dyes,[22] and luminescent complexes,[23] which provides MOFs materials with broader luminescence properties. At present, a large number of LMOFs have been synthesized and used for sensing applications.[24] Zhang *et al.*[25] successfully synthesized ZJU-108 containing fluorescence emission belonging to organic ligand. Based on the singlet energy transfer process from tryptophan to the ligand, ZJU-108 was used as luminescent turn-up sensor for discriminating tryptophan from other natural amino acids in aqueous solution with a detection limit of 42.9 nM. Normally, the sensing function of LMOF sensor with a single emission window is often affected by environmental disturbances such as fluctuations of excitation, intensity of light source, uneven concentration, etc., resulting in quantitative errors.[26] However, the dual-emission ratiometric LMOF sensor could eliminate the influences of apparatus and detection environment with self-calibration function, thus avoiding false response and improving signal-to-noise ratio.[27] LMOF with dual emission centers can be mainly constructed in the following two ways: (1) luminescent guest-luminescent ligand, (2) double luminescent guests. Comparing to other luminescent guests, Lanthanides[28] display a high coordination number, connectivity, and diverse coordination modes, and therefore exhibiting great potential in constructing a wide variety of LMOFs. Zhou *et al.*[29] developed a dual-emitting ratiometric temperature sensor by imparting Eu^{3+} to UiO-bpydc with inherent emission. The Eu^{3+} emission is sensitized by the UiO-bpydc via energy transfer from the ligand to Eu^{3+} . Owing to the back energy transfer (BEnT) between organic linkers and Eu^{3+} , with the temperature increasing, the Eu^{3+} emission declined and the ligand emission increased. Zhang *et al.*[30] prepared $\text{Tb}^{3+}/\text{Eu}^{3+}$ -functionalized bio-MOF-1 containing double emissions belonging to Eu^{3+} and Tb^{3+} for visual colorimetric sensing of dipicolinic acid (DPA) for the first time. The addition of DPA leads to the enhancement of emission intensity of Tb^{3+} (I_{545}) through the energy transfer between ligand and metal. On the contrary, owing to the interruption of energy transfer from Tb^{3+} to Eu^{3+} , the emission intensity of Eu^{3+} (I_{615}) is decreased.

Herein, in this work, through the hydrothermal post-synthesis modification method, Eu^{3+} and Ag^+ are incorporated into 2D Ni-MOF nanosheets respectively to synthesize Ag/Eu@Ni-MOF with double luminescence centres of Eu^{3+} ion (615 nm) and organic ligand (524 nm) for the first time. And a ratiometric luminescence sensor is constructed based on Ag/Eu@Ni-MOF for sensitive detection of various thiol species in aqueous solutions (Scheme 1). The molar ratio of Ag^+ and Eu^{3+} was changed to study its effect on the fluorescence emission, also the effects of temperature and pH on the fluorescence of Ag/Eu@Ni-MOF were investigated. After addition of the thiol species to the double emission luminous

Ag/Eu@Ni-MOF solution, due to the strong binding of Ag^+ with -SH, the emission of organic ligand (524 nm) was significantly inhibited by weakening the Ag^+ influence on the energy transfer process in the MOFs. A highly sensitive and selective ratiometric luminescence sensor was established for detection of biothiols. Furthermore, the thiol species content in human serum was determined. This method for the detection of Cys and GSH can be interpreted by naked eyes to realize visual detection, also the low cost of the reagents in the steps make it very suitable for application in point-of-care testing (POCT).

Experimental

Materials

$\text{Ni}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$, Terephthalic acid (BDC, 99%+), NaOH, N, N-dimethylformamide (DMF, 99%), methanol, arginine (Arg), cysteine (Cys), glutathione (GSH), glutamic acid (Glu), glycine (Gly), histidine (His), phenylalanine (Phe), tryptophan (Trp), tyrosine (Tyr), NaCl, NaNO_3 , and KNO_3 were purchased from Sinopharm Chemical Reagent Co., Ltd (Shanghai, China). $\text{Eu}(\text{NO}_3)_3 \cdot 6\text{H}_2\text{O}$ and AgNO_3 were purchased from Aladdin Reagent Co. Ltd. (Shanghai, China). Human serum samples were obtained from Subei People's Hospital of Jiangsu province.

Preparation of Ni-MOF

To synthesize the nickel-based metal-organic framework, BDC (0.166 g) and $\text{Ni}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$ (0.096 g) were added to DMF (20 mL) and stirred at room temperature until the solid powder was completely dissolved.[31, 32] Then, NaOH aqueous solution (2mL, 0.4 M) was gradually added dropwise to the above-mixed solution, and stirred at room temperature for 30 min. Subsequently, the mixture was transferred to a 50 mL Teflon-lined stainless steel autoclave and heated at 100°C for 8 hours. After cooling to room temperature, the products were centrifuged at 8500 rpm for 5 min, washed with DMF and ethanol three times, and dried under vacuum for 6 h.

Preparation of Eu@Ni-MOF

The luminescent MOF is prepared by modifying Eu^{3+} into the above-mentioned synthesized Ni-MOF. Ni-MOF (50 mg) was added to a solution (10 mL) containing $\text{Eu}(\text{NO}_3)_3 \cdot 6\text{H}_2\text{O}$ (5 mM, 50 mM, 100 mM), then transferred to a single-necked flask equipped with a reflux condenser, and reacted at 60 °C for 24 h.[33] The white powder product was separated by centrifugation at 8500 rpm, washed with deionized water several times, and vacuum dried at 30°C for 6 h.

Preparation of Ag/Eu@Ni-MOF

Similarly, the ratiometric luminescent MOF is prepared by co-modifying Ag^+ and Eu^{3+} into the above-mentioned synthesized Ni-MOF. Ni-MOF (50 mg) was added to a solution (10 mL) containing $\text{Eu}(\text{NO}_3)_3 \cdot 6\text{H}_2\text{O}$ (0.5 mmol) and different contents of AgNO_3 (0.125, 0.25, 0.375, and 0.5 mmol), and then transferred to a single-necked flask equipped with a reflux condenser, react at 60°C for 24 h. The white powder product was separated by centrifugation at 8500 rpm, washed with deionized water several times,

and vacuum dried at 30°C for 6 hours. For convenience, we define the Ag/Eu@Ni-MOF materials synthesized with the molar ratio of $\text{Eu}^{3+}/\text{Ag}^+$ as 1: 0.25, 1: 0.5, 1: 0.75, and 1:1 respectively as P1, P2, P3, and P4, respectively. The synthesized P2 sample is used for after detection of Cys.

Characterization of Materials

The fluorescence spectra were detected by the spectrofluorometer (FS-5, Edinburgh Instruments), the FTIR spectra of MOFs were obtained by Fourier transform infrared spectroscopy (FT-IR, Antaris II), the crystal structure analysis of MOFs was conducted by the X-ray powder diffraction (XRD, D8 Advance diffractometer with Cu K α radiation), the morphology and elemental analysis of MOFs were observed by the transmission electron microscopy (TEM, JEM-2100) and the high-resolution TEM (HRTEM) with elemental mapping analysis and energy-dispersive X-ray spectroscopy (EDS) (Tecnai G2 F30S-TWIN).

Detection of Cys and GSH

For selectivity test, P2 powder samples (0.5 mg) were added to solutions containing Arg, Cys, GSH, Glu, Gly, His, Phe, Trp, Tyr, NaCl, NaNO_3 , and KNO_3 , respectively, and the mixture was sonicated for 5 min to form a uniformly dispersed solution for luminescence test. For sensitivity test, Cys and GSH solutions with different concentrations (5, 10, 20, 50, 100, 150, 200, 250, 500, 1000 μM) were added to the P2 (0.25 mg/mL) solution. The fluorescence spectra at 450–750 nm were measured at 20°C in 10 mM HEPES buffer solution (pH 8.0) with an excitation wavelength of 315 nm.

Detection of biothiols in serum samples

The standard addition method was used to detect biothiols in diluted serum samples. To avoid autofluorescence interference of serum, serum samples were diluted 20 times with 10 mM HEPES buffer solution (pH 8.0) and then used for testing. A 100 μL serum sample was diluted to 2 mL with ultrapure water, and then 0.5 mg of P2 was added and sonicated for 5 min for fluorescence detection. Then, different concentrations of GSH (20, 40, 60 μM) were added, and the fluorescence spectra were measured with an excitation wavelength of 315 nm.

Result And Discussion

Materials synthesis and characterization

In this work, a facile solvothermal method was used to synthesize Ni-MOF nanosheet, and then lanthanide ions Eu^{3+} ions were doped into the Ni-MOFs using a hydrothermal and post-synthesis modification method. The fluorescent spectra of Eu@Ni-MOF reveal strong fluorescence emission at 615 nm upon 315 nm excitation (Fig. 1A). The sharp characteristic peaks of 590, 615, 651, and 700 nm corresponding to the $^5\text{D}_0\text{--}^7\text{F}_j$ ($j = 1\text{--}4$) transitions.[34] This is caused by the “antenna effect”[35, 36] between the rare-earth metal and the organic ligand of Ni-MOFs. The organic ligand absorbs energy and transits into an excited state, and then transfers the energy to the rare-earth ion through a resonant coupling, resulting in the luminescence of the rare-earth ion. It is worth noting that there is no ligand-

based emission in the 450–590 nm range, which indicates that there appears an effective energy transfer process from the organic ligand to the Eu^{3+} . It is also found that the fluorescence emission intensity gradually increased with the increase of the Eu^{3+} amount, and reached the maximum when the amount of Eu^{3+} increased to 50 mM (Figure S1). Subsequently, transition metal ion Ag^+ was introduced onto Eu@Ni-MOF using a hydrothermal method. Figure 1B shows the physical picture of the fluorescence for Eu@Ni-MOF and Ag/Eu@Ni-MOF synthesized at different molar ratio of Eu^{3+} and Ag^+ under the UV lamp irradiation at 254 nm, and the fluorescence color gradually transited from red to green with the increase of Ag^+ amount. As shown in Fig. 1C, the gradual increase of Ag^+ doping amount caused the gradual weakening of luminescence intensity belonging to Eu^{3+} . Meanwhile, the fluorescence emission peaks at ~ 487 , ~ 524 , and ~ 560 nm which are similar to that of those fluorescent coordination polymers reported previously appeared,[37] and the fluorescence emission peaks appearing at 450–590 nm are due to vibrationally-resolved emission (VRE). VRE is due to a transition from a unique excited state that is generated by ligand-to-metal charge transfer (LMCT) and/or ligand-to-metal-metal charge transfer (LMMCT). Numerous studies have shown that LMCT is one of the most plausible mechanisms for the luminescence of d^{10} metal complexes. Besides, shorter metal-to-metal (M-M) distances may induce the emission of LMMCT transitions.[37] The phenomenon suggests that the doping of silver reduces the energy transfer efficiency from organic ligands to Eu^{3+} that leads to the enhancement of the emission intensity belonging to the ligand.[27] As shown in Fig. 1D, the characteristic luminescence peak intensity of the ligand (I_{524}) gradually enhanced with the increase of silver content, while that belonging to Eu^{3+} (I_{615}) gradually weakened.

The products of MOFs after doping with Eu^{3+} and Ag^+ were further characterized by XRD, HRTEM, TEM and EDS-mapping. XRD was used to verify the crystal structures changes of products after $\text{Ag}^+/\text{Eu}^{3+}$ modification, the XRD patterns of Ni-MOF, Eu@Ni-MOF , and Ag/Eu@Ni-MOF are shown in Fig. 2A. It shows that the XRD pattern of the synthesized Ni-MOF is in agreement with the previously reported $[\text{Ni}_3(\text{OH})_2(\text{C}_8\text{H}_4\text{O}_4)_2(\text{H}_2\text{O})_4]\cdot 2\text{H}_2\text{O}$ (CCDC No.638866)[32]. The diffraction peaks of the previously reported Eu-BDC (CCDC No.1241234)[38] and Ni-MOF were observed in the spectrum of Eu@Ni-MOF . By comparing the XRD spectra of P1, P2 and P4, some diffraction peaks which coincide with the $[\text{Ag}(\text{BDC})_{1/2}]_n$ (CCDC No.198096)[39] and Ag_2O (JCPDS No.42–0874) appeared and gradually became stronger with the increase of Ag content, where the 2θ of 13° and 31° are attributed to the (100) and (121) crystal planes of Ag-BDC,[37] and the 2θ of 34° is attributed to the (003) crystal planes of Ag_2O respectively. It indicates that Ag^+ and Eu^{3+} are successfully incorporated into the MOF by replacing the nickel ions and hydrogen ions on the ligands. The morphology of the prepared MOFs was analyzed by TEM. It can be seen from Fig. 2B and 2C that both Ni-MOF and Eu@Ni-MOF are nanosheet materials. Figure S2 and Fig. 2D shows the TEM images of the Ag/Eu@Ni-MOF (P1, P2, P4), respectively. After the introduction of Ag^+ , numerous spherical nanoparticles with a diameter of ~ 25 nm attached around the lamellar layer. It is noteworthy that as $\text{Ag}^+/\text{Eu}^{3+}$ increases from 0.5: 1 to 1: 1, smaller spherical particles with diameter of ~ 5.1 nm are dispersed on the surface of MOF and eventually cover the lamellae completely. High-resolution TEM (HRTEM) images of the P2 in Fig. 2D reveals that the d-spacing of the

two spherical particles around the lamellae was different. The d-spacing of 0.261 nm for the spherical particles with diameter of ~ 25 nm could be indexed as (003) plane of Ag_2O . The d-spacing of 0.209 nm for the smaller spherical particles with diameter of ~ 5.1 nm could be indexed as (032) plane of Ag-BDC. Elemental mapping (Fig. 2E) of Ag/Eu@Ni-MOF demonstrates the presence of uniformly distributed C, Ni, Eu, O, and Ag atoms in nanosheets and the bigger spherical particles with diameter of ~ 25 nm are Ag_2O . Combining the above characterization results, with the doping of Ag^+ , the formation of Ag-BDC is accompanied by the presence of Ag_2O . The successful modification of metal ions into Ni-MOF was also demonstrated by FT-IR analysis. In the FT-IR spectrum (Figure S3), the band at 3597 cm^{-1} was attributed to the stretching vibration of OH^- , the absorption peaks of 3427 , 3344 , and 3070 cm^{-1} indicate that coordinated H_2O molecules in Ni-MOF. Moreover, for Eu@Ni-MOF and Ag/Eu@Ni-MOF, the lack of bands at 1683 cm^{-1} corresponding to the $-\text{COOH}$ group, indicating a portion of the guest metal ions is coordinated to the free carboxyl group. The strong bands of 1577 , 1508 and 1380 cm^{-1} attributed to the asymmetric and symmetric stretching modes of $-\text{COO}^-$ groups. The number of bands present in this spectral region suggests more than one coordination mode of carboxylate group. The characteristic peak of 752 cm^{-1} is due to the deformation vibration of C-H on the benzene ring in the organic ligand. By comparing the spectra of MOFs before and after guest metal cation doping, the band of the Ni-O at 819 cm^{-1} is weakened after doping with metal ion. We speculate that there appeared ions exchange in the organic ligand which coordinated with metal ions, leading to the loss of Ni^{2+} ions in the MOFs.

The effect of pH, temperature on the fluorescence of Ag/Eu@Ni-MOF

Considering the experimental environment such as pH, temperature and etc. may have effects on the fluorescence of Ag/Eu@Ni-MOF. pH and temperature were varied to investigate their effects on the dual-emission fluorescence of Ag/Eu@Ni-MOF. According to Fig. 3A, it can be seen that the Ag/Eu@Ni-MOF exhibits emission quenching at both 524 nm and 615 nm when the pH is about 3. It may be that the structure of the Ag/Eu@Ni-MOF has been disrupted, resulting in the quenching of dual emission. Figure 3B showed the I_{524}/I_{615} remained almost unchanged when the pH of the solution was in the range of 4.0–7.0, and then gradually increased with the increase of pH. When the pH increases from 8.0 to 9.0, the emission of Eu^{3+} is weakened and the luminescent color becomes green when the pH reaches 9.0. The results indicate that the fluorescence of Ag/Eu@Ni-MOF keep stable with a pH in the range of 4.0–8.0. Later, we studied the effect of temperature on the fluorescence of the Ag/Eu@Ni-MOF. Upon increasing the temperature, the emission spectra of dual-emission luminous MOFs recording at different temperature revealed a gradual quenching of ligand emission (Fig. 3C). It is noteworthy that the emission intensity of the Eu^{3+} did not change. By linear fitting, it was found that I_{524}/I_{615} showed a good linear relationship with temperature (Fig. 3C inset). $I_{524}/I_{615} = 0.162 - 1.72 \times 10^{-3}T$ ($R^2 = 0.986$). The CIE coordinates (Fig. 3D) display the luminescence color of Ag/Eu@Ni-MOF is systematically changed from the yellow to red in the temperature range of 0–80°C. According to the literature, when the temperature

increases, the vibrational mode of MOF also expands, which leads to an increase in the non-radiative complex. As previously reported for other fluorescent MOFs, the change in temperature affects the distance and coupling between the ligand and the metal cluster, which leads to the weakening of the ligand fluorescence.[40]

The ratiometric luminescence sensor based on Ag/Eu@Ni-MOF for Cys and GSH detection

In order to validate the potentials of ratiometric luminescence sensor in the field of analytical sensing, Ag/Eu@Ni-MOF probe was used for the detection of biothiols (GSH/Cys). As shown in Fig. 4A and Fig. 4C, it was found that the fluorescence of Ag/Eu@Ni-MOF changed from yellow to red in the biothiols solution. It also can be seen that the fluorescence emission intensities at 524 nm and 615 nm corresponding to ligand and Eu^{3+} decreased with the addition of biothiols. Especially a substantial quenching of the emission intensity (I_{524}) belonging to ligand was observed, thus only displaying the red fluorescence of Eu^{3+} for Ag/Eu@Ni-MOF in presence of biothiols. It indicated dual-emission fluorescent probe of Ag/Eu@Ni-MOF can be used for ratiometric detection of GSH and Cys. Furthermore, the fluorescence change also can be observed with naked eyes, which is very suitable for point-of-care testing (POCT).

The reaction conditions for RSH species detection were first optimized to improve the sensing performance, the effects of Ag/Eu@Ni-MOF concentration, pH, reaction time, and reaction temperature on the ratiometric fluorescence sensing system were studied. As shown in Figure S4A, GSH and Cys were added to the solutions containing different concentration of Ag/Eu@Ni-MOF respectively. The results showed that the fluorescence intensity I_{524}/I_{615} decreased most at a concentration of 0.25 mg/mL of Ag/Eu@Ni-MOF. The reaction time was also optimized, it indicates the fluorescence intensity I_{524}/I_{615} decreased with time increased and reached platform at 5 min (Figure S4B). Figure S4C showed that the optimal temperature was around 20°C. Figure S4D displayed the ratiometric fluorescence intensity I_{524}/I_{615} decreased most when the reaction system was in pH 8.0. Herein, 0.25 mg/mL of Ag/Eu@Ni-MOF, 5 min, 20°C and pH 8.0 were the optimal reaction conditions for the ratiometric fluorescent sensing system, and subsequent experiments were performed under the above conditions. Under the above optimal conditions, the detection of GSH and Cys at different concentrations based on the fluorescence emission spectra of Ag/Eu@Ni-MOF ratiometric fluorescent probe were shown in Fig. 4A and C. It can be seen that the fluorescence at 524 nm gradually decreased with the increase of GSH/Cys from 5 to 1000 μM . As displayed in Fig. 4B and D, the good liner regression curve could be obtained for GSH and Cys concentration in the range of 5-250 μM . The linear equations were $I_{524}/I_{615} = 0.149 - 5.928 \times 10^{-4} [\text{GSH}]$ ($R^2 = 0.997$) and $I_{524}/I_{615} = 0.150 - 5.174 \times 10^{-4} [\text{Cys}]$ ($R^2 = 0.995$), and the limit of detection (LOD) of 0.17 μM and 0.20 μM was obtained on the basis of the 3σ rule for GSH and Cys. The analytical performance of GSH and Cys detection using this ratiometric fluorescent sensor was compared with other MOF based fluorescent sensors (Table S1 and S2), which indicated our analytical parameters are satisfactory.

Therefore, the dual-emission fluorescence properties of Ag/Eu@Ni-MOF make it promising for fluorescence ratiometric sensing applications.

The fluorescence quenching mechanism was further investigated by FT-IR, XRD and UV-vis absorption analysis. By FT-IR characterization (Figure S5), for Ag/Eu@Ni-MOF with addition of Cys and GSH, the absorption peak of $\sim 2550\text{ cm}^{-1}$ attributing to the sulfhydryl group in the thiol species and disappeared, which indicates that the fluorescence discoloration is due to the binding of the ratiometric fluorescent probe to the sulfhydryl group in the biothiols, resulting in the quenching of the emission for organic ligand (I_{524}). Combined with the XRD patterns shown in Figure S6A, the diffraction peak intensity of Ag-BDC in P2 was weakened, indicating that Ag-BDC crystal phase is decreasing. According to the TEM image of P2 after combining with Cys and GSH (Figure S6B and S6C), the particles scattered on the nanosheets were agglomerated and their morphology changed compared with that of Ag-BDC without Cys/GSH. It may be that the combination of -SH in the cysteine with Ag^+ results in the breakage of the coordination bond of Ag-BDC, inducing the decrease of Ag-BDC crystal. As shown in Figure S7, the absorption peaks at 240 nm and 280 nm belong to terephthalic acid. Comparing the UV-vis absorption spectra of Ag/Eu@Ni-MOF before and after the addition of cysteine and glutathione, it can be seen that the absorption peaks at 240 nm and 280 nm are significantly enhanced, and a new absorption peak appears at 356 nm. It may be that the coordination bond of Ag-BDC is broken and terephthalate protonated, resulting in an increase in the absorption peak at 240 nm. According to previous literature reports[41, 42], the absorption peaks at 280 nm and 356 nm may be due to the energy absorption caused by the combination of Ag^+ and Cys/GSH. Therefore, the mechanism of the fluorescent material for the thiol species detection can ultimately be explained by the recombination of Ag^+ and -SH in the biothiols and the breakage of the coordination bond of Ag-BDC. So, the dissociation of the Ag^+ blocks the LMCT, which results in the quenching of the ligand fluorescence.

Having high selectivity is quite important for a sensor to identify the target object in many interferences. The interference of different biological molecules on the biothiols detection for this fluorescence ratiometric sensor was investigated. While in other amino acid solutions of Glu, Tyr, Phe, Arg, His, Trp, Gly, the fluorescence color remained unchanged. It also can be seen that the fluorescence emission intensities at 524 nm corresponding to ligand decreased with the addition of the target RSH species (Fig. 4E and Figure S8). In summary, this ratiometric fluorescent probe had good selectivity and strong anti-interference ability for biothiols (Figure S9).

In order to evaluate the feasibility of ratiometric fluorescent sensor in actual samples, it was used to detect biothiols in human serum samples. Ag/Eu@Ni-MOF was dispersed in human serum sample to record the fluorescence change, and then glutathione standard solution was added to the above solution with three times, the fluorescence change was recorded for testing (Fig. 4F). Results indicated the biothiols contents of three human samples was $878 \pm 28\text{ }\mu\text{M}$ (Table S3), respectively, which were slightly higher than the measured value reported by previous work.[8] It may be results from the presence of other mercapto compounds in serum. The values of recovered ratio for the assay of 20, 40, and 60 μM GSH

added in the serum samples are between 92% and 105%. This shows that the ratio fluorescence sensor can be used for routine analysis of biothiols in actual serum samples with good accuracy and precision.

Conclusions

In summary, dual-emission Ag/Eu@Ni-MOF which exhibits the fluorescence of Eu^{3+} and ligand was synthesized by functionalization of 2D Ni-MOF nanosheets with Eu^{3+} and Ag^+ , respectively, in which the doping of Ag^+ reduces the energy transfer efficiency from organic ligands to Eu^{3+} that leads to the enhancement of the ligand's emission intensity. The molar ratio of Ag^+ and Eu^{3+} was changed to study the effect on the fluorescence emission, it is found that the emission peak intensity at 615 nm for Eu^{3+} decreased, while that at 524 nm for ligand enhanced, and the fluorescence color transitioned from red to green with the increase of Ag^+ amount. At the same time, we found that Ag/Eu@Ni-MOF is a temperature-sensitive material and the fluorescence intensity decreased with increasing temperature. Furthermore, the fluorescence of Ag/Eu@Ni-MOF can keep stable over a wide pH range from 4.0 to 8.0. Due to the binding of Ag^+ with -SH in the thiol species, the ratiometric fluorescent probe can be used for detection of Cys and GSH by using the emission intensity ratio of ligand to Eu^{3+} as a detection signal. Also the fluorescence change can be observed with naked eyes. The sensor has the advantages of fast response, low detection limit, high selectivity, and the ability to detect biomolecular thiols from actual serum samples. This work proves that the 2D Ni-MOF nanosheets can be used as a stable scaffold for construction of luminescent MOFs and also shows the great potential of Ag/Eu@Ni-MOF as a ratiometric fluorescent probe for POC testing and biomolecules detection in living cells and *in vivo*.

Declarations

Supplementary Information The online version contains supplementary material available at

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Figures

Figure 1

(A) Emission and excitation spectra of Eu@Ni-MOF ($\lambda_{\text{ex}}=315\text{nm}$, $\lambda_{\text{em}}=615\text{nm}$). (B) The fluorescence physical picture of Eu@Ni-MOF and Ag/Eu@Ni-MOF which dispersed in ultrapure water under 254 nm UV-light irradiation. a: Eu@Ni-MOF, b-e: Ag/Eu@Ni-MOF (P1-P4). (C) The emission spectra of Eu@Ni-MOF and Ag/Eu@Ni-MOF synthesized at different molar ratio of $\text{Eu}^{3+}/\text{Ag}^{+}$. (D) The luminescence intensities of the ligand at 524 nm (black bar) and Eu^{3+} at 615 nm (red bar).

Figure 2

(A) XRD patterns of Ni-MOF, Eu@Ni-MOF and Ag/Eu@Ni-MOF synthesized at different Ag: Eu ratio. (B) TEM image of Ni-MOF. (C) TEM image of Eu@Ni-MOF. (D) TEM image of Ag/Eu@Ni-MOF (P2). Inset: HRTEM images of Ag-BDC and Ag₂O in P2. (E) EDS-mapping images of Ag/Eu@Ni-MOF (P2).

Figure 3

(A) The emission spectra of Ag/Eu@Ni-MOF at different pH. (B) I_{524}/I_{615} of Ag/Eu@Ni-MOF at different pH and the insets are photos of Ag/Eu@Ni-MOF at different pH under 254 nm UV-light irradiation. (C) Emission spectra of Ag/Eu@Ni-MOF at different temperatures and the inset is the fitting linear curve of I_{524}/I_{615} for Ag/Eu@Ni-MOF with temperature. (D) CIE of Ag/Eu@Ni-MOF at different temperatures.

Figure 4

(A, C) The emission spectra of Ag/Eu@Ni-MOF after addition of different concentration of GSH and Cys. Inset: photos of Ag/Eu@Ni-MOF in corresponding solutions under 254 nm UV-light irradiation. (B, D) I_{524}/I_{615} of Ag/Eu@Ni-MOF in different concentrations of GSH and Cys. Inset: the linear fitted curve of I_{524}/I_{615} with GSH and Cys concentration. (E) The emission spectra of Ag/Eu@Ni-MOF in presence of GSH, Cys and other different amino acid solutions. Inset: photos of Ag/Eu@Ni-MOF in corresponding

solutions under 254 nm UV-light irradiation. (F) Emission spectra of Ag/Eu@Ni-MOF (a), Ag/Eu@Ni-MOF in human serum (b) Ag/Eu@Ni-MOF with addition of different concentrations of GSH (c: 20 μ M, d: 40 μ M, e: 60 μ M). Inset: photos of materials in corresponding solutions.

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