



Research Article

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An enhanced boronic acid-functionalized bimetallic metal-organic-framework fluorescent probe for rapid and selective fluorescence detection of epinephrine in human serum and urine

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Abstract: Epinephrine (EP) is a pivotal hormone and neurotransmitter, and its accurate quantification is crucial for evaluating stress responses, diagnosing pathological conditions, and maintaining physiological homeostasis. However, conventional analytical methods are often constrained by limited sensitivity, long detection times, and high costs, necessitating innovative strategies that reconcile analytical rigor with practical applicability. In this work, we present a boronic acid-functionalized bimetallic Zn-Eu metal-organic framework (Zn-Eu-MOF) as a highly sensitive fluorescent probe for EP detection. Owing to the synergistic Zn-Eu bimetallic architecture and an efficient light-harvesting ligand, the probe exhibits intense fluorescence and a rapid response toward EP. The integration of boronic acid groups facilitates selective recognition of the cis-diol structure of EP's, ensuring reliable performance in complex biological matrices. The sensor developed here offers a wide linear detection range (0.4-500 $\mu\text{mol/L}$), high sensitivity (LOD=0.12 $\mu\text{mol/L}$), and excellent selectivity. It successfully quantified EP in human serum and urine samples, achieving average recovery rates of 94.8%-115.1%. This study provides a high-performance platform for the rapid and sensitive fluorescence-based determination of EP, offering significant potential for biomedical diagnostics and point-of-care testing.

Key words: Epinephrine; Fluorescence sensor; Metal organic frameworks; Boric acid functionalized

1 Introduction

Epinephrine (EP), a pivotal catecholamine neurotransmitter synthesized and secreted predominantly by the adrenal medulla (Bandyopadhyay P et al., 2020), exerts profound effects on both the central and peripheral nervous systems (Huang S et al., 2023; Shinde et al., 2025). It is intimately involved in emotional regulation, memory formation, and the physiological stress response. Clinically, quantitative determination of EP in biological samples (e.g., serum and urine) is gaining importance due to the strong correlation between its fluctuating levels and diverse pathological conditions, including neurodegenerative diseases (e.g., Alzheimer's and Parkinson's), endocrine disorders, and cardiovascular dysfunction (Wang L and Chen Y, 2025). Serum EP levels may serve as early biochemical indicators of autonomic dysregulation (Aslam et al., 2015; Yadav et al., 2023), whereas urinary EP levels can reflect chronic disease progression or acute catecholamine hypersecretion syndromes (Inoue et al., 2021). Therefore, the development of rapid, sensitive, and accessible methods for EP is of

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critical value for early diagnosis, therapeutic monitoring, and patient risk assessment.

Current analytical techniques, including high-performance liquid chromatography (HPLC) (Xiao D et al., 2016), capillary electrophoresis (Roychoudhury et al., 2020), and immunoassays (Wang Y et al., 2024) offer high reliability, but are often constrained by labor-intensive sample preparation, expensive instrumentation, and prolonged analysis times. These limitations hinder their applicability for rapid clinical screening or point-of-care testing (POCT) (Mohammadipoor-Ghasemabad et al., 2024). Meanwhile, trace-level concentrations of EP and the complex biological matrices (serum and urine contain abundant proteins, salts, and metabolites), present challenges to achieving high sensitivity, selectivity, and reproducible detection. Consequently, it is essential to develop detection strategies that combine high sensitivity, selectivity, rapidity, and operational simplicity, while remaining compatible with real biological samples. Fluorescence-based sensing has emerged as a promising approach, offering inherent high sensitivity, rapid response, operational simplicity, and cost-effectiveness (Luo C et al., 2024; Zhang J et al., 2025). Specifically, nanomaterial-based probes that are designed to integrate molecular recognition units with a signal-amplification mechanism enable rapid, sensitive, and accurate detection of EP in complex serum and urine matrices with minimal sample pretreatment (Xu C et al., 2025).

Among the various fluorescent probes, metal-organic frameworks (MOFs) have been utilized as fluorescence probes, owing to their ordered porous structure, unparalleled structural diversity, and tunable pore environment (Zhu N et al., 2023). Their modular ligands can be tailored for selective binding, while intrinsic or doped fluorescence components enable sensitive "turn-on" or "turn-off" responses (Pal TK, 2023). For instance, Shi et al. synthesized an iron-based single-atom nanozyme (Fe-SAzyme) via a microwave-assisted strategy. The nanozyme demonstrated enhanced laccase-like catalytic activity and enabled visual, rapid, and highly sensitive dual-mode detection of EP (Shi YH et al., 2024). Similarly, Shen et al. developed a ratiometric nano-probe (CDs@LZIF-8-Eu³⁺) by integrating carbon dots and Eu³⁺ into LZIF-8 with a one-pot method; the probe showed high sensitivity (2.94-4.46 ng/mL), rapid response (≤ 10 s), and visible color changes for tetracyclines (Shen Y et al., 2025). Despite these advantages, the existing probes often suffer from limited signal controllability and compromised selectivity in complex biological samples. In this context, lanthanide-based MOFs (Ln-MOFs) present distinct advantages for bioanalytical applications, because their photophysical properties include large Stokes shifts, long luminescence lifetimes, and sharp emission peaks (Li XN et al., 2024; Yu Z et al., 2024; Zhao FH et al., 2025). However, the practical utility of Ln-MOFs is frequently constrained by the weak intrinsic emission of lanthanide ions, resulting from parity-forbidden f-f transitions. This necessitates efficient energy transfer from suitable "antenna" ligands or co-metal additives to sensitize the luminescence (Li SQ et al., 2026).

Recent studies have revealed that incorporating transition metals such as Zn²⁺ into heterometallic Ln-MOF systems can significantly enhance energy-transfer efficiency and fluorescence intensity (Wu D et al., 2025; Yamamoto M et al., 2016). Notably, Yin et al. synthesized 4f-3d heterometallic one-dimensional coordination polymers using α -furancarboxylic acid as the ligand, demonstrating that polymers which included Zn²⁺ ions exhibited superior energy-transfer efficiency compared to Eu³⁺ alone, thereby enhancing fluorescence intensity. Nevertheless, whether other ligands or transition metals confer similar fluorescence-sensitization effects still requires further exploration. Furthermore, functionalizing MOFs with boronic acid ligands offers a strategic approach to achieve highly specific cis-diol binding. This not only enables selective recognition of EP, but also tunes the electronic environment to improve signal transduction (Hui Y et al., 2025; Zhu S et al., 2025). For instance, Yu et al. introduced boronic acid ligands into a MOF framework, achieving high selectivity for and sensitivity to tannic acid through boronate-diol interactions. This approach highlights the potential of boronic-acid functionalization to confer specific molecular recognition and signal amplification within MOF frameworks (Yu Z et al., 2024).

In this work, a boronic-acid-functionalized bimetallic Zn-Eu-MOF was synthesized via a one-pot solvothermal method (Fig. 1). Zn²⁺ ions were introduced into the Eu-MOF framework to enhance Eu³⁺ lumines-

cence through energy-transfer sensitization, while 3,5-dicarboxyphenylboronic acid served as both an organic linker and a specific recognition unit for cis-diol-containing molecules. Benefiting from the integration of amplified fluorescence and boronate-affinity molecular recognition, the developed Zn-Eu-MOF provides an efficient fluorescence platform for selective EP detection. The sensing performance, fluorescence mechanism, and practical applicability were systematically investigated in human serum and urine samples.

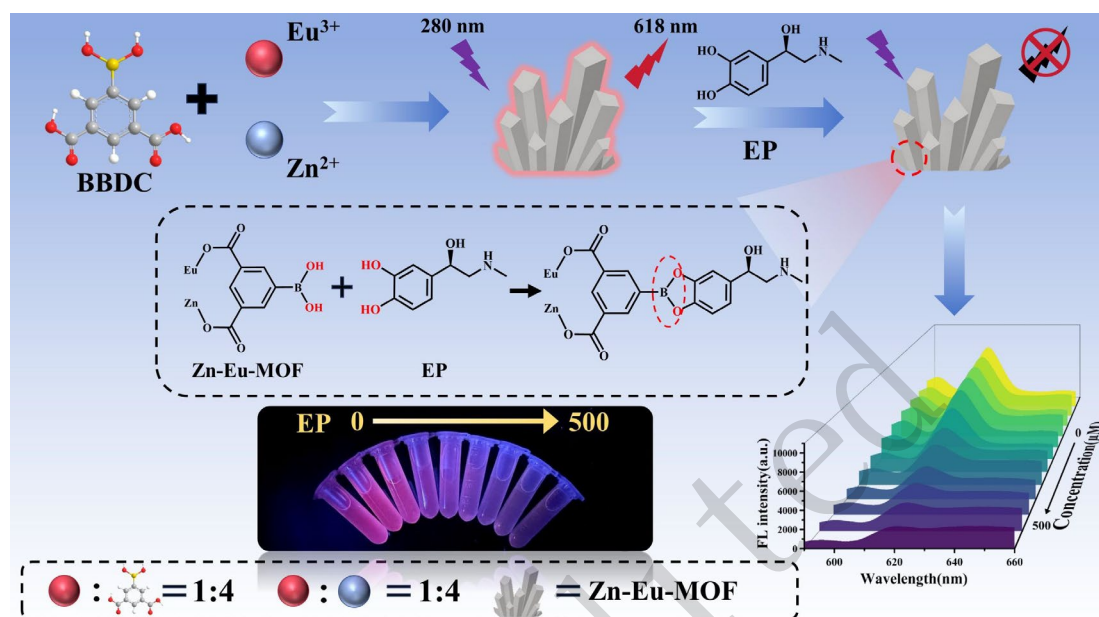


Fig. 1 Schematic illustration of the Zn-Eu-MOF-based sensor for epinephrine (EP) detection

2 Materials and methods

2.1 Synthesis of Zn-Eu-MOF

Synthesis of Zn-Eu-MOF was performed based on a previously reported method (Wu D et al., 2025), with some modifications. Zn-Eu-MOF was synthesized via one-step self-assembly of $\text{Eu}(\text{NO}_3)_3 \cdot 6\text{H}_2\text{O}$ and $\text{Zn}(\text{CH}_3\text{COO})_2 \cdot 2\text{H}_2\text{O}$ as metal precursors, and BBDC as the organic ligand. Briefly, $\text{Zn}(\text{CH}_3\text{COO})_2 \cdot 2\text{H}_2\text{O}$ solution (1 mL, 0.2 mol/L) was mixed with BBDC solution (1 mL, 0.2 mol/L), using 1 mL of DMF solution under vigorous stirring for 2 min. Then, $\text{Eu}(\text{NO}_3)_3 \cdot 6\text{H}_2\text{O}$ (1 mL, 50 mmol/L) solution was added dropwise and the mixture was stirred for 1 h. The resulting solution was transferred into a sealed pressure-resistant bottle and heated at 120 °C for 24 h. After cooling to room temperature, the precipitate was collected and washed twice with DMF, followed by two washes with methanol and two washes with ultrapure water, to remove unreacted materials and byproducts. Finally, the Zn-Eu-MOF was stored at 4 °C for further use.

For comparison, we prepared a series of Eu-based MOFs containing different metal ions under the same synthetic conditions, including Eu-MOF, Hg-Eu-MOF, Co-Eu-MOF, Cd-Eu-MOF, Ag-Eu-MOF, Cu-Eu-MOF, and Fe-Eu-MOF. We replaced Zn^{2+} with 1 mL of ultrapure water or 0.2 mol/L solutions of Hg^{2+} , Co^{2+} , Cd^{2+} , Fe^{3+} , Cu^{2+} and Ag^+ , respectively. Additionally, a series of Zn-Eu-based MOFs incorporating various organic ligands (3-carboxyphenylboronic acid (3-CPBA), 4-carboxyphenylboronic acid (4-CPBA), 3,5-dicarboxyphenylboronic acid (BBDC), 1,3,5-benzenetricarboxylic acid (BTC), phenylboronic acid (PBA), 3-carboxy-5-nitrophenylboronic acid (CNPBA), and 2,5-dicarboxyphenylboronic acid (2,5-DCPBA)) were prepared, in which BBDC was replaced with an equimolar amount of each alternative ligand while maintaining the same Zn^{2+} concentration.

2.2 Fluorescence detection of Epinephrine using Zn-Eu-MOF

During the subsequent detection process, a 1 mg/mL Zn-Eu-MOF solution was first prepared and ultrasonically dispersed. Then, 1 mL of the Zn-Eu-MOF solution was transferred into a 2 mL centrifuge tube. Different concentrations of EP solution were added, and the mixture was subsequently diluted to a final volume of 2 mL with HEPES buffer (10 mmol/L, pH 8.0). The mixture was vortexed at 2500 rpm for 15 min, and the fluorescence spectra were recorded with an excitation wavelength of 280 nm and an emission wavelength of 618 nm. The slit width for both excitation and emission was 5.0 nm.

2.3 EP detection in real samples

Serum and urine samples were collected from healthy individuals and centrifuged at 3000 rpm for 30 min. The supernatant was collected and diluted 50-fold with buffer solution (10 mmol/L, pH 3.0), followed by the addition of EP standard solutions at different concentrations (5, 20, and 200 $\mu\text{mol/L}$). The resulting mixtures were analyzed according to the procedure described above.

3 Results and Discussion

3.1 Synthesis and Screening of Zn-Eu-MOF

Aromatic carboxylic acids are widely known for their strong light absorption and efficient energy-transfer characteristics (Liu D et al., 2026; Yin M et al., 2006). To integrate molecular recognition with luminescent property, we also introduced boronic acid groups for their specific affinity toward cis-diol-containing EP. Accordingly, a series of ligands containing both aromatic carboxylic acid and boronic acid groups were systematically investigated to evaluate their effects on the fluorescence performance of Zn-Eu-MOFs, including 3-CPBA, 4-CPBA, BBDC, BTC, PBA, CNPBA, and 2,5-DCPBA (Fig. 2a). Of these, BBDC emerged as the most effective ligand, significantly enhancing fluorescence intensity. This superior performance can be attributed to synergistic effects: one is stronger coordination of the dicarboxyl groups with Eu^{3+} , which improves the rigidity of the framework and suppresses vibrational quenching; another is the antenna effect facilitated by the boronic acid moiety, which efficiently transfers energy from the ligand to Eu^{3+} . Moreover, the meta-substitution pattern of the boronic acid group was found to be more effective than the ortho-substitution. Therefore, we selected BBDC as the optimal ligand.

Subsequently, a series of X-Eu-MOF ($\text{X}=\text{Ag}^+$, Cd^{2+} , Co^{2+} , Cu^{2+} , Fe^{3+} , Zn^{2+}) were synthesized using BBDC as the ligand to investigate the influence of different metal ions on the fluorescence performance of Zn-Eu-MOF. As shown in Fig. 2b, the introduction of Zn^{2+} significantly enhanced fluorescence intensity, while other metal ions induced varying degrees of quenching. The fluorescence intensity of Zn-Eu-MOF was approximately 2.5 times higher than that of pristine Eu-MOF. We attribute this enhancement primarily to the closed-shell ($3d^{10}$) electronic configuration of Zn^{2+} . In addition, the ability of Zn^{2+} to coordinate well with carboxylate ligands facilitates formation of a relatively rigid and well-defined framework. Such structural rigidity effectively suppresses non-radiative vibrational relaxation pathways, thereby enhancing energy transfer from the ligand to Eu^{3+} centers (Yin M et al., 2006). In contrast, Cd^{2+} , with a larger ionic radius, tends to form more flexible coordination environments, while Ag^+ typically exhibits low coordination numbers. Both factors are less favorable for constructing stable and efficient luminescent frameworks. Consequently, Zn^{2+} was selected as the optimal auxiliary metal ion for construction of the Zn-Eu-MOF system.

The amount of ligand is a critical factor influencing the antenna effect, so we optimized the molar ratio of Eu^{3+} to BBDC (Fig. 2c). Fluorescence intensity was maximized at a Eu:BBDC ratio of 1:4, while higher or lower BBDC content led to decreased fluorescence. We also investigated the Eu:Zn molar ratio (Fig. 2d), as Zn^{2+} can enhance the fluorescence of Zn-Eu-MOF. Fluorescence intensity reached its maximum at a Eu:Zn ratio

of 1:4, and further increasing the ratio to 1:6 showed no additional enhancement. This can be attributed to the triangular spatial configuration of Zn, whose vacant orbitals can accept lone pairs from the ligands. At a 1:4 ratio, the coordination sites of the complex were saturated; lower Zn^{2+} content resulted in decreased fluorescence. Therefore, optimal synthesis was achieved at a 1:4 ratio for both Eu:BBDC and Eu:Zn.

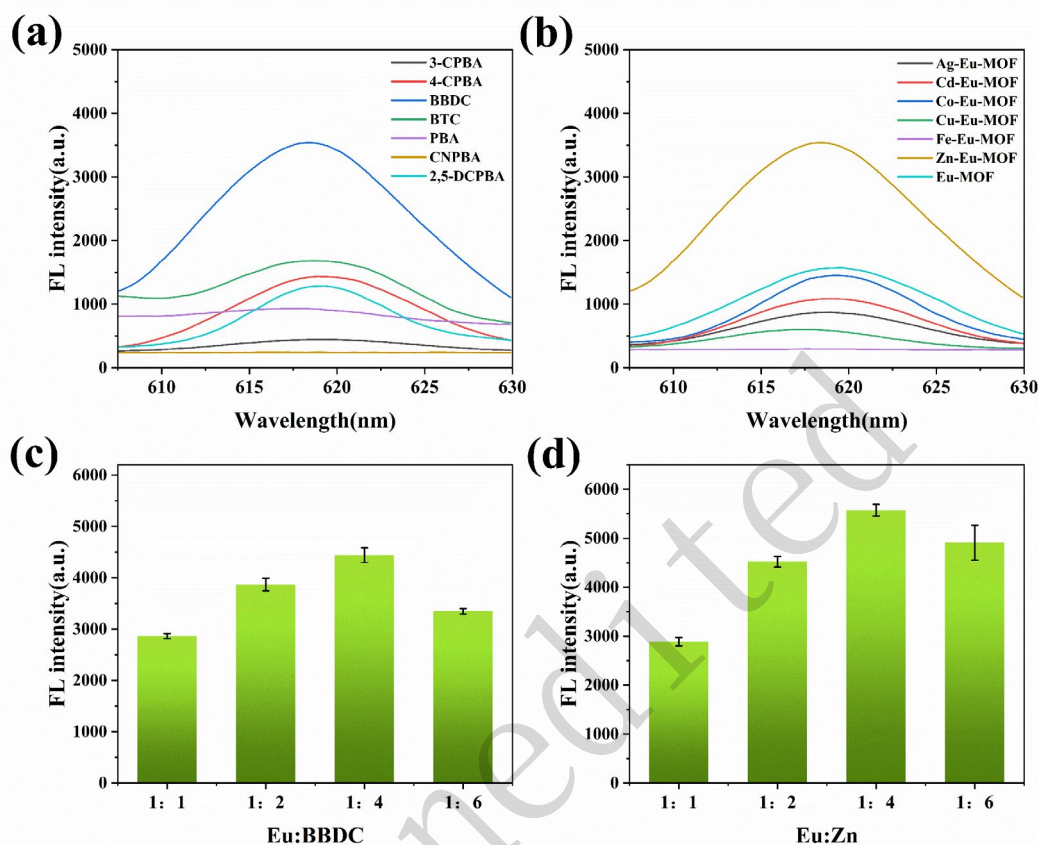


Fig. 2 Effect of different ligands, including 3-carboxyphenylboronic acid (3-CPBA), 4-carboxyphenylboronic acid (4-CPBA), 3,5-dicarboxyphenylboronic acid (BBDC), 1,3,5-benzenetricarboxylic acid (BTC), phenylboronic acid (PBA), 3-carboxy-5-nitrophenylboronic acid (CNPBA), and 2,5-dicarboxyphenylboronic acid (2,5-DCPBA) (a), Effect of various metal ions, including Ag^+ , Cd^{2+} , Co^{2+} , Cu^{2+} , Fe^{3+} , and Zn^{2+} (b), different Eu:BBDC molar ratios (c), and different Eu:Zn molar ratios (d) on the fluorescence performance of Zn-Eu-MOF. The values are expressed as mean $\pm$ standard deviation (SD), $n=3$.

3.2 Characterization

The scanning electron microscopy (SEM) image (Fig. 3a) reveal that the Zn-Eu-MOF exhibits a tubular fibrous morphology with an approximate average diameter of 25 nm. The powder X-ray diffraction (PXRD) pattern of the synthesized Zn-Eu-MOF (Fig. 3b) displays characteristic diffraction peaks at 8.4° , 9.56° , 12.9° , 19.2° , 25.3° , and 29.4° , which are in agreement with those reported for Eu-MOF (Du Q et al., 2023; Yu Z et al., 2024). We attribute the minor variations observed in peak intensity and position to lattice distortion and alterations in the coordination environment induced by Zn^{2+} incorporation. The Fourier transform infrared (FT-IR) spectra (Fig. 3c) provide further evidence of successful coordination. The spectrum of the ligand BBDC displays a broad absorption band around 3000 cm^{-1} , corresponding to the O-H stretching vibration of the -COOH group (Wang ZP et al., 2024). Upon Zn-Eu-MOF formation, the characteristic C=O stretching vibration of

BBDC at 1700 cm^{-1} disappeared, and two new peaks emerged at 1615 and 1545 cm^{-1} , which can be attributed to the asymmetric and symmetric stretching vibrations of -COO^- (Liu P et al., 2021; Yu Z et al., 2024). Additionally, a peak observed at 470 cm^{-1} in Zn-Eu-MOF can be assigned to the metal-oxygen (Zn/Eu-O) vibrational mode (Li SQ et al., 2025). All the results indicated successful coordination of -COOH groups with the metal centers. In addition, bending vibration peaks for B-O-H at 1370 and 1312 cm^{-1} in both BBDC and Zn-Eu-MOF confirmed that active boronic acid sites were retained in the synthesized Zn-Eu-MOF (Yu H et al., 2021).

To further investigate the elemental composition and chemical states of Zn-Eu-MOF, X-ray photoelectron spectroscopy (XPS) analysis was performed (Fig. 3d), and were able to confirm the presence of Zn, Eu, C, O, and B. In the C 1s spectrum (Fig. 4a), the peak corresponding to the -COO^- shifted from 289.2 in the ligand BBDC to 288.6 eV in the Zn-Eu-MOF and became broader, which can be attributed to deprotonation of -COOH and its subsequent coordination with the metal centers, which alters the chemical environment of the carbon atoms. In the B 1s spectrum (Fig. 4b), the binding energy associated with B-C/B-O shifted from 186.9 to 189.6 eV after Zn-Eu-MOF formation, which we attribute to electron redistribution induced by coordination of carboxylate groups with metal centers, leading to decreased electron density around boron atoms. Moreover, upon Zn-Eu-MOF formation, the binding energies of Zn 2p increased from 1140.8 and 1017.7 eV to 1142.7 and 1019.7 eV (Fig. 4c), while those of Eu 3d decreased from 1160.0 and 1131.4 eV to 1158.9 and 1128.8 eV (Fig. 4d), confirming the coordination between metal ions and -COOH groups. Collectively, these results validate the successful synthesis of Zn-Eu-MOF.

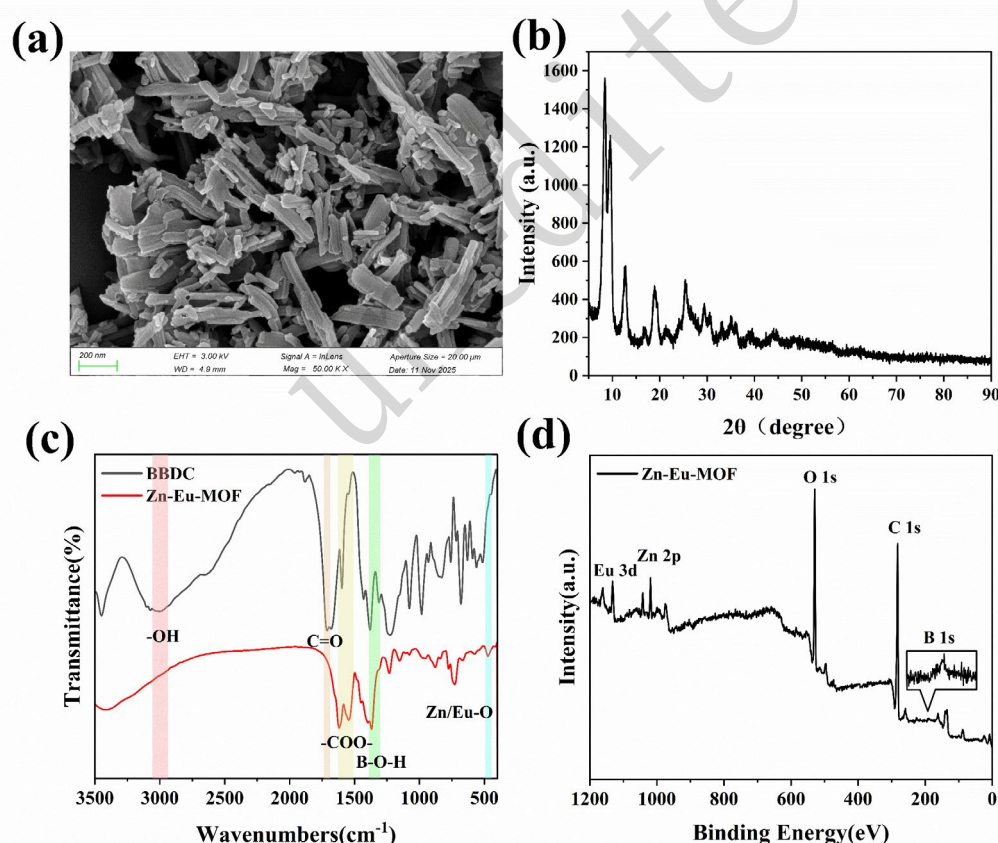


Fig. 3 Scanning electron microscopy (SEM) image of Zn-Eu-MOF (a); Powder X-ray diffraction (PXRD) pattern of Zn-Eu-MOF (b); Fourier transform infrared (FT-IR) spectra of Zn-Eu-MOF and BBDC (c); X-ray photoelectron spectroscopy (XPS) spectra of Zn-Eu-MOF (d).

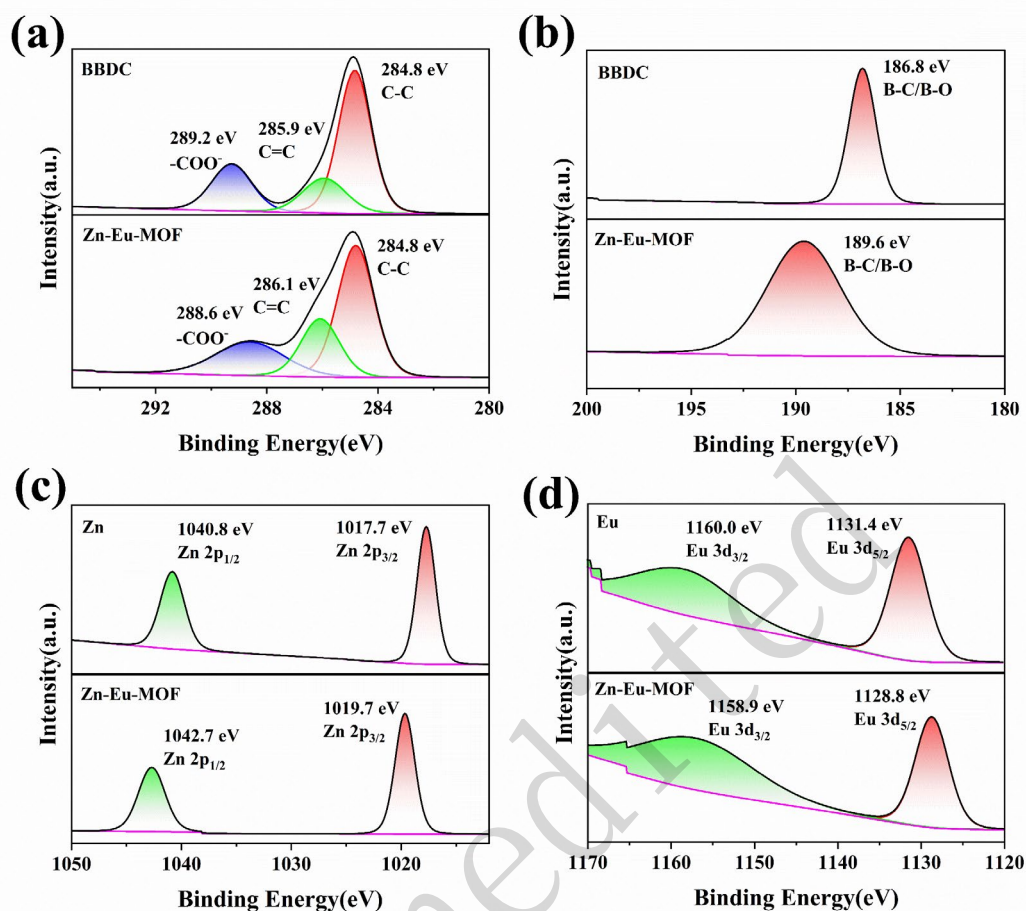


Fig. 4 High-resolution X-ray photoelectron spectroscopy (XPS) spectra of Zn-Eu-MOF, (a) C 1s, (b) B 1s, (c) Zn 2p and (d) Eu 3d.

3.3 Optimization of experimental parameters

To maximize detection performance, we systematically investigated key experimental parameters (reaction time, pH, temperature, and probe dosage) using fluorescence-quenching efficiency as the evaluation metric. The fluorescence-quenching efficiency is defined as $(F-F_0)/F_0$, where F and F_0 represent the fluorescence intensities of Zn-Eu-MOF in the presence and absence of EP, respectively.

As shown in Fig. 5a, fluorescence-quenching efficiency increased significantly within the first 3-15 min and then plateaued. One-way ANOVA revealed that reaction time had a statistically significant effect on quenching efficiency ($F=68.17$, $P<0.05$). Post hoc analysis confirmed that the efficiency at 15 min was significantly higher than at shorter time points, while no significant difference was observed beyond 20 min, indicating that binding equilibrium was attained within 15 min. Therefore, a reaction time of 15 min was selected for subsequent experiments.

Given the pH dependence of the coordination interaction between boronic acid groups and the cis-diol

moiety of EP, we evaluated the effect of pH over a range of 5.0 to 9.0. As shown in Fig. 5b, quenching efficiency increased markedly from pH 5.0 to pH 8.0, followed by a decrease under more alkaline conditions. One-way ANOVA indicated that the efficiency at pH 8.0 was significantly higher than at other tested pH values (5.0, 6.0, 7.0, and 9.0) ($F=21.65$, $P<0.05$). The occurrence of maximum response at pH 8.0 corresponds to the optimal ionization state of the boronic-acid groups, which facilitates the formation of a cyclic boronate ester with EP. At higher pH, excessive deprotonation destabilizes the complex, reducing the quenching response. Accordingly, pH 8.0 was chosen as the optimal condition for further experiments.

The influence of temperature on fluorescence-quenching efficiency in EP detection is shown in Fig. 5c. Over the tested range (20–50 °C), quenching efficiency showed no significant variation. One-way ANOVA confirmed that temperature did not have a statistically significant effect ($F=0.07$, $P>0.05$), indicating that the fluorescence response of Zn-Eu-MOF to EP is essentially temperature-independent within this range. These results highlighted the excellent thermal stability of the Zn-Eu-MOF-based sensing platform. Therefore, all subsequent fluorescence measurements were carried out at room temperature (25 °C).

Finally, the dosage of Zn-Eu-MOF was optimized within the range of 0.1 to 0.6 mg/mL. As illustrated in Fig. 5d, at very low concentrations (<0.2 mg/mL), the intrinsic fluorescence of EP exceeded that of Zn-Eu-MOF, resulting in negative quenching-efficiency values. As the MOF concentration rose from 0.2 mg/mL to 0.6 mg/mL, the fluorescence-quenching intensity gradually increased, reaching a plateau at 0.5 mg/mL. One-way ANOVA showed that MOF concentration had a statistically significant effect on quenching efficiency ($F=1547$, $P<0.05$). Post hoc analysis identified 0.5 mg/mL as the optimal dosage, which provided maximum quenching efficiency without excessive material use. Thus, 0.5 mg/mL was selected as the optimal probe concentration for subsequent assays.

In summary, the optimal conditions for EP detection using Zn-Eu-MOF were established as follows: 15 min of reaction time, pH value of 8.0, ambient temperature (25 °C), and a probe concentration of 0.5 mg/mL. This configuration offered an effective balance of sensitivity, selectivity, and operational simplicity, making it suitable for further analysis.

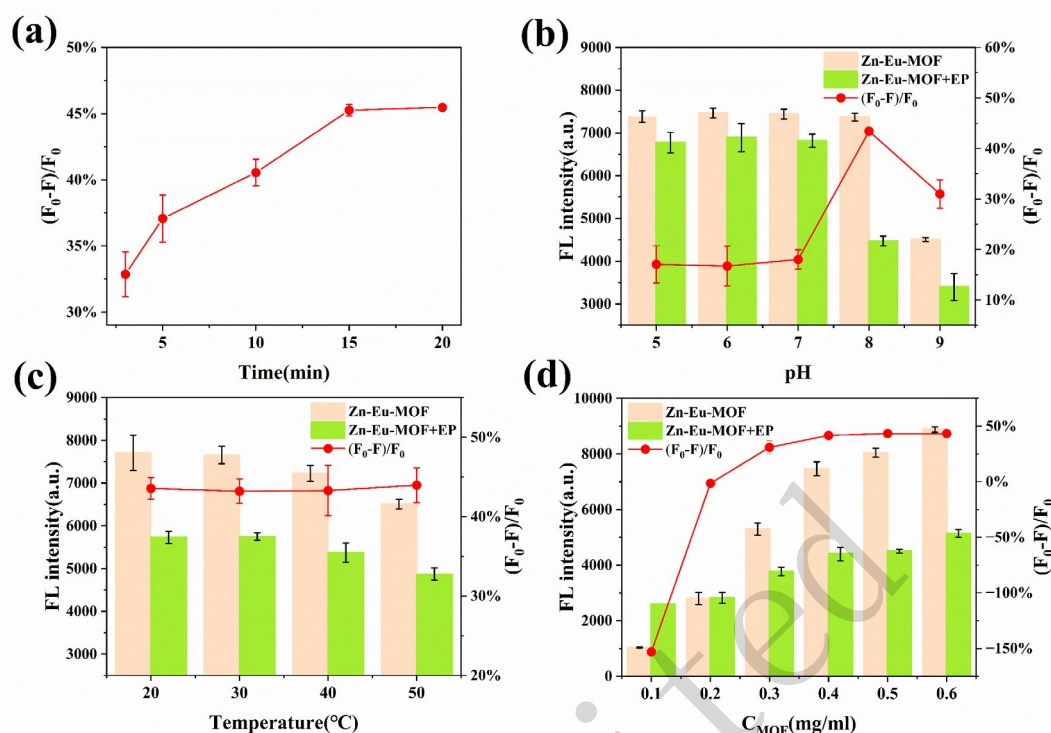


Fig. 5 The effects of (a) reaction time, (b) pH, (c) temperature, and (d) amount of MOF on epinephrine (EP)-induced fluorescence-quenching efficiency. Fluorescence-quenching efficiency was calculated as $(F-F_0)/F_0$, where F and F_0 represent the fluorescence intensities of Zn-Eu-MOF in the presence and absence of EP, respectively. The values are expressed as mean $\pm$ standard deviation (SD), $n=3$.

3.4 Fluorescence detection of EP using Zn-Eu-MOF

Under the optimized conditions, we investigated the fluorescence response of Zn-Eu-MOF to different concentrations of EP. As shown in Figs. 6a and 6b, the fluorescence intensity of Zn-Eu-MOF gradually decreased as the EP concentration increased from 0.4 $\mu\text{mol/L}$ to 500 $\mu\text{mol/L}$. A good linear relationship was obtained between the fluorescence intensity and EP concentration in the ranges of 0.4–200 $\mu\text{mol/L}$ and 200–500 $\mu\text{mol/L}$, with calibration equations of $y=8561.76-19.04x$ ($R^2=0.997$) and $y=6493.99-8.66x$ ($R^2=0.991$), respectively. The limit of detection (LOD) was calculated to be 0.12 $\mu\text{mol/L}$ ($\text{LOD}=3\sigma/k$, where σ is the standard deviation of 10 replicate measurements at low concentration and k is the slope of the calibration curve), and the limit of quantification (LOQ) was 0.40 $\mu\text{mol/L}$ ($\text{LOQ}=10\sigma/k$). The difference in the slopes observed in the two linear response regions can be attributed to a transition in the dominant quenching mechanism within the system. At low concentrations, fluorescence quenching is primarily governed by dynamic quenching, along with partial static interactions between EP and the boronic-acid sites of the MOF, resulting in higher quenching efficiency. At higher concentrations, however, the boronic-acid binding sites gradually become saturated, and additional EP molecules contribute less significantly to fluorescence quenching. Meanwhile, enhanced absorption of excitation light by EP leads to a more pronounced inner filter effect (IFE), which decreases the effective excitation of the MOF and lowers quenching sensitivity. These combined effects account for the observed slope variation. To evaluate the stability and reproducibility of the Zn-Eu-MOF sensor, we monitored the fluorescence intensity at 618 nm after incubation in human serum and urine. As shown in Figs. S1a and S1b, the fluorescence intensity remained nearly unchanged over 7 days, indicating good stability. In addition, repeated measurements at the

same EP concentration showed almost identical quenching efficiency (Fig. S2), demonstrating excellent reproducibility. Compared with previously reported methods (Table 1), the proposed fluorescence-quenching strategy thus exhibits higher sensitivity and a broader linear range for EP detection.

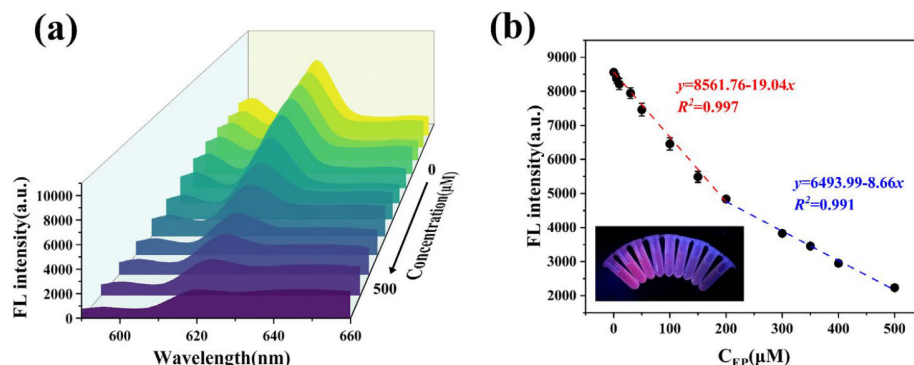


Fig. 6 (a) Fluorescence spectra of Zn-Eu-MOF in the presence of different concentrations of epinephrine (EP); (b) Linear relationship between EP concentration and the fluorescence intensity of Zn-Eu-MOF. The values are expressed as mean $\pm$ standard deviation (SD), $n=3$.

Table 1 Comparison of different methods for EP detection

Method	Material	Linear range ($\mu\text{mol/L}$)	LOD ($\mu\text{mol/L}$)	References
Electrochemical	Pt/POM/NCS	2.59-1109.59	0.25	(Cai C et al., 2024)
Electrochemical	LDHzyme	2.5-200	0.27	(Li ZY et al., 2025)
Electrochemical	NiO/CuCo ₂ O ₄ /GQDs	0.02-500	0.01	(Uruc S et al., 2025)
Fluorescence	Fe-SAzymes	1-1000	0.39	(Shi YH et al., 2024)
Fluorescence	Anionic Cyanine	2-75	0.40	(Luo C et al., 2024)
Fluorescence	Zn-Eu-MOF	0.4-500	0.12	this work

EP: epinephrine; LOD: limit of detection.

3.5 Selectivity for fluorescence determination of EP

To ensure that the proposed fluorescence detection strategy is not affected by potential interferents in real sample analysis, common substances present in serum and urine were selected, including nor-epinephrine (NE), dopamine (DA), glycine (Gly), cysteine (Cys), glutamic acid (Glu), glucose (Glc), uric acid (UA), ascorbic acid (AsA), NaCl, and KCl, all at the same concentration as EP. As shown in Fig. 7, the fluorescence intensity in the presence of these interferents was nearly identical to that of EP alone, indicating that this fluorescence detection method possesses excellent anti-interference capability in human serum and urine.

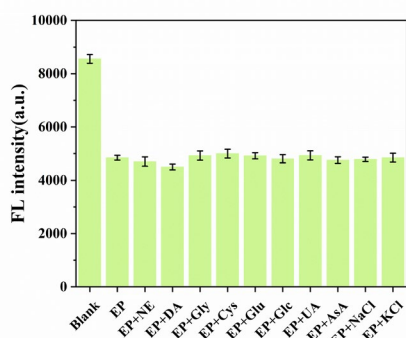


Fig. 7 Fluorescence-quenching response of Zn-Eu-MOF toward epinephrine (EP) in the presence or absence of potential interfering substances, including nor-epinephrine (NE), dopamine (DA), glycine (Gly), cysteine (Cys), glutamic acid (Glu), glucose (Glc), uric acid (UA), ascorbic acid (AsA), NaCl, and KCl. The values are expressed as mean $\pm$ standard deviation

(SD), n=3.

3.6 Detection of EP in real samples

To further evaluate the practical applicability of the Zn-Eu-MOF, spiked recovery experiments were performed in human serum and urine samples. As shown in Table 2, the recovery of EP in both serum and urine was in the range of 94.8%-115.1%. This range is considered to be acceptable for biological analysis, with the observed variation being attributable to matrix effects inherent in such complex samples. Furthermore, we compared the analytical performance of the Zn-Eu-MOF sensor with the standard HPLC method. The relative standard deviations (RSDs) (Table S1) for the Zn-Eu-MOF-based method (1.2%-4.3%) were comparable to those for the HPLC method (1.3%-3.0%). These results confirm that the proposed Zn-Eu-MOF sensor offers good precision and reproducibility.

Table 2 Recovery of EP detection in serum and urine (n=3)

Samples	Add (μmol/L)	Found (μmol/L)	Recovery (%)	RSD (%)
Blood 1	5	5.32	106.4	3.1
	50	55.87	111.8	4.0
	200	192.78	96.4	4.3
Blood 2	5	5.25	104.9	4.5
	50	53.86	107.7	3.1
	200	198.20	99.1	1.4
Blood 3	5	4.95	99.0	3.2
	50	52.93	105.9	4.7
	200	200.97	101.7	0.9
Urine 1	5	5.37	107.4	2.9
	50	50.24	100.5	2.8
	200	198.12	99.1	3.7
Urine 2	5	4.74	94.8	2.6
	50	54.68	109.4	3.6
	200	196.00	98.0	0.7
Urine 3	5	5.76	115.1	4.2
	50	53.74	107.5	3.3
	200	193.07	96.5	1.6

EP: epinephrine; RSD: relative standard deviation.

3.7 Investigation of the detection mechanism

To elucidate the EP sensing mechanism of the Zn-Eu-MOF probe, we systematically investigated the interactions between the MOF and EP using ultraviolet-visible (UV-vis) absorption spectroscopy, fluorescence spectroscopy, fluorescence lifetime measurements, FT-IR, XPS analysis, and density functional theory (DFT) calculations. The inherent fluorescence of Zn-Eu-MOF arises from an efficient antenna effect, whereby the organic linker (BBDC) absorbs excitation energy and non-radiatively transfers it to the central Eu^{3+} ion, resulting in sharp energy emission. The introduction of EP leads to significant fluorescence quenching, which can be attributed to the formation of cyclic boronate esters that interrupt this energy-transfer pathway.

The primary interaction mechanism involves the covalent reaction between the boronic acid groups $-\text{B}(\text{OH})_2$ on the MOF's linker and the cis-diol moiety of the EP molecule, and forms a stable five-membered boronate ester (Chen Y et al., 2019; Pan L et al., 2022). This specific bond is the foundation for the probe's selectivity. First, we investigated the FT-IR spectra before and after the addition of EP, as shown in Fig. 8a. The characteristic B-O-H stretching bands of the boronic acid ligand at 1370 cm^{-1} and 1312 cm^{-1} shifted to 1368 cm^{-1} and 1313 cm^{-1} , respectively, indicating the formation of covalent bonds between the $-\text{B}(\text{OH})_2$ groups and the

cis-diol moiety of EP. Then, we examined the XPS spectra before and after the addition of EP (Figs. 8b-8c). As shown in Fig. 8c, the O 1s spectrum revealed that the binding energy of the B-O bond increased from 529.7 eV to 530.8 eV, accompanied by varying degrees of shifts in the C-O and C=O peaks. Meanwhile, the binding energy of B-C/B-O decreased from 189.60 eV to 189.10 eV when EP was added (Fig. 8d). These results further confirm the boronate-affinity interaction between Zn-Eu-MOF and EP.

To further elucidate the fluorescence-quenching mechanism of Zn-Eu-MOF, UV-vis absorption spectra were recorded before and after the addition of EP (Fig. 9a). Upon the introduction of EP, a noticeable redshift in the absorption peak of Zn-Eu-MOF was observed, indicating the formation of a new ground-state complex. This is consistent with the covalent interaction between the -B(OH)_2 groups and the cis-diol moiety of EP. This result suggests that the fluorescence-quenching process involves a static quenching (SQE) mechanism. In addition, we noted a significant spectral overlap between the absorption spectrum of EP and the excitation spectrum of Zn-Eu-MOF (Fig. 9b), which indicated competitive absorption of the excitation light by EP. This phenomenon can be attributed to the IFE (Chen D et al., 2023), which further reduces the fluorescence intensity of the system. We also performed fluorescence lifetime measurements of Zn-Eu-MOF before and after the addition of EP (Fig. 9c), and found that the fluorescence lifetime decreased from 3.78 ns to 2.05 ns when EP was added, indicating that the detection process involved dynamic quenching. To gain deeper insight into the fluorescence-quenching mechanism, we performed DFT calculations at the B3LYP/6-31G* level to analyze the frontier molecular orbitals of BBDC and EP. As shown in Fig. 9d, the LUMO energy level of BBDC (-1.99 eV) was lower than that of EP (-0.28 eV), indicating that electron transfer from BBDC to EP is energetically unfavorable, which excludes a photoinduced electron transfer (PET) pathway (Yan Y et al., 2025).

In summary, the fluorescence quenching of Zn-Eu-MOF induced by EP is dominated by dynamic quenching and the IFE, while static quenching contributes to a lesser extent through the formation of a ground-state complex. The specific covalent interaction between boronic acid groups and the cis-diol structure of EP governs the recognition process and disrupts the antenna effect. Meanwhile, DFT calculations rule out a PET mechanism. These factors collectively account for the observed quenching behavior.

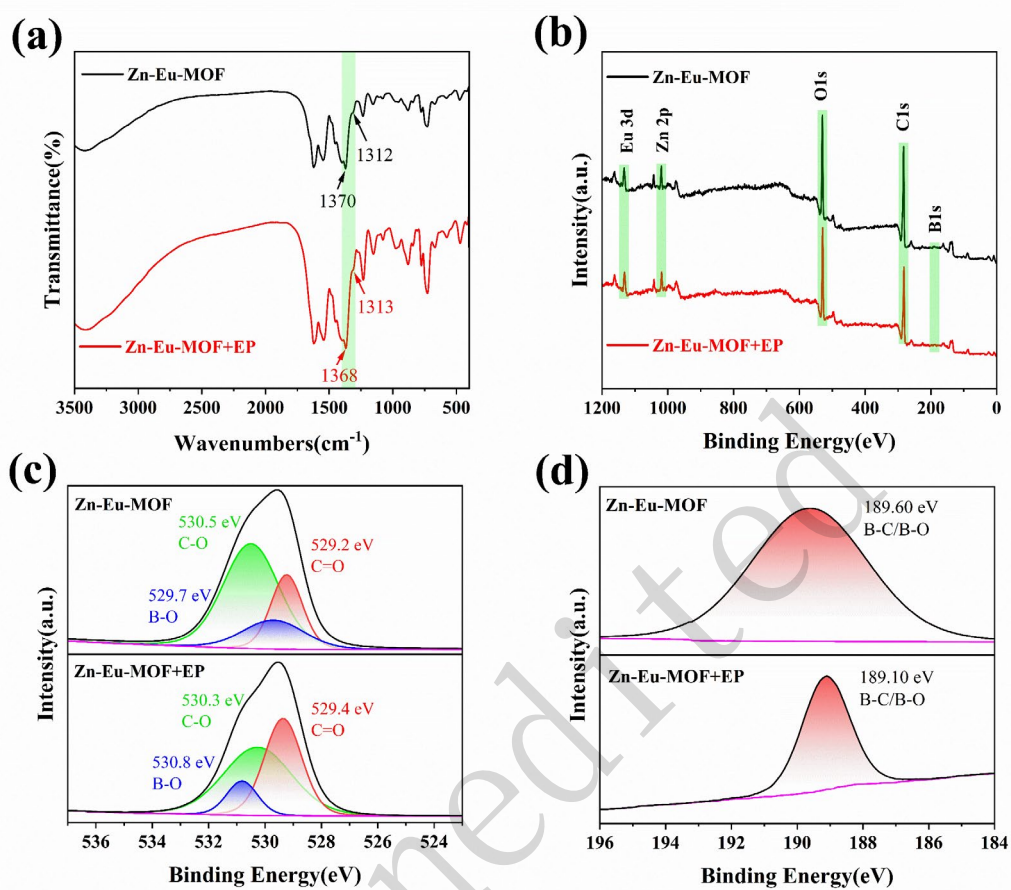


Fig. 8 (a) Fourier transform infrared (FT-IR) spectra, (b) X-ray photoelectron spectroscopy (XPS) spectra, (c) O 1s, and (d) B 1s of Zn-Eu-MOF before and after the addition of epinephrine (EP).

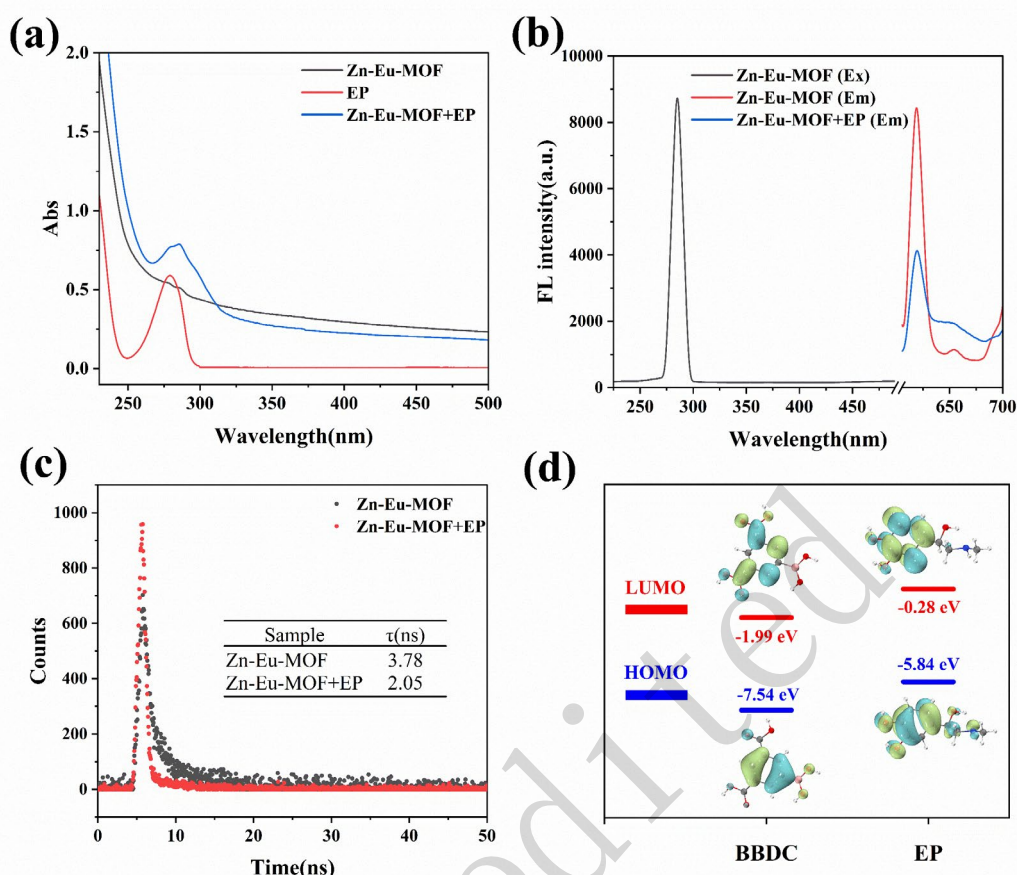


Fig. 9 (a) Ultraviolet-visible (UV-vis) absorption spectra of Zn-Eu-MOF, epinephrine (EP), and Zn-Eu-MOF+EP; (b) Excitation and emission spectra of Zn-Eu-MOF; (c) Fluorescence lifetimes of Zn-Eu-MOF in the presence and absence of EP; (d) Highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) energy-level diagrams for 3,5-dicarboxyphenylboronic acid (BBDC) and EP.

4 Conclusions

In summary, this study reports a boronic acid-functionalized bimetallic Zn-Eu-MOF as a highly sensitive and selective fluorescent probe for EP detection in human serum and urine via a fluorescence quenching mechanism. The incorporation of Zn^{2+} ions enhances Eu^{3+} luminescence through an antenna-mediated energy-transfer process, yielding an approximately 2.5-fold amplification in fluorescence intensity compared to the monometallic Eu-MOF counterpart. The 3,5-dicarboxyphenylboronic acid ligands enable specific recognition of cis-diol-containing EP. The resulting sensor displays a wide linear range, low detection limit, and excellent anti-interference performance, with successful application in human serum and urine. This work provides a simple, efficient, and mechanism-guided strategy for constructing boronic-acid-functionalized lanthanide MOF sensors, offering promise for rapid catecholamine analysis in clinical diagnostics and point-of-care testing.

Materials and methods

Detailed methods are provided in the electronic supplementary materials of this paper.

Data availability statement

The data will be made available upon request.

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Author contributions

Yixuan NI performed the experimental research and data analysis, and wrote and edited the manuscript. Changyu CHEN, Baoqi LUO and Jianliang LI participated in experimental research and data analysis. Ming GUO, Qiao DENG, Jingjing XU and Dan WEI contributed to the study design, data analysis, and writing and editing of the manuscript. Xu WANG provided the original sample. All authors have read and approved the final manuscript, and therefore, have full access to all the data in the study and take responsibility for the integrity and security of the data.

Compliance with ethics guidelines

Yixuan NI, Changyu CHEN, Baoqi LUO, Jianliang LI, Ming GUO, Qiao DENG, Jingjing XU, Dan WEI, Xu WANG declare that they have no conflict of interest.

This study was approved by the Ethics Committee of Hangzhou Medical College (Approval No: LL2023-05).

Declaration on the use of generative AI tools

No generative AI tools were used in the preparation of this manuscript.

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Supplementary information:

Figs. S1-S3; Table S1