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Ultrasensitive detection of Cadmium ions using a microcantilever-based piezoresistive sensor for groundwater

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Abstract

In this paper, we proposed the selective and ultrasensitive detection of Cadmium ions using a Cysteamine functionalized microcantilever-based sensor with cross-linked DL-glyceraldehyde. The detection time for various laboratory-based techniques is generally 12-24 hours. The experiments performed to create the SAMs of Cysteamine (Cys) cross-linked with DL-glyceraldehyde on the Microcantilever surface to selectivity capture the targeted Cadmium ions. The proposed portable microfluidic platform able to achieve the detection in 20-23 minutes and having a Limit of Detection (LOD) of 0.56 ng (2.78 pM), which perfectly describes its excellent performance over other reported techniques. Many researchers used Nanoparticles (NPs)-Based sensors for Heavy metal ions detection, but day by day, increasing usage and commercialization of Nanoparticles are rapidly expanding their deleterious effect on human health and the environment. The proposed technique uses the blend of thin-film and microcantilever (MEMS)-technology to overdrive the disadvantages of the Nanoparticles-approaches for selective Cadmium ions detection and having LOD less than

WHO limit of 3 μg/L. The fabricated sensor can achieve the limits efficiently well below the standards set by the WHO and helpful for the early detection of HMIs polluted source.

Keywords

Piezoresistive Sensors; BioMEMS; Microfluidics; Microcantilevers; SAM (Self Assembled Monolayer's); Heavy Metal Ions (HMIs); Limit of detection (LOD); WHO (World Health Organization), Micro-ElectroMechanical Systems (MEMS)

Introduction

Water is fundamentally essential to sustaining life, and an increase in the global population led to an exponential increase in waste disposal, which definitely may cause significant stress on water quality demand [1]. Water quality monitoring, clean water is one of the main priorities of the 21st century–worldwide, and negligence to this may have a significant effect on maintaining the safety and security of human beings [2,3]. Water contamination caused by cadmium ions is a common issue and has contributed to enlarging the water quality demands. Industrial wastewater, mining industry, fossil fuels, iron and steel industry, cement manufacturing unit, electroplating industry, manufacturing unit of PVC plastic and pipes, Ni-Cd batteries, fertilizers, and pesticides use in agriculture, photovoltaic devices, soil, and sediments are the sources of cadmium in groundwater. Cadmium is one of the highly toxic HMI, and its poisoning may cause fatigue, headaches, nausea, vomiting, abdominal cramps, bone degeneration, diarrhea, osteoporosis, renal dysfunction, cancer, anemia, and neurological disorders such as Parkinson's disease, Alzheimer's disease[4,5]. The water contamination due to different HMIs is one of the major issues out of which cadmium (Cd^2), is very hazardous, and WHO has provided limits 3 (μg/L) [6]. Therefore, we conclude from the WHO limit that cadmium is very dangerous, and small mass below the limit is also hazardous and detrimental to life. Hence, it is very much essential to sense the Cadmium ions in picomolar (pM) range well below the specified WHO limit.

The Ion-Selective Electrodes (ISEs) fabricated by [7] is stable and precise for HMIs detection, but the measurement is done by using laboratory-based equipment. Nanotubes, nanorods, nanoneedles, and nanoplates based sensor is also used to detect the HMIs selectively but up to nanomolar range[8-11]. Many authors using adsorption methods to extract the heavy metals from groundwater [12-16] but only useful to eliminate the dangerous heavy metals when a polluted source is identified. Luminescence(fluorescent)-based sensors have been used by many researchers to selectively detect the HMIs [17-22] but this method required lab-based equipment for analysis and detection. Also, most of the reported fluorescent probe reply only on the absorption and fluorescence change and need to acquired dynamic procedure [23]. A magnetic field powered pressure sensor proposed by Khan et al.[24] is capable of measuring pressure in kPa range but need to check the suitability for very low pressure caused by HMIs. A reduced graphene oxide (RGO) based sensor and a microfluidic platform fabricated by [25-27] can be used with some surface modification for HMIs application but mostly capable of detecting μMol sample. The polymer-based microcantilever using an encapsulated piezoresistor is proposed by Kale et al.[28], but not suitable and sustainable during other high-temperature sputtering processes. Microcantilevers based on SiO_2 have been manufactured by Tang et al.[29] to enhance the sensitivity of cantilever sensors. Many authors use the optical setup for microcantilevers, but optical output has several disadvantages when operating in the water environment; when the refractive index of water changes [30,31].

Many authors have proposed the electrode-based approaches for selective sensing of cadmium ions [32], but the limit of detection is always in μM to nM ranges. Some of the authors used fluorescent [5,33] and calorimetric [34] approach to selectively detect the Cadmium ions required laboratory-based equipment for analysis and LOD is also in the nanomolar range. These methods were susceptible and reliable for the qualitative and quantitative determination of Cadmium ions, but they are time-consuming, expensive, and not suitable for on-site determination. The calorimetric approach proposed by [34-37], free from these problems but not capable of differentiating between two nearby ranges and LOD is also on the higher side. The electrochemical sensor is a good approach[38], but required a lab instrument for measurement.

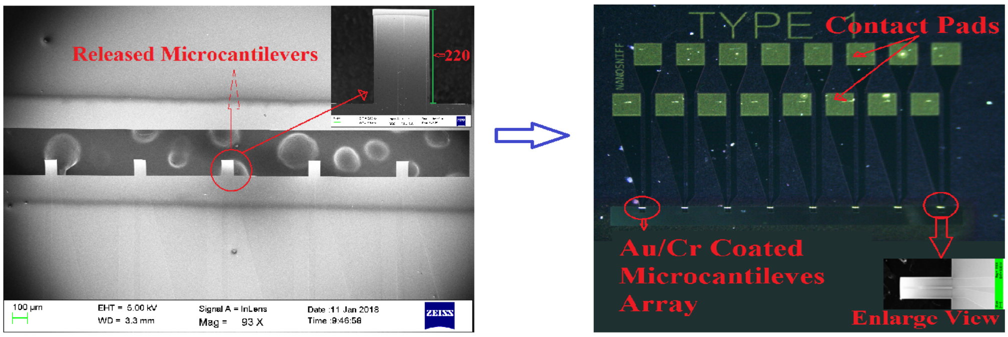
We have previously investigated SAM of Homocysteine (HCys)-pyridinedicarboxylic acid (PDCA) for selective sensing of the Hg^2 ions using a portable piezoresistive platform [39,40] and experimental results confirmed that proposed setup is capable of picomolar sensing. In this paper, we have used the previously designed portable piezoresistive platform to selectively capture the Cadmium ions in the picomolar range. The preliminary result shows that the fabricated device has an excellent response for selective sensing of cadmium ions within 20-23 minutes with 0.56 ng/mL (2.78 pM) LOD, which is well below the limit set by WHO for cadmium ions.

The paper flow describes the methodology, the formation of SAM for Ultra-selective Cadmium ions detection and its characterization using Field Emission Scanning Electron Microscopy (FE-SEM), use of the portable experimental platform for the MEMS-based piezoresistive device to selective capture the cadmium ions at the picomolar level and verification of the experimental results using Energy Dispersive X-ray (EDX).

Fabrication and calibration of Piezoresistive device

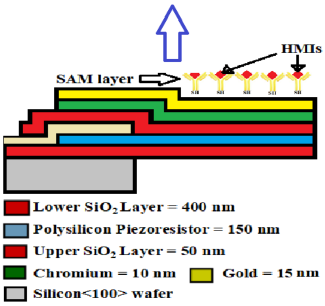
We have previously fabricated the Polysilicon-based piezoresistive sensor using a standard microfabrication process and also perform the calibration using Atomic force microscopy (AFM) [40]. The stiffness (k) of the fabricated piezoresistive sensor calculated using the AFM technique is 131.18-146 mN/m, which is well below the stiffness required for the BioMEMS application (1000 mN/m[41]). We have also used COMSOL 5.3 software for design and simulation of the piezoresistive sensor to verify the stiffness and sensitivity with respect to fabricated device [42]. The fabricated piezoresistive sensor layer structure with thickness, FESEM image, PCB, and the experimental platform is shown in Fig.1.

To use the microcantilever device for selective Cadmium ions detection required surface modification. The surface modification of the sensor basically used selective thiol coating on top gold surface. Here, we have developed SAM of cysteamine-glyceraldehyde on top of Microcantilever-based sensors with integrated piezoresistive readout to get the change in resistance due to changes in surface stress. Until now, many people used lab-based optical setups to measure the change in surface stress of cantilever sensors. Moreover, the proposed piezoresistive device has capabilities to directly capture the surface stress make this better option for HMIs applications.

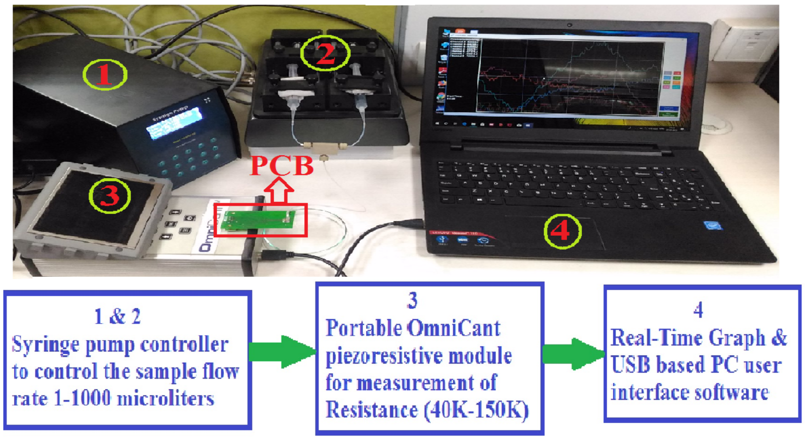


(b) FESEM image of piezosensor

(c) Optical microscope view of PCB



(a) Fabricated piezosensor layer structure & thickness



(d) Portable Experimental Setup for Cadmium detection

Figure 1: Fabricated piezoresistive sensor and experimental platform for cadmium ion detection

Microfluidic platform for piezosensor to selectively capture cadmium ions

Methodology

In this proposed method, we have combined the benefits of three different technologies, namely thin-film, Nanoparticles (NPs), and MEMS, to selectively target the cadmium ions at the picomolar (pM) ranges. Also, we know that excessive commercialization of Nanoparticles leads to increasing their harmful effect on life and the environment by[43-45]. In this article, we try to expand the AuNPs-based technology proposed by [34] for ultrasensitive sensing of Cadmium ions with cysteamine functionalized DL-glyceraldehyde (Cys-DL-GC) using the remarkably advanced MEMS-based piezoresistive platform. We know that the MEMS-based sensor has very high sensitivity compared to any other technique and prove the importance of this hypothesis for ultrasensitive application. The complete process flow for the piezoresistive microcantilever-based biosensor to enhance the sensitivity and selectivity for Cadmium ions shown in Fig.2.

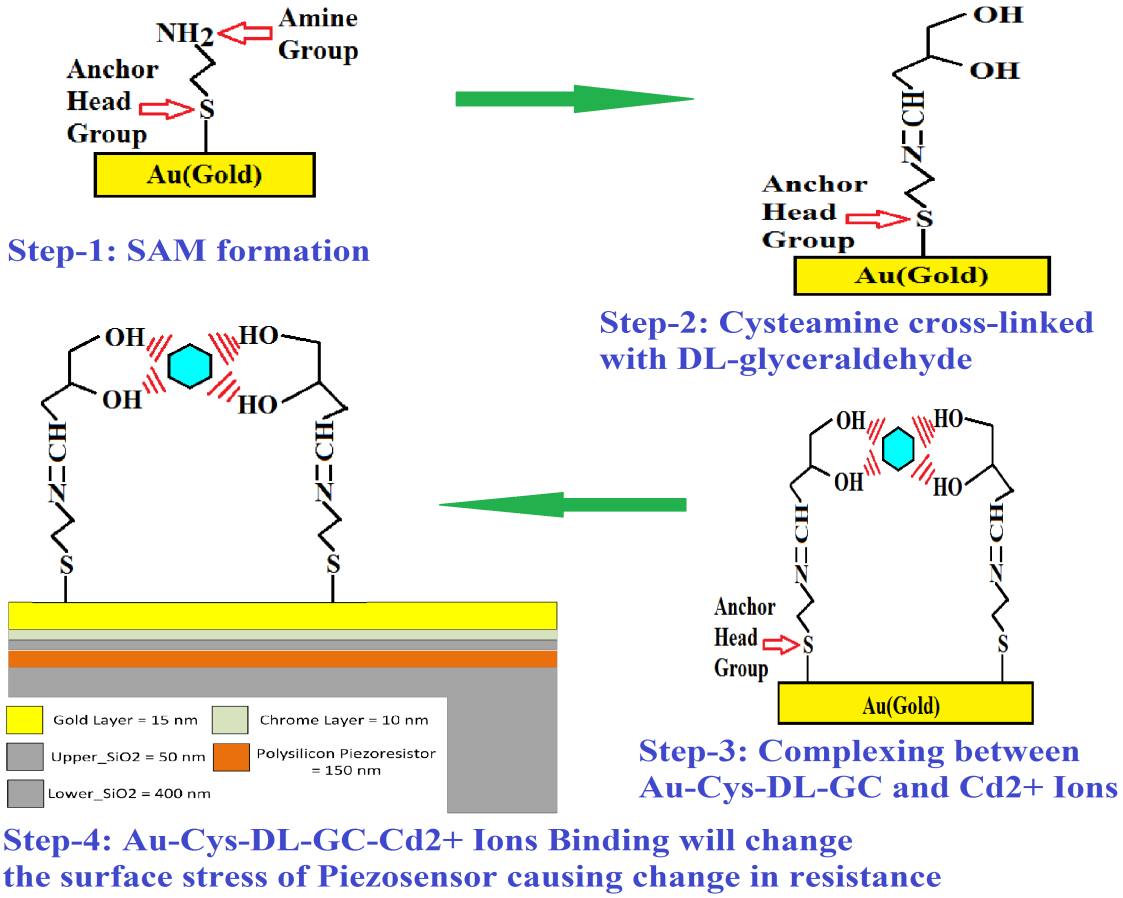
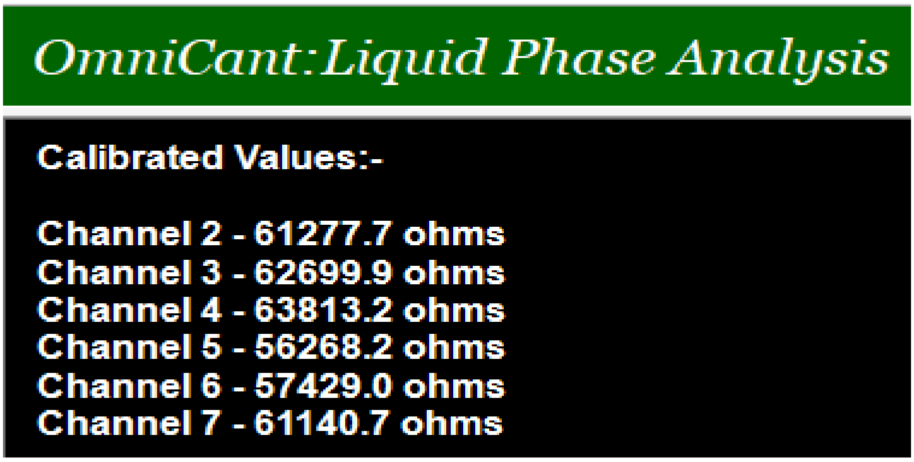


Figure 2: Process flow of biosensor for selective Cd^2 ions detection

Here, we have used the fabricated microfluidic platform with a microcantilever-based piezoresistive sensor to capture the targeted Cadmium ions at the picomolar range.

Experimental results and discussion

We have evaluated the performance of fabricated Microcantilever-based device for selective Cadmium ions detection in the microfluidic environment using the OmniCant setup shown in Fig.1(d). The non-stressed calibrated resistance values of Piezoresistive sensor using SAM of cysteamine cross-linked DL-glyceraldehyde (Cys-DL-GC) is in the range of 56268-63813 ohms. The Non-stress resistance value of fabricated piezoresistive die shown in Fig.3 using OmniCant microfluidic platform. The block cantilever used as a reference. The microcantilever-2 selected as a reference for Cys-DL-GC experiments. The calibrated value of Cys-DL-GC SAM shows that some of the microcantilever (1,8) broken during the wire bound and not present in the analysis.



OmniCant:Liquid Phase Analysis

Calibrated Values:-

Channel 2 - 61277.7 ohms
Channel 3 - 62699.9 ohms
Channel 4 - 63813.2 ohms
Channel 5 - 56268.2 ohms
Channel 6 - 57429.0 ohms
Channel 7 - 61140.7 ohms

Figure 3: Non-stress calibrated values for used piezoresistive die

These piezoresistive MEMS-devices show a fast response to change in the resistance depending on the additional HMIs mass (Cadmium ions) loaded on the surface at deficient concentration, i.e., picomolar range.

Experimental results for SAM of cysteamine with cross-linked DL-glyceraldehyde to selectively detect cadmium ions

The proposed microfluidic platform provides the chance of real-time monitoring of Cadmium ions in groundwater. We have performed the experiment to selectively capture the targeted Cadmium ions using the thiol coating of cysteamine with cross-linked DL-glyceraldehyde (Cys-DL-GC). Also, we have already discussed that the Au/Ag nanoparticles (NPs)-based methods required the lab-based equipment such as fluorescence spectroscopy, which ultimately leads to the non-portable platform. Hence, we have focused our research on selective detection of the cadmium ions using the portable experimental platform.

Experimental Procedure:

1. We have prepared the stock solution of cysteamine (Cys=10mM/10mL).
2. Gently dip the piezoresitive devices in a petri-dish containing cysteamine thiol.
3. Keep the petri-dish for at least 12-24 hours, but more time gives you better packing density of SAM layer.
4. Furthermore, 2% W/V (0.2g/10mL) DL-glyceraldehyde (DL-GC) prepared in phosphate buffer saline (PBS) buffer at pH 7 according to [34].
5. The SAM of cysteamine were allowed to cross-link with DL-glyceraldehyde solution at least for 2-3 hours by covering the container using silver foil.
6. Now, we have prepared the stock solution of 1mM/10mL for different HMIs ($AlCl_3$, $MnCl_2$, $CrCl_3$, $HgCl_2$, $PbCl_2$, $CdCl_2$).
7. The flow rate = 30μL/minute is constant for complete experiments.

DI water initially began to stabilizing the microcantilever-based sensor in a liquid environment and then injecting different heavy metals through the microfluidic pumps. So, after this injection event, the real influence of the HMIs began to change the piezoresistance of the microcantilever device. The change in piezo-resistance (ΔR) is calculated using a formula:

$$\Delta R = \Delta R_{Block} - \Delta R_{Unblock} \tag{1}$$

Where ΔR_{Block} is the change in piezoresistance of block microcantilever with Acetyl Chloride and $\Delta R_{Unblock}$ is the change in piezoresistance of unblocking microcantilever.

The change in piezoresistance of unblocked microcantilever regarding block microcantilever of Acetyl Chloride(2) is shown in Fig.4.

Initially, we have used DI water to settle-down the microcantilever in a liquid environment for the 7-minutes duration; the piezo-resistance change is stable during this period of time on a particular value. When we started to inject different heavy metals after 7-minutes except for the cadmium ions, the change in piezoresistance minimal (5-30 ohms). When we injected cadmium ions after 7-minutes, the change in piezoresistance is around 200-300 ohms for each microcantilever. These results show the selectivity of the proposed method for Cadmium ions with respect to other HMIs. It is also evident that microcantilever-5 (Fig.4(c)) shows a non-linear response. The rationale behind this is that no binding sites available for Cadmium ions over microcantilever surface. From Fig.4(b,d), It is also observed that two microcantilever shows a decrease in resistance because of tensile stress due to small no. of biomolecule (Cadmium ions) binding on the surface gives tensile stress and other three microcantilever (Fig.4(a,c,e)) shows an increase in the resistance because of compressive surface stress when large no. of biomolecule binding with microcantilever surface [46].

Fig. 5 demonstrates the average change in piezoresistance of Au-Cys-DL-GC coated cantilever-based sensor for different heavy metals ($AlCl_3$, $MnCl_2$, $CrCl_3$, $HgCl_2$, $PbCl_2$, $CdCl_2$).

The average value of change in piezoresistance is the difference between the average change in piezoresistance for DI water and particular heavy metal injected. This difference shows that SAM of cysteamine with cross-linked DL-glyceraldehyde(Cys-DL-GC) has a higher selectivity for Cadmium ions as compared with other heavy metals. The average value of change in piezoresistance of Au-Cys-DL-GC coated microcantilever is approximately 130-240 ohms for Cadmium ions and 5-30 ohms range for other injected heavy metals. The total value of average change in piezoresistance for the concentration of 0.56 ng (see the appendix for LOD calculation) Cadmium ions is 877.72 ohms.

Verification of performed experiment results using EDX (Energy Dispersive X-ray Analysis) tools for selective detection of Cadmium ions

As we know, thiols can bind to all types of HMIs. So, to selectively bind and detect the cadmium ion, we have to modify or functionalize the thiol with some material which has selectivity only for Cadmium ions. From the performed experiment results, it is observed that the fabricated MEMS-based sensor is capable of selective Cadmium ions detection using SAM of cysteamine with cross-linked DL-glyceraldehyde(Cys-DL-GC). If we have to characterize the SAM above microcantilever device has minimal analytical techniques available because of its fragile nature. The FESEM/EDX is the pre-eminent tool to characterize the SAM on the top surface of the cantilever without damaging the device. Therefore we conducted the characterization of proposed MEMS-device using FESEM/EDX to validate these findings. The EDX spectra of the microcantilever-based MEMS sensor with SAM of cysteamine cross-linked DL-glyceraldehyde (Cys-DL-GC) on top Au-surface shown in Fig. 6.

From the EDX spectra of cysteamine cross-linked DL-glyceraldehyde (Cys-DL-GC), it is clear that no cadmium ions detected before exposer to $CdCl_2$ during the experiment. The EDX spectra of the microcantilever-based MEMS sensor with SAM of cysteamine cross-linked DL-glyceraldehyde (Cys-DL-GC) on top Au-surface after exposer to $CdCl_2$ shown in Fig. 7.

The EDX spectra in tabular form say about the percentage mass of the respective entity in a given scan region, explicitly showing the presence of Cadmium ions and the percentage number of molecules capture in that scan region.

Table 1 represents a comparative analysis of different techniques to selectively capture Cadmium ions in the picomolar range. For selectivity, we have taken 1 mM concentration of all the HMIs (Al, Mn, Cr, Hg, Pb, Cd) and prepare the stock solution of 10 mL. Now, diluted all the HMIs 10 μL concentration taken from a stock volume in 5 mL. From the experiment findings, we observed the fact that fabricated piezoresistive sensor needs an utmost 20-23 minutes for selectively capture the targeted cadmium ions. So, maintaining the flow rate = 30μL/minute, the total injected concentration is 0.69 mL for a maximum of 23 minutes during the performed experiment. Therefore, the corresponding mass for $AlCl_3$, $MnCl_2$, $CrCl_3$, $CdCl_2$, $PbCl_2$, and $HgCl_2$ is 0.67 ng, 0.55 ng, 0.74 ng, 0.56 ng, 0.77 ng, and 0.75 ng respectively.

From the comparison table 1, it is clearly observed that proposed microfluidic platform has the power and ability to selectively capture the targeted Cadmium ions as small as 2.78 pM/mL (LOD) and outperform other approaches that require sophisticated measuring instruments. The methods proposed by [4,56] have outstanding potential for a picomolar range of detection but required

Table 1: Comparison with different methods for cadmium detection

Reference	Analyte (HMI)	Limit of Detection (LOD)	Method Used	Detection Technique
Sabrina Heng et al. 2017 [4]	Cadmium ions	100 pM	Microstructured/optical fiber	Fluorescence/ Absorption spectra (Lab based)
Ali Ourari et al. 2018 [32]	Cadmium ions	1 μM	Carbon Paste Electrode	XRF/XRD/anodic stripping voltammetry (Lab based)
Yu-Feng Zhu et al. 2017 [33]	Cadmium ions	2.15 nM	fluorescent aptamer probe	F-4500 fluorophotometer/UV-2450 spectrophotometer /Lab based
Jing Qian et al. 2017 [5]	Cadmium ions	0.5 nM	Ratiometric fluorescence	UV-vis spectroscopy/fluorescence spectra/(Lab based)
R. Yadav et al. 2018 [34]	Cadmium ions	21 nM	AuNP based probes	Colorimetric/FT-IR/DLS/(Lab based)
Na Chen et al. 2016 [35]	Cadmium ions	10 μM	AuNP based electrode	Colorimetric/UV-vis spectroscopy/(Lab based)
M. Ghanei-Motlagh et al. 2018 [38]	Cadmium ions	1.33 nM	polymeric-NPs/sol-gel technique	Anodic stripping voltammetry (ASV)/FT-IR/(Lab based)
Papiya Dhara et al. 2019 [47]	Cadmium ions	800 μM	Localized Surface Plasmon Resonance technique (LSPR)	Optical fiber setup (Lab based)
Adarsh Nigam et al. 2019 [48]	Cadmium ions	2.26 nM	AlGaN/GaN HEMT	High Electron Mobility Transistor (HEMT)
Cheng Ju et al. 2018 [49]	Cadmium ions	65 μM	Gold nanoclusters/graphene based	Fluorescent probe/UV-vis spectroscopy/(Lab based)
Ling Wong et al. 2017 [50]	Cadmium ions	1 μM	Gold Bioluminescent based	Fluorescent/Microalgae-Based(Lab based)
Safari et al. 2020 [51]	Cadmium ions	1.062 μM	FRET probe-ZnS QD	FT–IR/UV–Vis/DLS/TEM/(Lab based)
Gan et al. 2020 [52]	Cadmium ions	5.56 nM	AuNPs-based	colorimetric system/UV–vis spectra/TEM/(Lab based)
Pham et al. 2019 [53]	Cadmium ions	18.5 μM	Fluorometric Chemosensor	colorimetric/UV-visible/Fluorescent spectra/(Lab based)
Kava et al. 2020 [54]	Cadmium and Lead ions	2.23 nM	carbon stencil printed electrode (GC-SPE)	Raman scattering
Jabariyan et al. 2019 [55]	Cadmium ions	4.95 μM	silver nanoparticles (AgNPs)	UV-visible/FT-IR/TEM/(Lab based)
Mandoc et al. 2017 [56]	Cadmium, Copper, Mercury, Lead ions	10-100 pM	Electrochemical sensors	PGSTAT Potentiostat
This Work	Cd^2	2.78 pM	Piezoresistive sensor	Portable setup

costly, sophisticated analytical tools for measurements [4] and selectivity problem [56]. Many authors used the colorimetric/fluorescence technique for selective HMIs detection but highly sensitive to pH variation by [57]. In a colorimetric sensor, the concentration variation is shown by different shades of color and challenging to identify shads for the different ranges of concentrations. Both the colorimetric/fluorescence technique uses NPs and excessive commercialization of Nanoparticles, quickly expanding their harmful effect on life and environment, as discussed earlier in methodology.

Conclusions

The proposed microcantilever-based device is tested on a microfluidic setup for selective detection of cadmium and found competent in achieving the sensing in 20-23 minutes. The 0.56 ng/mL (2.78 pM) limit of detection is possible with SAM of cysteamine cross-linked DL-glyceraldehyde (Cys-DL-GC), which is well below the standards set by WHO for the Cadmium ions. The average value of change in piezo-resistance of Au-Cys-DL-GC coated microcantilever is approximately 130-240 ohms for Cadmium ions and 5-30 ohms range for other injected HMIs. The total value of average change in piezo-resistance for the concentration of 0.56 ng (see the appendix for LOD calculation) Cadmium ions is 877.72 ohms. The most critical feature of this approach is the need for a sample volume of one milliliter. It is also evident from EDX spectra that no other HMIs except Cadmium ions have been found. This EDX finding means that fabricated microcantilever-based piezoresistive sensor does not have cross selectivity. In conclusion, this approach could serve as a portable framework for on-site, ultrasensitive, and selective identification of Cadmium ions at the picomolar range.

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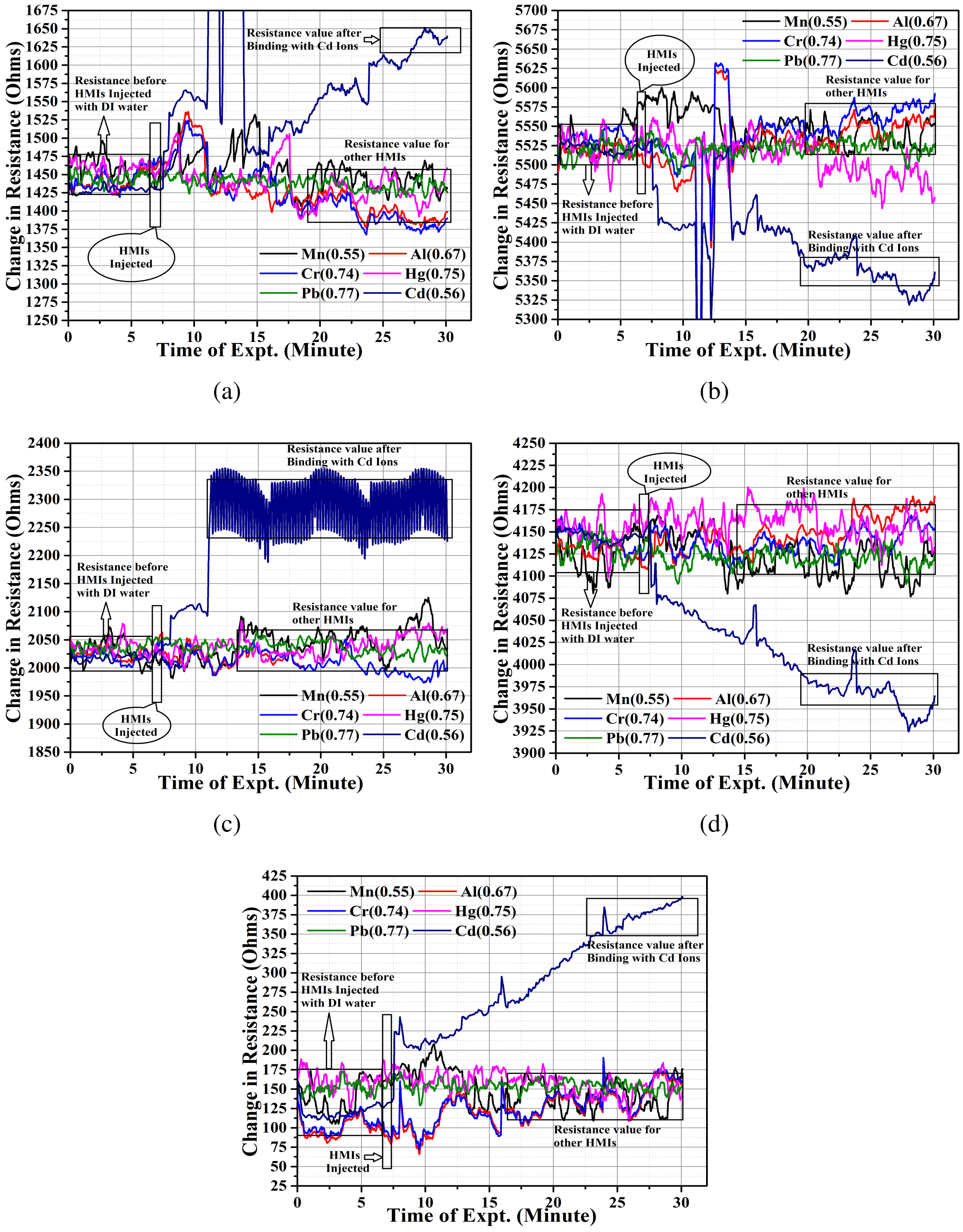
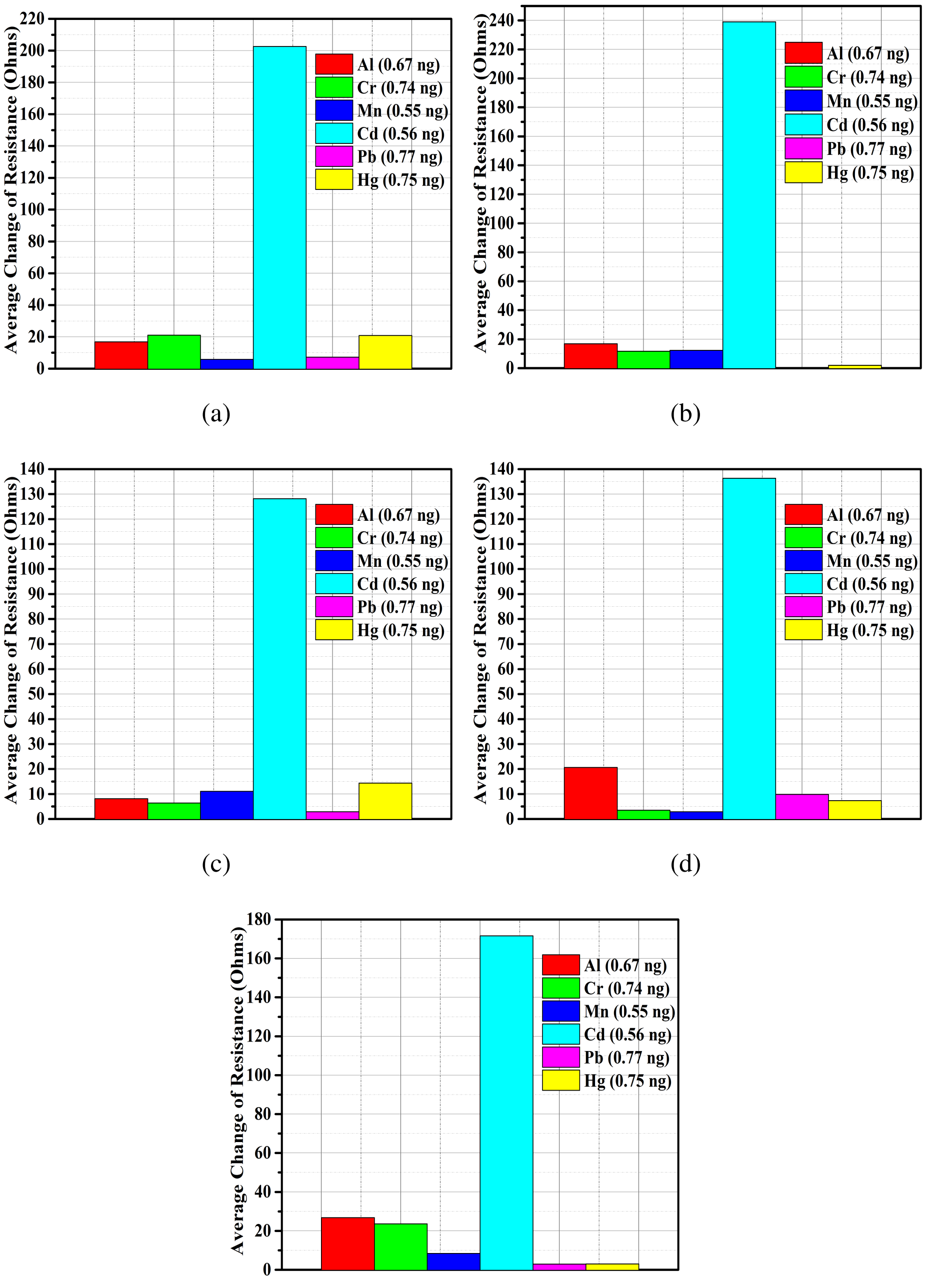


(a) (b)

(c) (d)

(e)

Figure 4: The change in piezoresistance of unblock cantilever (a) Cys-DL-GC(3), (b) Cys-DL-GC(4), (c) Cys-DL-GC(5), (d) Cys-DL-GC(6) and (e) Cys-DL-GC(7) with respect to block cantilever of Acetyl Chloride(2)

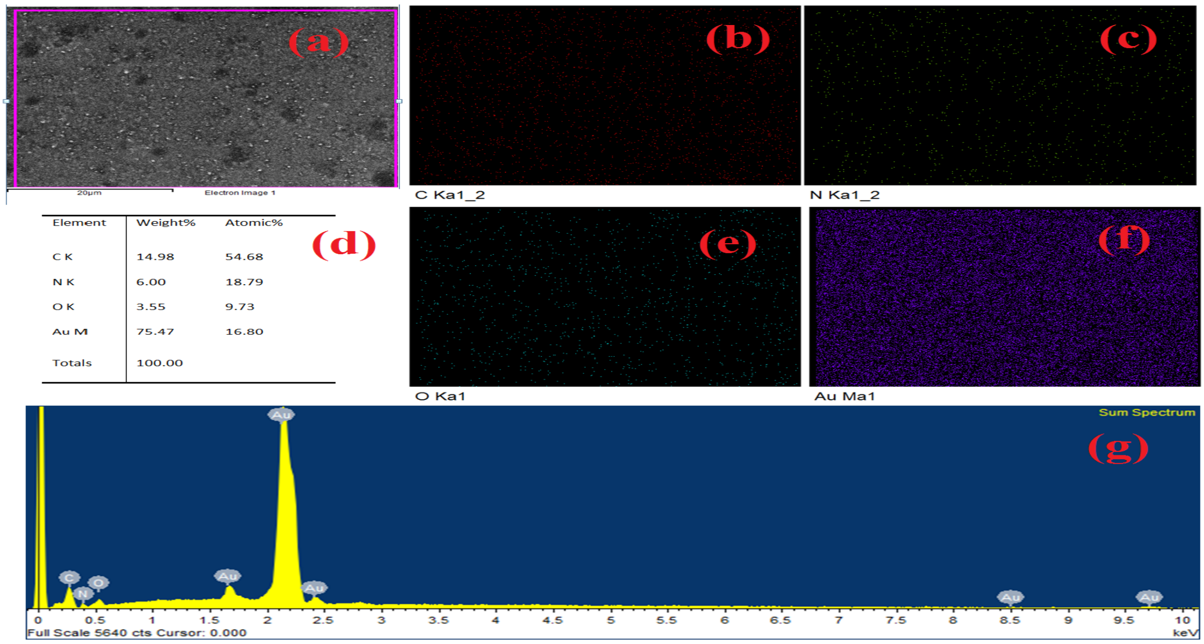


(a) (b)

(c) (d)

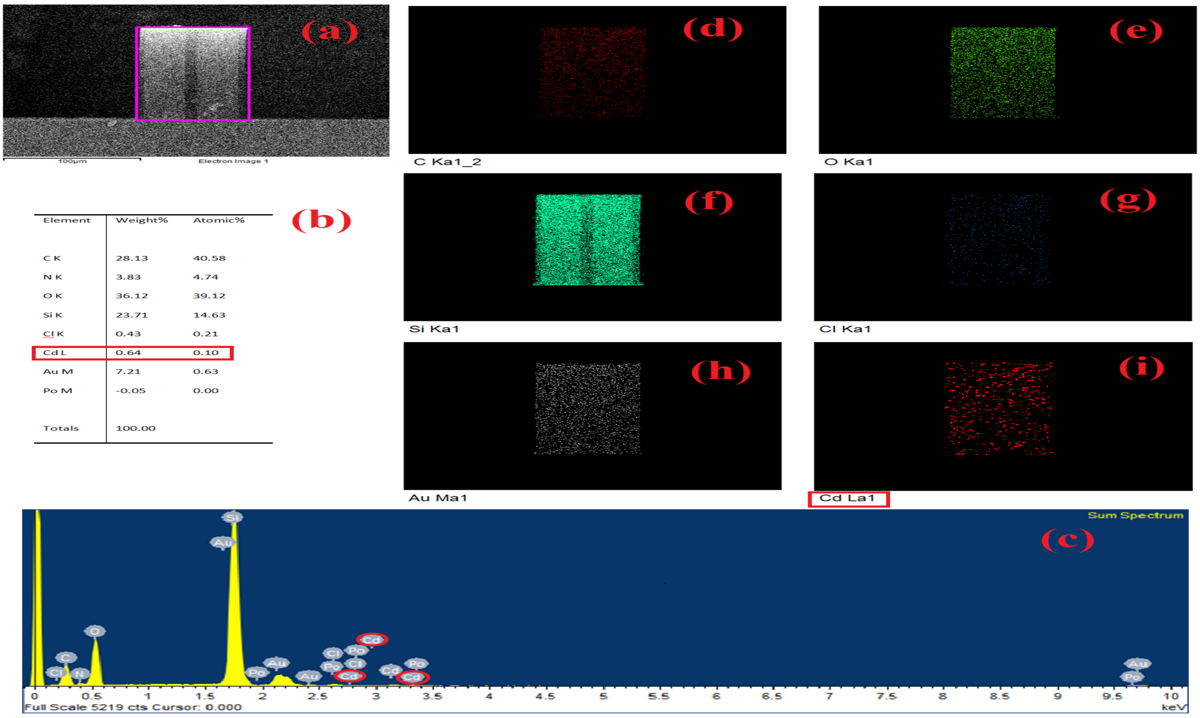
(e)

Figure 5: The average change in piezoresistance of Microcantilever a) Au-Cys-DL-GC(3) b) Au-Cys-DL-GC(4) c) Au-Cys-DL-GC(5) d) Au-Cys-DL-GC(6) e) Au-Cys-DL-GC(7)



Element	Weight%	Atomic%
C K	14.98	54.68
N K	6.00	18.79
O K	3.55	9.73
Au M	75.47	16.80
Totals	100.00	

Figure 6: EDX spectra for SAM of Cysteamine (Cys)-cross-linked DL-glyceraldehyde (Cys-DL-GC) (a) Scan area for analysis, (d) Tabular form of element detected (g) Spectra of elements detected, and (b,c,e,f) are colour mapping of different element detected during EDX analysis



Element	Weight%	Atomic%
C K	28.13	40.58
N K	3.83	4.74
O K	36.12	39.12
Si K	23.71	14.63
Cl K	0.43	0.21
Cd L	0.64	0.10
Au M	7.21	0.63
Po M	-0.05	0.00
Totals	100.00	

Figure 7: EDX spectra for SAM of Cysteamine (Cys)-cross-linked DL-glyceraldehyde (Cys-DL-GC) after exposer to Cd^2 ions (a) Scan area for analysis (b) Tabular form of element detected, (c) Spectra of elements detected, and (d,e,f,g,h,i) are colour mapping of different element detected during EDX analysis

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Appendix

LOD calculation for cadmium ions

- The molecular weight of cadmium $\left(CdCl_2H_2O\right) = 201.32\frac{g}{mole}$.
- The 1mM concentration of cadmium $\left(CdCl_2H_2O\right) = 0.2013\frac{g}{mole}$ in 1000 mL.
- For the 10 mL stock solution, the required concentration is $\left(x\right) = \frac{0.2013\times 10mL}{1000mL}$ g = 0.002013 g =2.013 mg in 10 mL.
- Take the 10 μL sample from the stock solution, So, the concentration in the 10 μL is $\left(x\right) = \frac{2.013\times 10^{-3}\times 10\times 10^{-6}}{10\times 10^{-3}}$=2.013 μg for 10 μL.

- Dilute this 10 μL concentration in 4.99 mL volume using Dilution Formula: $N_1 \times V_1 = N_2 \times V_2$: $N_1 \times 4990\ \mu L = 2.013\ \mu g \times 10\ \mu L$.
- $N_1 = \frac{2.013\mu g \times 10 \times \mu L}{4990\mu L}$= 4.034 ng in 5 mL.
- 1 mL volume contain 0.806 ng after dilution.
- So, with the constant flow rate = 30μL/minute, total sample volume is 0.69 mL for 23 minutes. Hence, the equivalent concentration= 0.56 ng for Cd.

Conversion of Grams to Moles for Cd

- As we know that, Moles=$\frac{Grams}{MolarMass}$=$\frac{0.56ng}{201.32\frac{g}{mol}} = 2.78 \times 10^{-12} Mol = 2.78pM$