

## MXene-supported Cobalt-MOF nanocomposite-printed electrochemical sensor with high sensitivity for blood creatinine detection under point-of-care settings

Debolina Roy<sup>a,b</sup>, Rajan Singh<sup>a,b</sup>, Soumen Mandal<sup>a,b</sup>, and Nripen Chanda<sup>a,b</sup>

\*Corresponding Author: somandal88@cmeri.res.in; n\_chanda@cmeri.res.in

<sup>a</sup>CSIR-Central Mechanical Engineering Research Institute, Durgapur, India.

<sup>b</sup>Academy of Scientific and Innovative Research (AcSIR), Ghaziabad, India.

**Table S1:** Performance comparison table for PoC/ chip based non-enzymatic electrochemical sensors reported for detection of creatinine in different biofluids

Creatinine oxidation site	Detection type	Current range & Sensitivity	Linear range & LOD	Application
MXene[1]	Square wave voltammetry (SWV)	NA; 0.015 $\mu\text{A } \mu\text{M}^{-1}$	10-400 $\mu\text{M}$ ; 1.2 $\mu\text{M}$	Human blood sample
Zn-MOF[2]	Electrochemical impedance spectroscopy (EIS)	NA; NA	50–2500 $\mu\text{M}$ 30 $\mu\text{M}$	Human serum
Paper-adsorbed iron (III) ions[3]	DPV	7.5-20 $\mu\text{A}$ ; NA	0.10 - 6.5 mM 0.043 mM	Urine
Nafion/polyacrylic gel-Cu <sup>2+</sup> /cuprous oxide NPs[4]	CV/DPV/EIS	225-275 $\mu\text{A}$ ; 0.034 $\mu\text{A } \mu\text{M}^{-1}$	1–2000 $\mu\text{M}$ ; 0.3 $\mu\text{M}$	Saliva
CuO/IL/ERGO[5]	CV	NA	0.01-2.0 mM; 0.22 $\mu\text{M}$	Blood serum
CuNPs[6]	CV	~35-85 $\mu\text{A}$ ; 0.2582 $\mu\text{A } \mu\text{M}^{-1}$	10-160 $\mu\text{M}$ ; 0.1 $\mu\text{M}$	Artificial saliva
SbNPs[7]	CV, Amperometry, and EIS	~3.5-4.2 $\mu\text{A}$ ; NA	0.6–1.0 $\mu\text{M}$ ; 0.74 $\mu\text{M}$	Human serum

## EXPERIMENTAL SECTION

### *Materials and Instruments*

Titanium aluminium carbide powder, 99% purity ( $\text{Ti}_3\text{AlC}_2$ ) was acquired from Nanoshel UK Ltd. Phosphate buffer solution (500 mL, 1M, pH 7.4,) and 2 Methylimidazole were purchased from Sigma-Aldrich, USA. Potassium hexacyanoferrate (III) ( $\text{K}_3[\text{Fe}(\text{CN})_6]$ ), potassium hexacyanoferrate (II) trihydrate ( $\text{K}_4[\text{Fe}(\text{CN})_6]\cdot 3\text{H}_2\text{O}$ ), creatinine, urea, sodium hydroxide, methanol and pH test strips were bought from Merck (India) Pvt. Ltd, while, dopamine, uric acid, and glutathione were procured from Himedia Laboratories Pvt. Ltd., India. Cobalt chloride ( $\text{CoCl}_2$ ) and silver conductive ink was purchased from AlfaAesar, USA. All chemicals used in this study were of analytical grade and used as received without any further treatment. The plasma separation membrane was obtained from Cobetter Filtration Equipment Co. Ltd., China. Single sided scotch tape was collected from Magic Tape, India. The printed circuit board/ PCB (FR1 grade), and silver/ silver chloride (Ag/AgCl) paste were purchased from Voltera (Canada) and Gwent Group of companies (UK), respectively. The carbon ink was bought from Bare conductive Ltd. UK. Digital multimeter, bolts & nuts, scissors, drilling machine, and wire were collected from a local supplier. The experimental solutions and buffers were prepared with ultrapure MilliQ water. Sheet resistance meter SRM-232-1000 was used to measure the sheet resistance. The coordinate measuring machine (CMM) was bought from Accurate gauging systems Pvt Ltd, India (Model: Spectra).

### ***Material characterization of the sensing material***

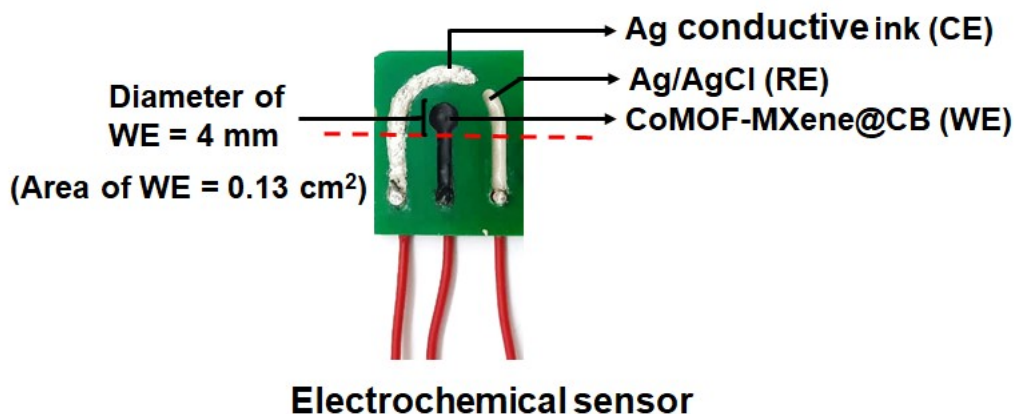
The dried newly synthesized nanocomposite powder was used for morphological characterization. Morphological topographies, surface microstructures, and elemental mapping were evaluated by Field-emission scanning electron microscope (FESEM) (Zeiss Sigma HD) and Transmission electron microscope (TEM) (JEOL JED 2300). The crystallinity of the sample was examined using the X-ray diffractometer (PANalytical Empyrean XRD) at  $2\theta$  Bragg's angle within the diffraction angle range of  $5^\circ$ - $70^\circ$ . RAMAN spectroscopy (WITEC 300 RAS instrument) was used to analyze the chemical structure of the nanocomposite. X-ray photoelectron spectroscopy (XPS) was utilized to analyze the surface properties of the CoMOF-MXene nanocomposite (Thermo fisher ESCALAB XI+).

### ***Application of developed sensor to human blood creatinine measurement and reusability studies***

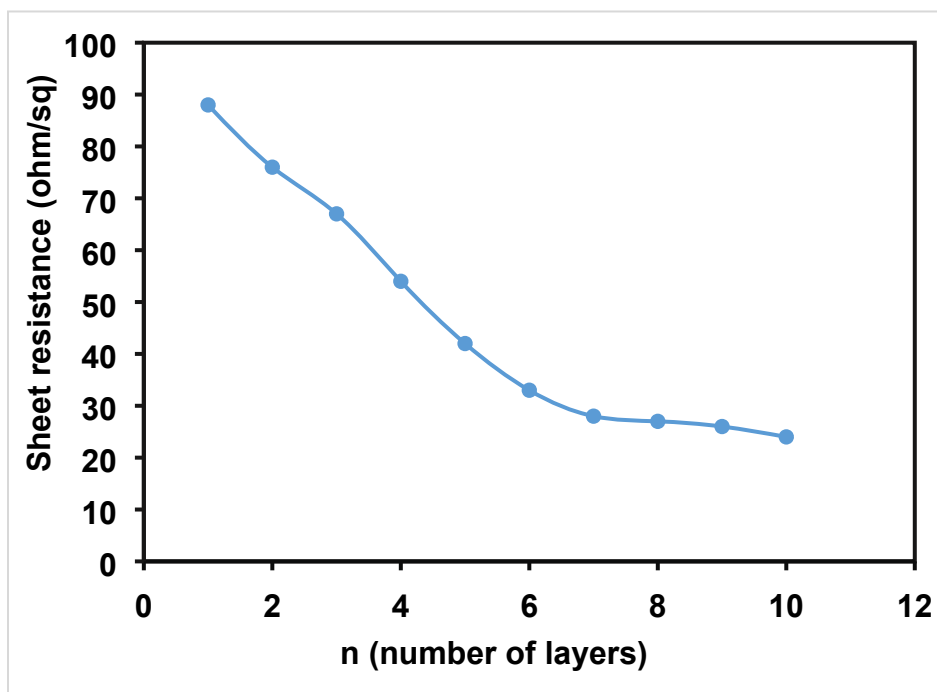
The real-time feasibility of the developed sensor was evaluated by testing it with real whole-blood samples. Blood samples were taken from three willing, healthy volunteers. The blood samples were used directly after collection without any further processing. 100  $\mu$ L of blood was dropped over the plasma separation membrane, which was attached to the electrodes to make them wet with the blood plasma. The plasma separation membrane caused the blood to separate and let the plasma come into touch with the electrodes. Thereafter the cyclic voltammetry experiment was performed at a scan rate of 40 mV/s to determine the response current density. The collected blood samples were additionally spiked with 150 and 200  $\mu$ M creatinine. The response current densities from the CV data were correlated with the sensitivity curve to calculate the recovery rate in blood creatinine measurement. The blood related experiments

were conducted with prior approval from institutional ethical committee (IEC) of CSIR-CMERI, Durgapur. The blood samples and biological waste were disposed of in a strong bag following autoclaving after completion of the experiments.

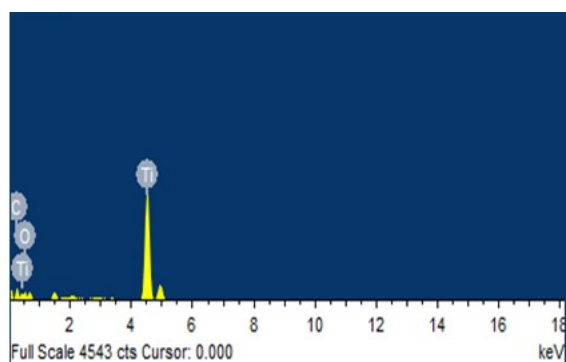
CV was performed to assess the reusability of the developed electrochemical sensor after washing. The plasma strip is not reusable as the plasma was deposited over it. After removing the plasma separation membrane, the electrodes of the used sensor were cleaned with 0.01M PBS (pH 7.4). After washing to determine the reusability of the sensor, the peak current density of the cleaned electrodes was recorded by performing a CV in the potential range of -1.0 V to +1.0V for 50 cycles at a scan rate of 40mV/s with the whole blood sample spiked with a known concentration of creatinine. All the experiments were performed under identical environmental conditions.



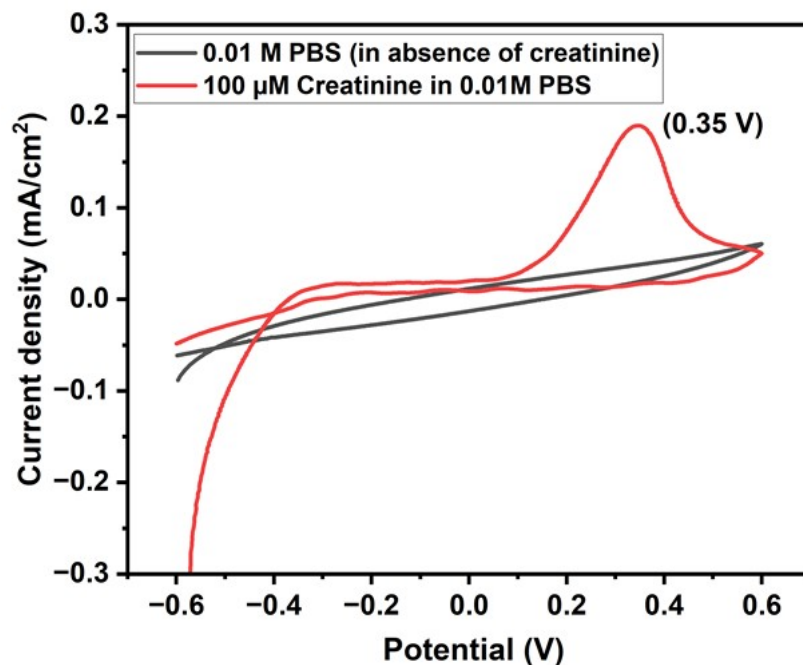
**Figure S1.** Detailed dimensions of the three-electrode electrochemical sensor



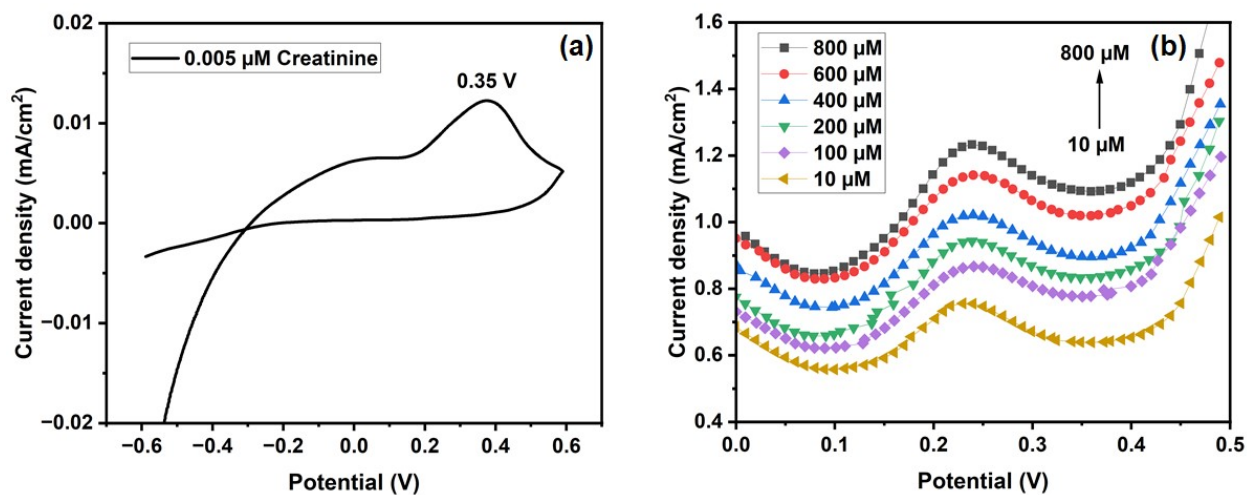
**Figure S2.** Variation of sheet resistance with number of printed nanocomposite layers



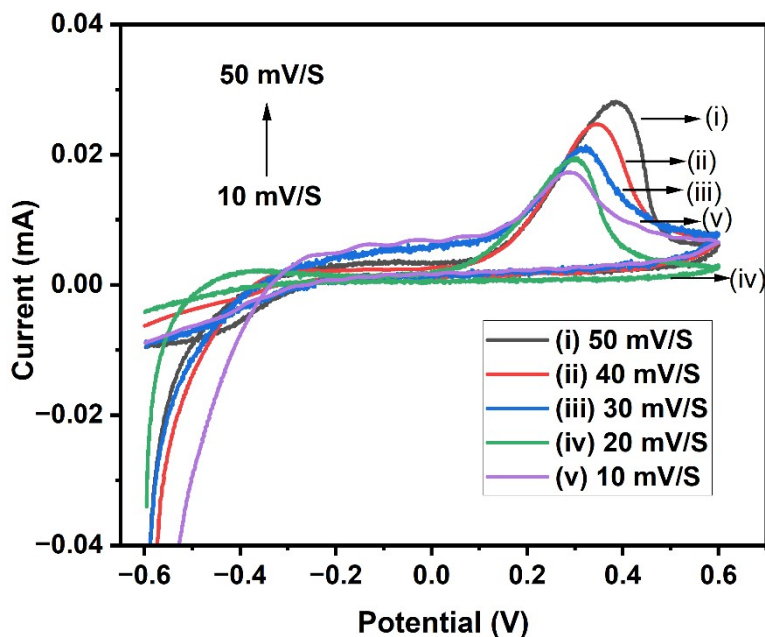
**Figure S3.** EDS mapping of the MXene



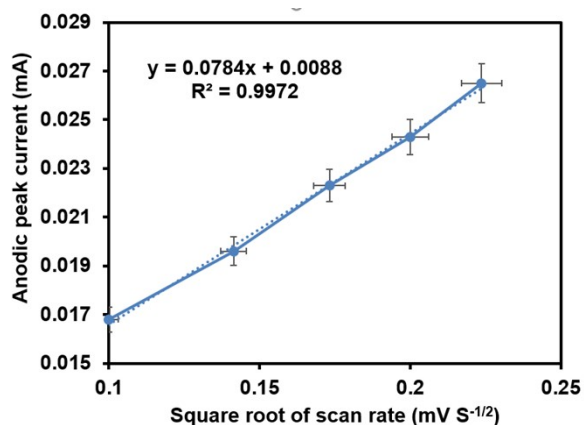
**Figure S4.** CV plots of CoMOF-MXene@CB electrode in the absence and presence of 100μM creatinine.



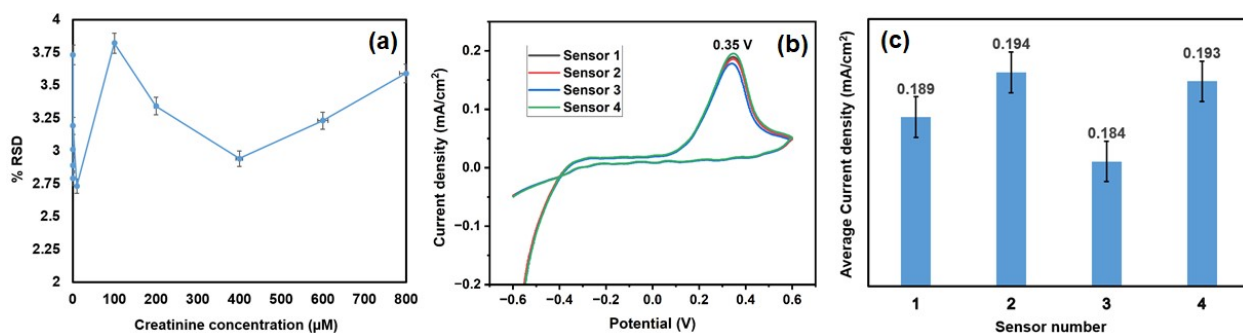
**Figure S5.** (a) CV plot showing the current density with 0.005 μM creatinine concentration using newly fabricated CoMOF-MXene@CB electrode, (b) DPV plots showing the variation of current density with creatinine concentration ranging from 10 μM to 800 μM using newly fabricated CoMOF-MXene@CB electrode.



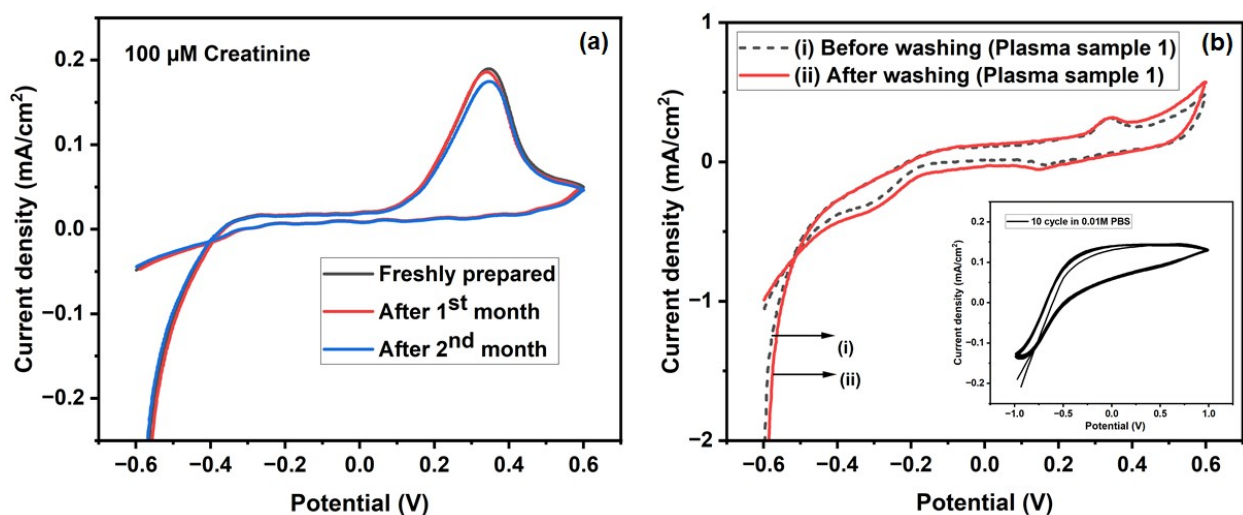
**Figure S6.** CV plots determining the effect of variation of scan rate (10, 20, 30, 40 50 mV/S) on the electrochemical oxidation of creatinine



**Figure S7.** Determination of reaction kinetics of creatinine oxidation on the CoMOF-MXene@CB electrode surface; Plot showing the dependence of anodic peak current on the square root of the scan rate ( $v^{1/2}$ ), (Conditions: 100  $\mu\text{M}$  creatinine in 0.01M PBS, pH  $\sim$ 7.4, within the potential range of -0.6 V to +0.6V).



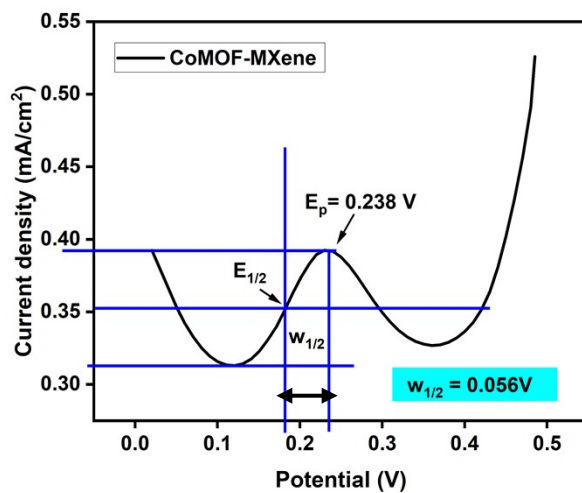
**Figure S8.** (a) Relative standard deviation (RSD) of the sensor for creatinine concentration values 10  $\mu\text{M}$  to 800  $\mu\text{M}$  repeated 10 times, (b) The reproducibility study of the CoMOF-MXene@CB electrode was performed using four different sensors named; Sensor-1,2,3,4 of same nature and tested by CV techniques. Each modified electrode was scanned in 0.01 M PBS containing 100  $\mu\text{M}$  creatinine, (c) Comparison of oxidation peak current density of each sensor with an error bar and the relative standard deviation (RSD) is found to be 2.4 %.



**Figure S9.** (a) The stability study; CV of 100  $\mu\text{M}$  creatinine recorded repeatedly with a single CoMOF-MXene@CB electrode for 2 months, (b) Reusability study of the electrochemical sensor (CoMOF-MXene@CB) after 0.01 M PBS washing and refreshing by performing 10 CV cycles at 40 mV/s scan rate within the range of -1 V to 1 V (Inset). CV results on reuse of the chip using



same unspiked blood sample after washing the tested blood using PBS for 10 times. (Conditions: pH ~7.4, -0.6 V to +0.6 V, the scan rate of 40 mV/s.).

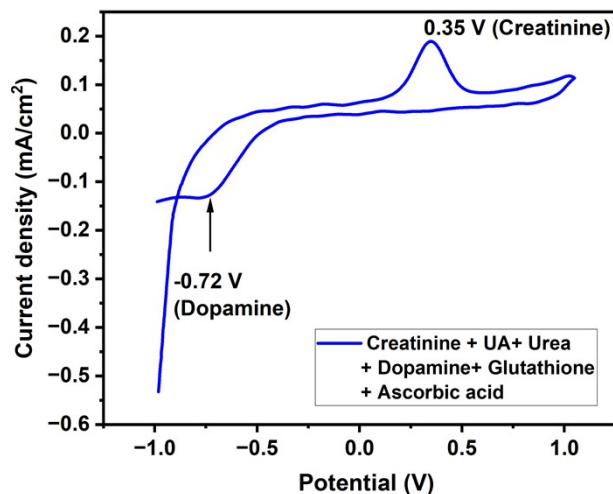


**Figure S10.** DPV for calculating the number of electrons involved in the creatinine oxidation.

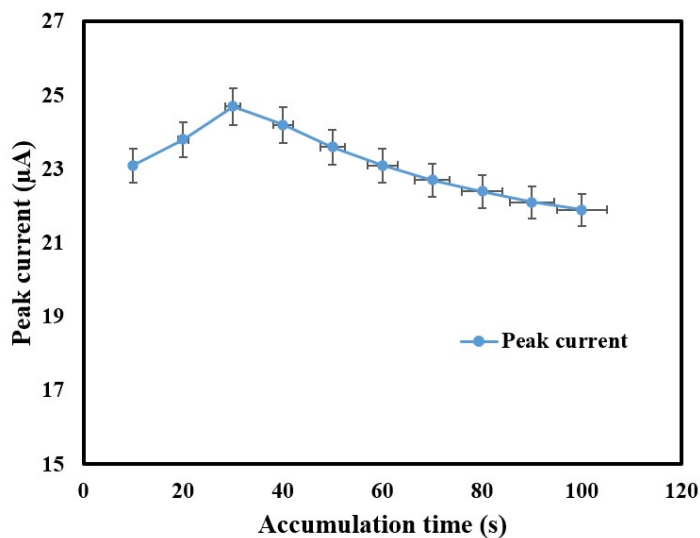
The number of electrons participated in the redox reaction ( $n$ ) from the Differential pulse voltammetry experiment by using the formula

$$w_{1/2} = \frac{90}{n}, \text{ where } n = \text{No. of electrons, } w_{1/2} = \text{peak width at half height (mV).}$$

$n = 1.6 \approx 2$  (for number of electrons).



**Figure S11.** Interference study of the CoMOF-MXene@CB sensor electrode: CV response in presence of uric acid, urea, dopamine, glutathione and ascorbic acid in 0.01 M PBS solution.



**Figure S12.** Effect of accumulation time on the oxidation peak current of creatinine over the CoMOF-MXene@CB electrode surface

The interference percentage of the various species has been estimated by using the following equation[8]:

$$Interference\% = \left( \frac{|I_f - I_i|}{I_i} \right) \times 100 \quad \text{Eq. S1}$$

Where,  $I_i$  and  $I_f$  are the oxidation peak currents recorded before and after adding interfering species to the creatinine solution.

**Table S2:** Current density and corresponding Creatinine concentration present in the tested blood plasma samples detected by the CoMOF-MXene@CB sensor, the standard clinical laboratory values and recovery percentage.

Human serum Sample	Before Spiking		After 1 <sup>st</sup> spiking (Spike X1= 150 μM)		After 2 <sup>nd</sup> spiking (Spike X2= 200 μM)		Clinical laboratory report (without spiking) μM
	Current density (mA/cm <sup>2</sup> )	Creatinine value from sensitivity plot (μM)	Current density (mA/cm <sup>2</sup> )	Creatinine value from sensitivity plot (μM)/ Recovery %	Current density (mA/cm <sup>2</sup> )	Creatinine value from sensitivity plot (μM)/ Recovery %	
Patient 1	0.166	61	0.331	213/ 100.2 %	0.545	415/ 100.6 %	62.4
Patient 2	0.183	73	0.34	220/ 97.6 %	0.552	421/ 98.6 %	75.4
Patient 3	0.202	102	0.382	248/ 97.5 %	0.583	453/ 99.7 %	104.2

## REFERENCES:

- [1] J. Liu, X. Jiang, R. Zhang, Y. Zhang, L. Wu, W. Lu, J. Li, Y. Li, H. Zhang, MXene-Enabled Electrochemical Microfluidic Biosensor: Applications toward Multicomponent Continuous

- Monitoring in Whole Blood, *Adv. Funct. Mater.* 29 (2019) 1–9. <https://doi.org/10.1002/adfm.201807326>.
- [2] T. Chakraborty, M. Das, C.Y. Lin, Y. Su, B. Yuan, C.H. Kao, ZIF-8 Nanoparticles Based Electrochemical Sensor for Non-Enzymatic Creatinine Detection, *Membranes (Basel)*. 12 (2022). <https://doi.org/10.3390/membranes12020159>.
- [3] E.L. Fava, T.M. do Prado, A. Garcia-Filho, T.A. Silva, F.H. Cincotto, F. Cruz de Moraes, R.C. Faria, O. Fatibello-Filho, Non-enzymatic electrochemical determination of creatinine using a novel screen-printed microcell, *Talanta*. 207 (2020) 120277. <https://doi.org/10.1016/j.talanta.2019.120277>.
- [4] S. Kalasin, P. Sangnuang, P. Khownarumit, I.M. Tang, W. Surareungchai, Salivary Creatinine Detection Using a Cu(I)/Cu(II) Catalyst Layer of a Supercapacitive Hybrid Sensor: A Wireless IoT Device to Monitor Kidney Diseases for Remote Medical Mobility, *ACS Biomater. Sci. Eng.* 6 (2020) 5895–5910. <https://doi.org/10.1021/acsbiomaterials.0c00864>.
- [5] S. Boobphahom, N. Ruecha, N. Rodthongkum, O. Chailapakul, V.T. Remcho, A copper oxide-ionic liquid/reduced graphene oxide composite sensor enabled by digital dispensing: Non-enzymatic paper-based microfluidic determination of creatinine in human blood serum, *Anal. Chim. Acta*. 1083 (2019) 110–118. <https://doi.org/10.1016/j.aca.2019.07.029>.
- [6] A. Domínguez-Aragón, A.S. Conejo-Dávila, E.A. Zaragoza-Contreras, R.B. Dominguez, Pretreated Screen-Printed Carbon Electrode and Cu Nanoparticles for Creatinine Detection in Artificial Saliva, *Chemosensors*. 11 (2023) 1–12. <https://doi.org/10.3390/chemosensors11020102>.
- [7] M. Jamil, B. Fatima, D. Hussain, T.A. Chohan, S. Majeed, M. Imran, A.A. Khan, S. Manzoor, R. Nawaz, M.N. Ashiq, M. Najam-ul-Haq, Quantitative determination of creatinine from serum of prostate cancer patients by N-doped porous carbon antimony (Sb/NPC) nanoparticles, *Bioelectrochemistry*. 140 (2021) 107815. <https://doi.org/10.1016/j.bioelechem.2021.107815>.

- [8] G.J. Kalaivani, S.K. Suja, Enzyme-less sensing of the kidney dysfunction biomarker creatinine using an inulin based bio-nanocomposite, *New J. Chem.* 43 (2019) 5914–5924. <https://doi.org/10.1039/C9NJ00594C>.