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# Postmodulation of the Metal–Organic Framework Precursor toward the Vacancy-Rich Cu<sub>x</sub>O Transducer for Sensitivity Boost: Synthesis, Catalysis, and H<sub>2</sub>O<sub>2</sub> Sensing

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Serge Cosnier, Junji Li, Wen-Li Xin, Yu-Xuan Dai, Guofang Shu, et al.. Postmodulation of the Metal–Organic Framework Precursor toward the Vacancy-Rich Cu<sub>x</sub>O Transducer for Sensitivity Boost: Synthesis, Catalysis, and H<sub>2</sub>O<sub>2</sub> Sensing. *Analytical Chemistry*, 2021, 93 (32), pp.11066-11071. 10.1021/acs.analchem.1c02183 . hal-03376495

**HAL Id: hal-03376495**

**<https://hal.science/hal-03376495v1>**

Submitted on 13 Oct 2021

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**Modulation of Crystalline Metal-organic Framework  
Precursor towards Carbon-based CuxO Electro-catalyst for  
Boosting Sensitive Hydrogen Peroxide Detection: Synthesis,  
Catalysis and Sensing Application**

Journal:	<i>Analytical Chemistry</i>
Manuscript ID	ac-2021-021836
Manuscript Type:	Technical Note
Date Submitted by the Author:	24-May-2021
Complete List of Authors:	Li, Junji; Nanjing University of Science and Technology, School of Environmental & Biological Engineering Xin, Wen-Li; Nanjing University of Science and Technology Dai, Yu-Xuan; Nanjing University of Science and Technology, School of Environmental & Biological Engineering Shu, Guofang; Southeast University Zhongda Hospital Zhang, Xueji; Nanjing University of Science and Technology, School of Environmental & Biological Engineering Marks, Robert; Ben-Gurion University of the Negev, Department of Biotechnology Engineering Cosnier, Serge; Universite Grenoble Alpes, Département de Chimie Moléculaire UMR CNRS 5250 Shan, Dan; Nanjing University of Science and Technology, School of Environmental and Biological Engineering

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4 1 **Modulation of Crystalline Metal-organic Framework**  
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6 2 **Precursor towards Carbon-based Cu<sub>x</sub>O Electro-catalyst for**  
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8 3 **Boosting Sensitive Hydrogen Peroxide Detection: Synthesis,**  
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10 4 **Catalysis and Sensing Application**  
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4 27 **Abstract:**  
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6 28 Metal-organic frameworks (MOFs) act as versatile coordinators for the  
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9 29 subsequent synthesis of high-performance electrochemical catalysts by  
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12 30 providing dispersed metal-ion distribution, initial coordination condition, and  
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15 31 modular dopant atom ratios, etc. In this work, a copper-based crystalline MOF  
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17 32 *trans*-[Cu(NO<sub>3</sub>)<sub>2</sub>(Him)<sub>4</sub>] was synthesized as a novel precursor of a  
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20 33 carbon-based electrochemical valence-alternating NC@Cu<sub>x</sub>O catalyst.  
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22 34 Through simple temperature modulation of the pyrolysis procedure, the  
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25 35 gradual transformation towards highly-active catalytic nanocomposite was  
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27  
28 36 characterized and investigated to ascertain the signal enhancing mechanism  
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31 37 during H<sub>2</sub>O<sub>2</sub> detection. Owing to its proprietary structure and ensuing  
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34 38 electrochemical reduction activity, a proof-of-principle sensor using  
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37 39 NC@Cu<sub>x</sub>O as transducer was able to provide an amplified sensitivity of 2330  
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40 40 μA mM<sup>-1</sup> cm<sup>-2</sup>. In addition, its facile one-vessel preparation and the intrinsic  
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43 41 non-enzymatic nature suggests a wide range of potential applications in  
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46 42 medical settings.

47 43 **Keywords:**  
48

49 44 Metal-organic framework derivate, Non-enzyme catalyst, Electrochemical  
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52 45 biosensor, Fenton-like signal amplification, One-pot synthesis  
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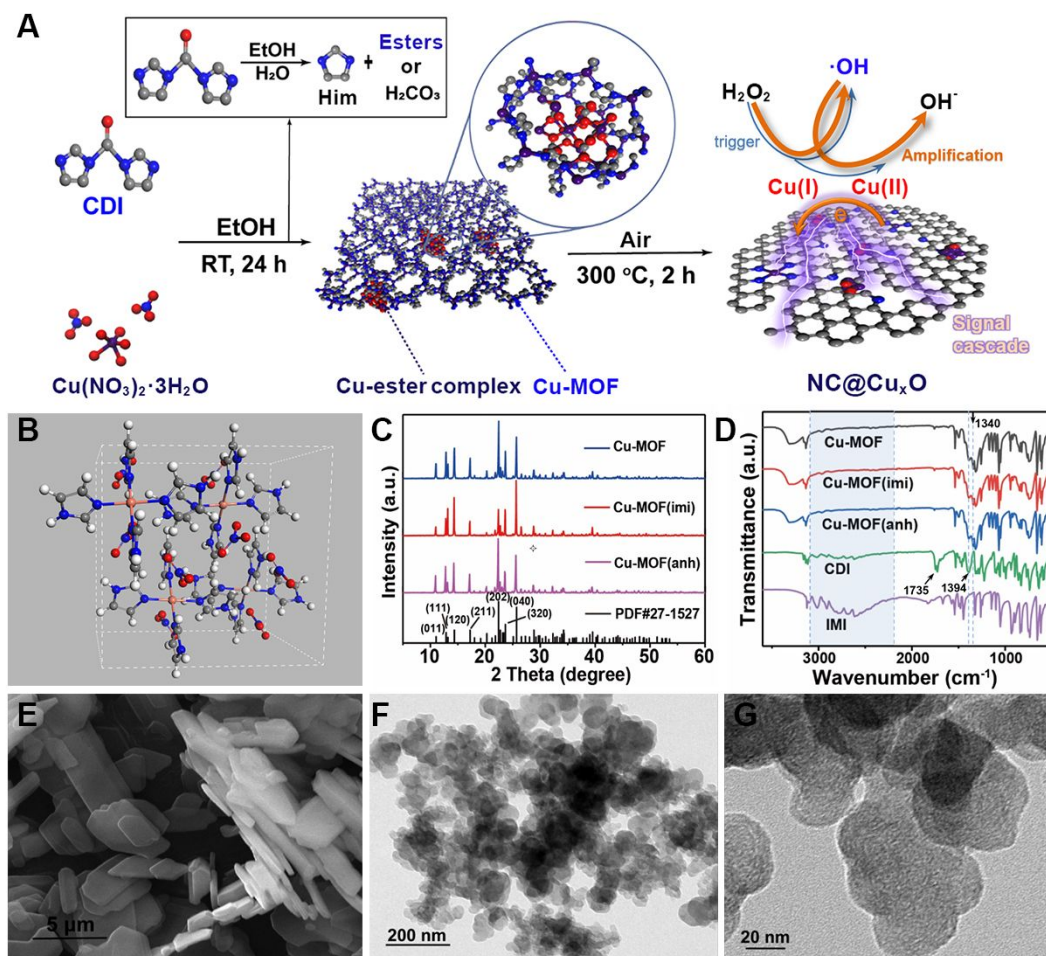
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4 47 The electrochemically active material, or rather the transducer, plays an  
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7 48 imperative role in the construction of an electrochemical biosensor <sup>1</sup>. Its  
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10 49 intrinsic properties, such as active center density, electron transfer ability, as  
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12 50 well as, internal structure and external morphology, set the fundamental  
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14 51 performance of the derived sensing systems or devices <sup>2-4</sup>. Use of  
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17 52 metal-organic frameworks (MOFs) as self-sacrificed precursors <sup>5, 6</sup> provides  
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20 53 invaluable properties, such as: 1) tunable initial coordination environment and  
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22 54 heteroatom doping, that can be easily achieved through the selection of  
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25 55 multitudinous ligand molecules; 2) atomic migration process can be accessed  
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28 56 and manually paused to obtain a series of products with diverse composite  
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31 57 configurations, including metal centers at different valence states or more  
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33 58 precisely the nuanced electronic regulation states, or carbon substrates with  
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36 59 various interconnecting degrees or doping ratios, and active catalysis clusters  
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39 60 with distinguished diameters; 3) porous characteristics can be inherited, thus  
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42 61 allowing high-throughput mass diffusion and interfacial contact <sup>7, 8</sup>. Already,  
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45 62 some state-of-the-art single atom catalysts (SACs) with satisfactory  
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48 63 performance have been synthesized using MOFs as starting templates <sup>9, 10</sup>.

48 64 Copper-based MOFs or derived nanomaterials have drawn conspicuous  
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51 65 attention due to their specific enzyme-like activities, reasonable cost efficiency  
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54 66 and robust stability <sup>11-13</sup>. According to the aforementioned advantages, these  
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57 67 copper-based enzyme mimics have been well accepted as signal transducers  
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60 68 to construct sensitive biosensor systems <sup>14</sup>. Copper species, no matter in

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4 69 forms of elementary clusters <sup>15, 16</sup>, compound nanoparticles <sup>17</sup> or even  
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6 70 secondary coordination units <sup>18</sup>, show prominent redox activity, with or without,  
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9 71 extra potential energy from the external circuit. In some latest articles, more  
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12 72 complex copper-based transducer materials with excellent and versatile  
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14 73 capabilities were synthesized from MOFs-contained composite precursors,  
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17 74 e.g. with several 2D materials like graphene, C<sub>3</sub>N<sub>4</sub> or MXene <sup>19</sup>. All these  
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20 75 treasures figure out an efficient clue of massively converting homogeneous  
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22 76 structural units inside the MOF crystal into highly disperse nano-catalysts  
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25 77 decorated upon a simultaneously generated substrate, and meanwhile  
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28 78 investigate the transiting procedure of some certain catalysis activity to the  
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30 79 other <sup>20</sup>.

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33 80 In the present communication, we designed the synthesis of a crystalline  
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35 81 MOF-derived Cu<sub>x</sub>O composite catalyst, serving as an electrochemical  
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38 82 peroxidase mimic. Inspired by the coordination structure of copper catalysts,  
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41 83 both the ligand atoms and the central metal valence state of the catalysis unit  
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44 84 were modulated simply using a short period of differential thermal treatment.  
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46 85 Thanks to the uniform texture of the crystalline precursor, the generation  
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49 86 process of a well-tuned transducer material was monitored and sought. An  
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52 87 electrochemical Fenton-like signal enhancing mechanism was herein  
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55 88 discussed, in view of the derived prototype biosensor and its corresponding  
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58 89 interfacial reactions (Fig. 1A). We expect that this novel and concise  
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60 90 transducer material will provide proprietary engineering insights in providing

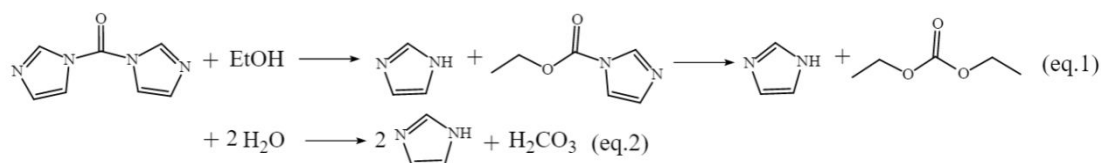
91 improved biosensor devices suitable for commercialization <sup>21, 22</sup>.



92  
93 **Fig. 1.** Stepwise modulation from crystalline MOF precursor to active electrochemical  
94 transducer. (A) Schematic overview of the preparation and signal amplification mechanism of  
95 the composite transducer material NC@Cu<sub>x</sub>O. (B) Crystal structure diagram of the MOF  
96 precursor *trans*-[Cu(NO<sub>3</sub>)<sub>2</sub>(Him)<sub>4</sub>]. (C) Three comparative routes to prepare MOF precursors  
97 with distinguished preferential crystallographic orientation and lattice shrinkage or bulge. (D)  
98 FT-IR spectra of the obtained crystalline precursors with arrows and blue dashed lines or  
99 region indicating critical changes of the transmittance peak. (E) SEM image of the board-like  
100 precursor crystals. (F and G) TEM images of the layered transducer material NC@Cu<sub>x</sub>O after  
101 a short period of pyrolysis under air atmosphere.

102 To ascertain that copper atoms were highly dispersed at the initial precursor  
103 stage, powder X-ray diffraction (PXRD) was performed immediately after  
104 lyophilization (Supplementary methods). All of the main peaks have been  
105 indexed as a well-defined orthorhombic phase of *trans*-[Cu(NO<sub>3</sub>)<sub>2</sub>(Him)<sub>4</sub>]

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4 106 crystal (PDF 27-1527)<sup>23</sup>, indicating that the copper ions were strictly  
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7 107 hexa-coordinated by four nitrogen atoms (from imidazole) and two oxygen  
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10 108 atoms (belonging to the nitrate ions) (Fig. 1B). The specific crystal herein was  
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12 109 obtained according to the following procedures: N,N'-carbonyldiimidazole (CDI)  
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14 110 underwent decomposition in some polar solvents like ethanol, thus, releasing  
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17 111 free imidazole (Him) molecules as well as di-esters of carbonic acid or  
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20 112 imidazole-N-carboxylic esters, as shown in *eq. 1*. Whereas, in the presence of  
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22 113 lattice water, CDI was possible to be hydrolyzed into carbonate ions (*eq. 2*)  
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25 114 which would further react with copper ions and generate stable basic  
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27 115 modalities<sup>24</sup>.



117 In order to know the priority of the aforementioned possible reaction routes,  
118 two contrast synthesis strategies were introduced. In detail, anhydrous copper  
119 nitrate with CDI and  $\text{CuNO}_3 \cdot 3\text{H}_2\text{O}$  with imidazole were each examined under  
120 the same ethanol-solvent condition and compared in terms of their respective  
121 diffraction peaks which almost kept the same with a slight peak shift of about  
122  $10^{-2}$  degrees, implying lattice shrinkage and bulge of these copper-imidazole  
123 frameworks due to the differences in accessory products (Fig. 1C and Fig. S1)  
124<sup>25</sup>. Interestingly, the preferential crystallographic orientations echoed by the  
125 diffraction peak intensities, however, were significantly different between the

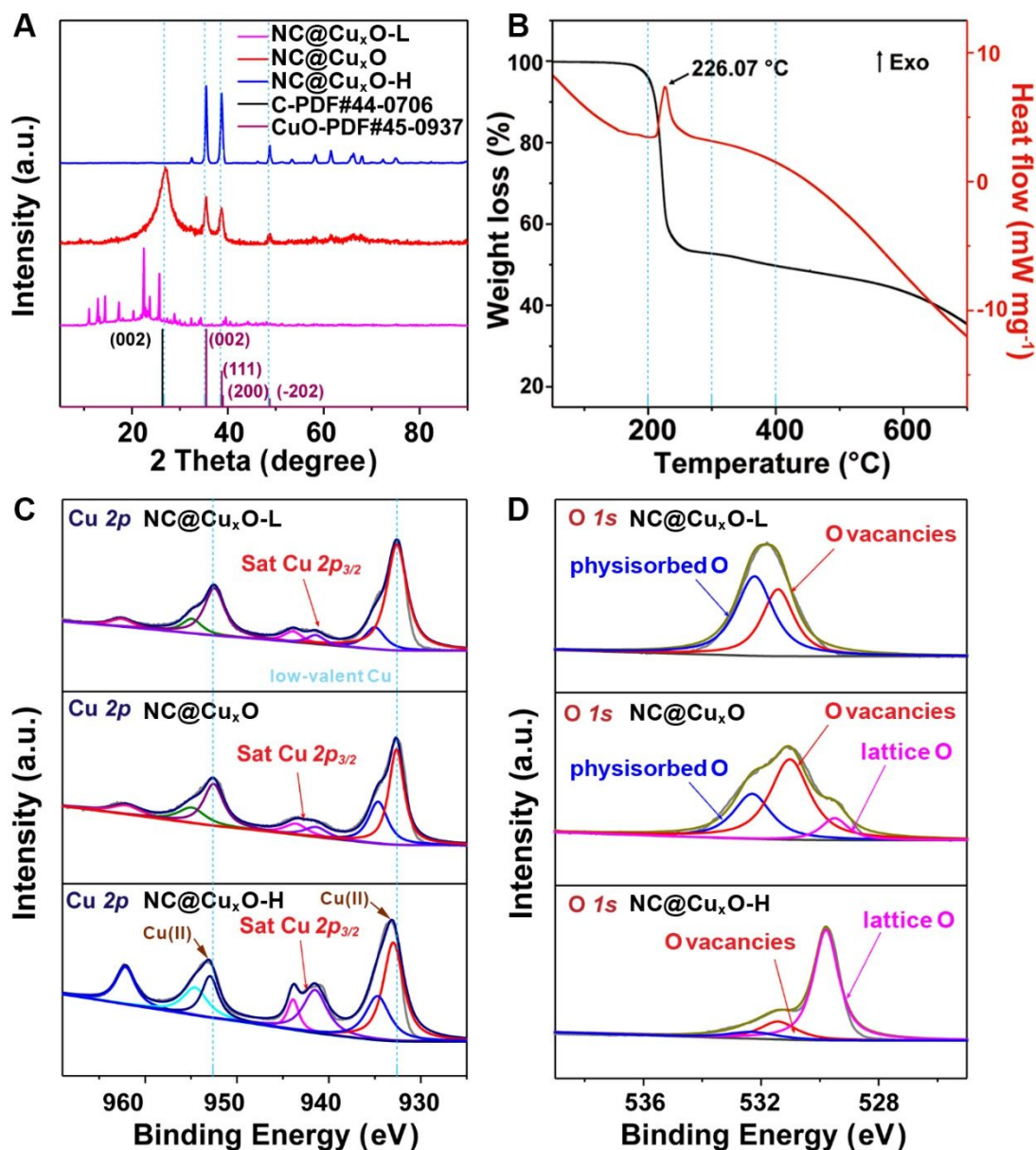


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4 126 two groups. From the Fourier transform infrared spectrometer (FT-IR) spectra,  
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7 127 it is clear that these Cu-MOFs acquired through different formulas maintained  
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10 128 perfectly identical chemical bonds. The transmittance peak variations from the  
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12 129 ligand monomers suggested probable reaction routes and the inner  
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14 130 connections of MOFs, detailed as follows: 1) the vanishing of carbonyl  
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17 131 stretching vibration at  $\sim 1735\text{ cm}^{-1}$ , as well as the strong broad band from 2200  
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20 132 to  $3100\text{ cm}^{-1}$ , respectively indicated the decomposition of CDI, and the  
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22 133 following coordination reaction of derived imidazole with copper ion which  
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25 134 accompanied the collapse of N–H $\cdots$ N hydrogen bonds; and 2) the strong  
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28 135 vibration peak at  $1394\text{ cm}^{-1}$  that can be assigned to the amide C–N of CDI  
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31 136 red-shifted to  $1340\text{ cm}^{-1}$  as a result of the formation of ester C–O bonds in all  
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33 137 MOF samples (Fig. 1D and Fig. S2)<sup>26</sup>. These results imply that regardless of  
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36 138 the presence of lattice water, CDI reacts with ethanol thereby generating ester  
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38 139 species.

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41 140 The bluish violet Cu-MOF powder exhibited tabular hexagon-like  
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43 141 morphology with a thickness of hundreds of nanometers in scanning electron  
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46 142 microscope (SEM) images (Fig. 1E). After the pyrolysis process under air  
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48 143 atmosphere, the resulting NC@Cu<sub>x</sub>O catalyst, showed an obviously  
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51 144 decreased plane size down to 10-nm scale, according to the transmission  
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54 145 electron microscope (TEM) results (Fig. 1F and 1G). Furthermore, the  
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57 146 absence of aggregated nanoparticles suggested highly dispersed catalytic  
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59 147 sites. To further understand the transformation from a Cu-MOF precursor to a  
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4 148 copper-based catalyst and its accompanying H<sub>2</sub>O<sub>2</sub> reduction properties,  
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6 149 thermogravimetric-differential scanning calorimetry (TG-DSC) analysis was  
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9 150 conducted at a 5 °C min<sup>-1</sup> heating rate (Fig. 2B). A sharp weight loss was  
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12 151 noticed from 200 to 240 °C, accompanied with a clear exothermic peak at  
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15 152 226 °C. Thereafter, three representative temperature points (200, 300 and  
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17 153 400 °C) were set with their corresponding products named NC@Cu<sub>x</sub>O-L,  
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19 154 NC@Cu<sub>x</sub>O and NC@Cu<sub>x</sub>O-H respectively.

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22 155 When the Cu-MOF precursor was heated at 200 °C for 2 hours, the  
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25 156 obtained NC@Cu<sub>x</sub>O-L still preserved the typical lattice characteristics of  
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27 157 *trans*-[Cu(NO<sub>3</sub>)<sub>2</sub>(Him)<sub>4</sub>], and its weight loss can be attributed to the desorption  
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30 158 of solvent molecules and the decomposition of thermolabile esters. With a  
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33 159 further rise in temperature, broad peaks of graphite and copper oxide  
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35 160 appeared in the NC@Cu<sub>x</sub>O PXRD spectrum (Fig. 2A). By substituting the  
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38 161 measured value of full width at half maximum (FWHM) into the Scherrer  
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41 162 equation, the crystallite size of the newly formed copper oxide was calculated  
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43 163 to be several nanometers, which was in accordance with the lack of gathered  
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45 164 clusters in the TEM image <sup>27</sup>. *Via* calcination at 400 °C, the derived  
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48 165 NC@Cu<sub>x</sub>O-H showed striking peaks identical to that of CuO, owing to the  
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51 166 deep substitution of oxygen for the initial coordinated nitrogen through atomic  
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54 167 transfer.



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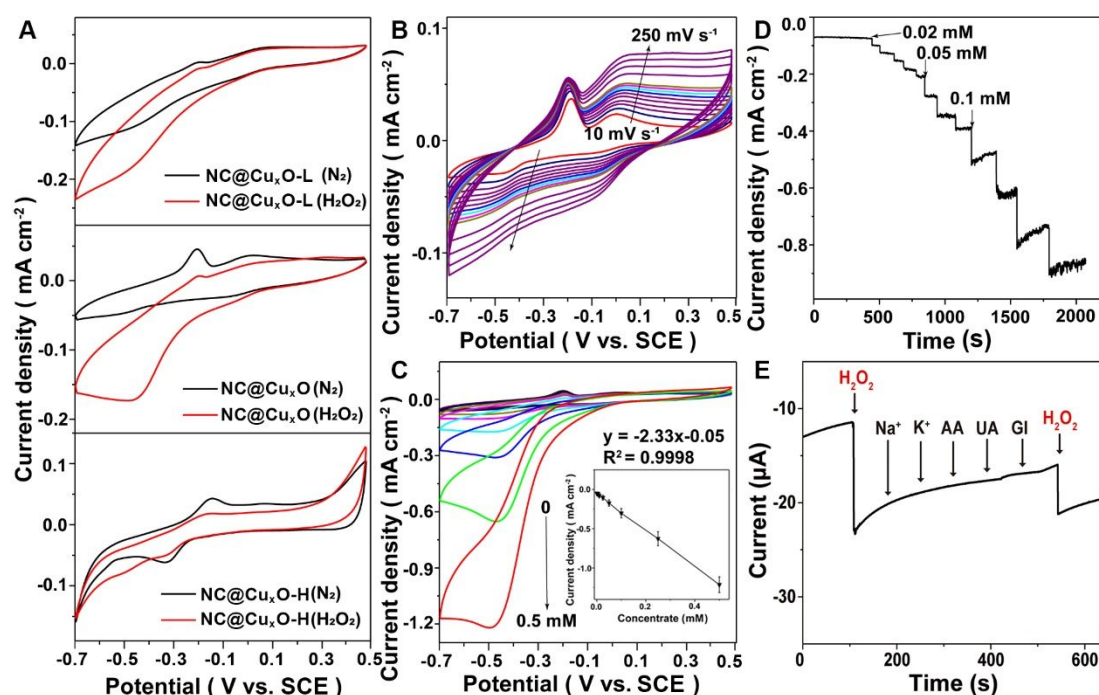
169 **Fig. 2.** Temperature modulation of the valence state of the central metal as well as the  
 170 neighboring ligand atoms and vacancies. **(A)** XRD spectra of the pyrolyzed samples under  
 171 different heat-treatment temperature. **(B)** TG-DSC curves of the self-sacrifice MOF precursor  
 172 in air atmosphere with the heating rate of 5 °C min<sup>-1</sup>. High-resolution XPS spectra of Cu 2p  
 173 **(C)** and O 1s **(D)** orbitals of the under-heated NC@Cu<sub>x</sub>O-L, experimental NC@Cu<sub>x</sub>O and  
 174 over-heated NC@Cu<sub>x</sub>O-H samples.

175 A mutually corroborating result was obtained by investigating the chemical  
 176 state alternations of atoms. In both NC@Cu<sub>x</sub>O-L and NC@Cu<sub>x</sub>O samples, the  
 177 high-resolution X-ray photoelectron spectroscopy (XPS) spectra of Cu 2p  
 178 orbitals displayed relatively weaker satellite peaks and slightly lower binding

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4 179 energies of both the  $2p_{1/2}$  and  $2p_{3/2}$  orbitals than that of NC@Cu<sub>x</sub>O-H (Fig. 2C).  
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7 180 Due to the existence of CuO nanocrystalline in NC@Cu<sub>x</sub>O, we surmised that  
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10 181 these features ought to be attributed to the abundant intermediate low-valent  
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12 182 Cu(I) rather than Cu(II) of coordinated state or compound state <sup>28</sup>. Taking O  
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14 183 1s spectra into consideration, on the other dimension, the gradual shift of the  
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17 184 predominant sub-peaks from 532.2 to 529.7 eV can help determine the exact  
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20 185 components of the aforementioned NC@Cu<sub>x</sub>O catalysts. In detail,  
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22 186 NC@Cu<sub>x</sub>O-L displayed Cu-MOF-like characteristics with respect to crystal  
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25 187 structure, and the chemical state of organic oxygen assigned as incompletely  
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28 188 decomposed esters. NC@Cu<sub>x</sub>O-H, at the other extreme, exhibited canonical  
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30 189 CuO properties with a standard XRD pattern and typical XPS spectrum  
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33 190 features, such as the intensive satellite peaks of Cu 2p and the nearly  
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36 191 complete conversion to lattice oxygen which belongs to the metal-oxide  
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38 192 compounds (Fig. 2D).

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40 193 The aforementioned under- or over- heating treatments exhibit variance in  
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43 194 the resulting functional ingredient of the composite catalyst NC@Cu<sub>x</sub>O. On  
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46 195 one hand, the crystalline framework collapsed and recombined as a N-doped  
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49 196 carbon substrate. The copper atoms, on the other hand, were gradually  
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52 197 aggregated and oxidized into nanoscale CuO nanoparticles, while preserving  
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54 198 an overall amorphous state with abundant oxygen vacancies (Fig. 2D) <sup>29</sup>.  
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56 199 Therefore, the uniformly dispersed catalytic centers of reductive copper oxide  
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59 200 in NC@Cu<sub>x</sub>O determined their high reaction activity towards oxidizing  
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substances. Simultaneously, the internal structural porosity is substantially retained which guarantees sufficient mass transfer during the catalyzing procedures (Fig. S3 and S4). The Cu-MOF precursor's periodic atom distributions and definite melting point enable the investigation of some critical catalyst-evolving processes, such as metal migration and oxygen transfer, by simply modulating temperature.



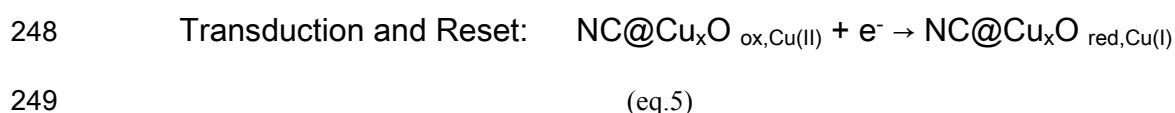
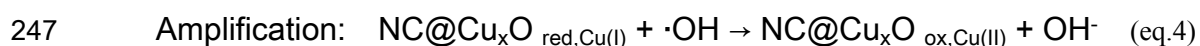
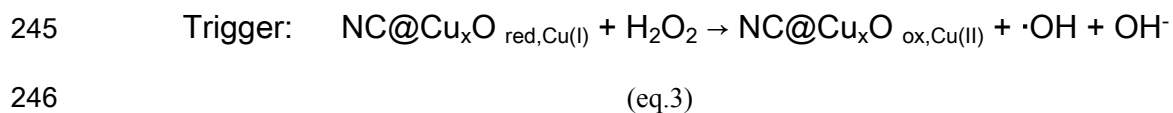
**Fig. 3.** Electrochemical catalysis behavior investigation of the transducer material to support sensitive sensing of H<sub>2</sub>O<sub>2</sub> concentration. **(A)** Electrochemical redox characteristics of the MOF-residual dominant (NC@Cu<sub>x</sub>O-L, top), O-vacancy abundant (NC@Cu<sub>x</sub>O, middle) and deeply oxidized (NC@Cu<sub>x</sub>O-H, bottom) samples as transducers in the absence and presence of 0.05 mM H<sub>2</sub>O<sub>2</sub>. **(B)** Cyclic voltammograms of NC@Cu<sub>x</sub>O electrode at different scan rates from 10 to 250 mV s<sup>-1</sup> in condition of saturated nitrogen without H<sub>2</sub>O<sub>2</sub>. **(C)** Cyclic voltammogram of NC@Cu<sub>x</sub>O electrode in response to H<sub>2</sub>O<sub>2</sub> concentrations of 0 to 0.5 mM with an insert exhibiting the linear fitting of the reductive peak-current density values. **(D)** Chronoamperometric responses of NC@Cu<sub>x</sub>O to stepwise addition of H<sub>2</sub>O<sub>2</sub> at -0.5 V (vs. SCE). **(E)** Selectivity test of the biosensor against some common interferences in body fluid, including 1 mM Na<sup>+</sup>, K<sup>+</sup>, ascorbic acid, uric acid and glucose.

Based on the characteristics of the NC@Cu<sub>x</sub>O catalyst species, their respective electrochemical behaviors were further examined using cyclic

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4 221 voltammetry (CV) (Fig. 3A). In the absence of H<sub>2</sub>O<sub>2</sub>, the lower-heated sample  
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6 222 showed inconspicuous redox peaks, implying an inert electron transfer ability  
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9 223 of the Cu-N coordinate-bond dominated MOF material. In contrast, the 400 °C  
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11 224 pyrolyzed product exhibited both obvious redox peaks (Cu<sup>I</sup>/Cu<sup>II</sup>,  $E_p = -0.34$  and  
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14 225  $-0.15$  V) due to the formation of conductive carbon substrates. In regard to the  
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17 226 NC@Cu<sub>x</sub>O, its undiscovered reduction peak at this particular potential window  
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19 227 indicated that copper existed in a low valence state in Cu<sub>x</sub>O and the  
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22 228 electrochemically oxidized copper ions would then be released into the liquid  
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25 229 phase, resulting in an irreversible procedure. When the solution contained  
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27 230 0.05 mM H<sub>2</sub>O<sub>2</sub>, a strong reduction peak appeared around  $-0.45$  V, significantly  
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30 231 deviating from the CV curve without adding H<sub>2</sub>O<sub>2</sub>. It is worth noting that the  
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33 232 oxidization peak, in the meanwhile, became quite indistinct especially when  
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35 233 the H<sub>2</sub>O<sub>2</sub> concentration increased. This result implied that reductive copper in  
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38 234 NC@Cu<sub>x</sub>O preferred to react with the oxidizing substances derived from H<sub>2</sub>O<sub>2</sub>  
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40 235 decomposition, prior to being electrochemically oxidized at the anode (*eq. 3*).

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43 236 The emphasis in sensitive H<sub>2</sub>O<sub>2</sub> detection lays on enhanced signal  
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46 237 transduction or an amplified feedback. Therefore, the catalysis mechanism  
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48 238 and its signal conversion process was studied first. The NC@Cu<sub>x</sub>O modified  
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51 239 glassy carbon electrode (GCE) was tested by cyclic voltammetry at different  
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53 240 scan rates in 0.1 M PBS and 0.3 M KCl solution (Fig. 3B). With increasing  
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56 241 scan rate from 10 to 250 mV s<sup>-1</sup>, both of the anodic and cathodic peak  
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59 242 currents were measured as linear with the square root of the scan rate (Fig.

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4 243 S5), indicating characteristic diffusion-controlled electrochemical redox  
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7 244 behaviors<sup>30</sup> from which we inferred a Fenton-induced enhancing mechanism:



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22 250 The highly dispersed Cu(I) catalysis centers of  $\text{Cu}_x\text{O}$  efficiently accelerated  
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25 251 the decomposition of  $\text{H}_2\text{O}_2$ , while releasing an equivalent amount of  $\cdot\text{OH}$   
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28 252 radicals. Thereafter, increased reductive copper sites would be oxidized  
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31 253 through rapid radical reactions. At the reduction potential, the newly generated  
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34 254 Cu(II) would then get reduced by capturing the electrons from the outer circuit.  
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37 255 More importantly, the electrochemical procedures at the electrodes were  
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40 256 shown to be rapid, which meant this redox cycle (eq.3-5) would continuously  
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43 257 proceed until the diffusion limit and simultaneously provide amplified current  
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46 258 response<sup>31</sup>. In addition, this catalytic process relied on not only the valence  
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49 259 state of copper centers, but also the structural configuration of ligand atoms  
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52 260 and defects, which can be supposed from the poor activity of both the  
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55 261  $\text{NC@Cu}_x\text{O-L}$  and  $\text{NC@Cu}_x\text{O-H}$  samples.

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58 262 By adding  $\text{H}_2\text{O}_2$  solutions of differing concentrations (Fig. 3C), the current  
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263 intensity of the reduction peak at -0.45 V was identified as a linear coefficient  
264 of the concentration, with a corresponding linear equation:  $j$  ( $\text{mA cm}^{-2}$ ) =

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4 265  $-2.33C$  (mM) - 0.05 ( $R^2=0.9998$ ), ranging from 10  $\mu$ M to 0.5 mM. The limit of  
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7 266 detection for the NC@Cu<sub>x</sub>O sensor, (LOD=  $3\sigma/S_d$ , where  $\sigma$  represents the  
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9 267 standard deviation of the current density value measured in blank solution, and  $S_d$   
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11 268 stands for the slope of linear regression calibration line), reached 6.67 nM. Fig. 3D  
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14 269 shows the amperometric response towards concentrated H<sub>2</sub>O<sub>2</sub> solutions. The  
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16 270 cathodic current rapidly achieved steady states and increased in pace with the  
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19 271 addition of H<sub>2</sub>O<sub>2</sub>. The selectivity and stability of this proof-of-principle  
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22 272 biosensor were also evaluated as these two important parameters could  
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25 273 reflect whether an artificial catalyst could mimic or even surpass natural  
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27 274 enzymes in practical use. From Fig. 3E, we can conclude that NC@Cu<sub>x</sub>O has  
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30 275 good selectivity towards H<sub>2</sub>O<sub>2</sub>. The i-t curve in Fig. S6 exhibited the stability of  
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32 276 this electrochemical sensor for long-term continuous detection. After dropping  
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35 277 in 1 mM H<sub>2</sub>O<sub>2</sub> solution, the output current could keep steady for more than 1 h,  
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37 278 indicating that the NC@Cu<sub>x</sub>O nanocomposite did not leach out from the  
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40 279 electrode during multiple cycles of electrochemical redox process, while  
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43 280 maintaining high catalytic activity. By simply modulating the thermal redox  
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45 281 condition of a well-characterized crystalline MOF precursor, both the chemical  
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48 282 valence and coordination environment of the central metal were adjusted to  
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51 283 render a transducer enhanced signal feedback. In comparison with previous  
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53 284 studies which introduced other functional materials or not, this NC@Cu<sub>x</sub>O  
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56 285 electrode offers a highly competitive sensitivity, as well as other decent  
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58 286 performances (Table 1).  
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**287 Table 1.** Comparison of copper-based electrochemical H<sub>2</sub>O<sub>2</sub> transducer materials on catalysis  
**288** mechanism and sensitivity performance.

Transducer material	Active-center type	Redox potential (V)	Additional materials	Sensitivity ( $\mu\text{A mM}^{-1} \text{cm}^{-2}$ )	LOD ( $\mu\text{M}$ )	References
CuO nanoflowers	monoclinic CuO	-0.4 (vs. Ag/AgCl)	n.a.	956.69	0.85	32
Cu <sub>2</sub> O nanoparticles	~100 nm size with (111) facets	-0.42 (vs. Ag/AgCl)	n.a.	28.0	0.2	33
3DIO Au/NiO@CuO	Ni <sup>3+</sup> species	0.5 (vs. Ag/AgCl)	CuO skeleton & AuNPs	650.2	0.0037	34
CuNPs@Y-1,4-NDC-MOF/ERGO	CuNPs supported by ERGO	-0.2 (vs. SCE)	Y-1,4-NDC-MOF & ERGO	8.8	0.43	35
Cu <sub>2</sub> O-rGO-P	cubic Cu <sub>2</sub> O	-0.4 (vs. Ag/AgCl)	rGO paper	77*	3.78	36
NCNT MOF CoCu	Co(0) & Cu(0)	0.5 (vs. Ag/AgCl)	Co(0)	639.5	0.206	37
Cu-Mo <sub>2</sub> C/C	Synergic Mo <sub>2</sub> C with Cu(0)	-0.4 (vs. SCE)	hexagonal $\beta$ -Mo <sub>2</sub> C	392.7	0.04	38
<b>NC@Cu<sub>x</sub>O</b>	<b>Amorphous Cu<sub>x</sub>O with oxygen vacancies</b>	<b>-0.45 (vs. SCE)</b>	<b>n.a.</b>	<b>2330</b>	<b>0.00667</b>	<b>This work</b>

**289** \* estimated from the offered linear regression curve.

**290** We presented, herein, a sensitive H<sub>2</sub>O<sub>2</sub> sensor constructed with a tailored  
**291** amorphous Cu<sub>x</sub>O composite catalyst. The corresponding mechanism of  
**292** enhanced signal transduction were stepwise investigated from the precursor  
**293** conformation, to its catalytic evolution, up to a final amplified electron  
**294** cascades. With the initial copper-nitrogen square domains converting into  
**295** low-valent amorphous copper oxide catalytic centers, the resulting current  
**296** remarkably increased due to its synergistic enhancement, contributed by both  
**297** rapid radical and electrochemical reactions. Moreover, the structural property  
**298** of specific neighboring ligand-atom configuration was proven to be a factor as  
**299** predominant as the valence state of central metals. From the perspective of  
**300** material, catalysis and the final sensing application, the way to design and

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4 301 modulate a proper copper-based transducer was comprehensively explored.  
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6 302 We envision that our work would hold the prospect for accurate bio-analyte  
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9 303 quantitation and promote the mainstreaming of precision diagnosis and  
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12 304 medicine.

### 15 305 **Acknowledgements**

17 306 The authors greatly acknowledge the financial support from National  
18  
19  
20 307 Natural Science Foundation of China (Grant No. 62001224), Natural Science  
21  
22  
23 308 Foundation of Jiangsu Province (Grant No. BK20190457), “Overseas  
24  
25 309 Academic Partnership Program” of Nanjing University of Technology (2019),  
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28 310 and Sino-French international research network “New nanostructured  
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