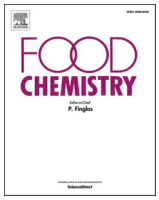
Food Chemistry 425 (2023) 136518

Contents lists available at ScienceDirect

Food Chemistry

journal homepage: www.elsevier.com/locate/foodchem



Review

Single-atom nanozyme-based electrochemical sensors for health and food safety monitoring

Jingru Sun, Zhenlu Wang *, Jingqi Guan *

Institute of Physical Chemistry, College of Chemistry, Jilin University, 2519 Jiefang Road, Changchun 130021, PR China

ARTICLE INFO

Keywords:
Single-atom nanozyme
Electrochemical sensor
Sensing mechanism
Food safety
Health monitoring

ABSTRACT

Electrochemical sensors and biosensors play an important role in many fields, including biology, clinical trials, and food industry. For health and food safety monitoring, accurate and quantitative sensing is needed to ensure that there is no significantly negative impact on human health. It is difficult for traditional sensors to meet these requirements. In recent years, single-atom nanozymes (SANs) have been successfully used in electrochemical sensors due to their high electrochemical activity, good stability, excellent selectivity and high sensitivity. Here, we first summarize the detection principle of SAN-based electrochemical sensors. Then, we review the detection performances of small molecules on SAN-based electrochemical sensors, including H_2O_2, dopamine (DA), uric acid (UA), glucose, H_2S, NO, and O_2. Subsequently, we put forward the optimization strategies to promote the development of SAN-based electrochemical sensors. Finally, the challenges and prospects of SAN-based sensors are proposed.

1. Introduction

Electrochemical sensors can transform chemical or biological signals into intuitive and readable electrochemical signals (Wu et al., 2022). Electrochemical sensors have attracted wide attention in the fields of food safety, medicine and environmental monitoring owing to their high sensitivity and high selectivity, quick response, good portability, low cost and in-situ monitoring (Kalambate, Rao, Wu, Shen, Boddula, & Huang, 2020). Since food pollution, unhealthy diet and high content of some substances may be harmful to human health, it is important for food industry to construct a sensor which can perform sensitive analysis in complex food matrix (Yang et al., 2018). In fact, electrochemical sensor contains an electrocatalytic process, which involves an effective energy conversion associated with the interface morphology and size effect of electrode materials (Lei, Zhang, Yuan, & Li, 2022).

The electrochemical detection performance greatly depends on the microstructure of electrode materials, and thus researchers have concentrated on using nanostructured materials in electrochemical sensors (Liang et al., 2022). There are many kinds of nanomaterials, including 0D (D: dimension), 1D, 2D, and 3D nanocomposites (Wu et al., 2022). Various nanomaterials composed of metal nanoparticles, carbon nanoparticles, nano-polymers and nano-composites have been adopted in electrochemical sensors (Sun, Zhang, et al., 2022). Therein, metal nanoparticles can improve mass and electron transfer, thus enhancing the electrode activity. SAN shows a unique microstructure and property, which contains isolated single-atom metals dispersed on a carrier (Ye, Zhang, Wang, & Li, 2020). SAN has the maximum value of atom utilization, which can realize reasonable usage of metal resources, becoming one of the most hopeful catalytic materials for heterogeneous catalysis (Ji, Chen, Wang, Zhang, Wang, & Li, 2020b). Compared with conventional nanomaterials, SANs have better catalytic performance and broader application prospect in electrochemical sensors (Niu et al., 2019). One of the most effective ways to improve the sensing property of electrochemical sensors is to decorate the surface of electrodes with SANs with high electrocatalytic activity.

However, isolated single metal atoms have high surface free energy and are easy to aggregate, which need to be anchored on substrates to generate a steady conformation. The doping of metal or nonmetal atoms can introduce defects, change the microstructure of substrate, enhance dipole polarization and interface polarization and provide a large number of active sites, thus improving electrocatalytic performance (Hamukwaya et al., 2022; Ping et al., 2023). Compared with nanoenzymes, SANs not only have higher catalytic activity and higher stability, but also have higher selectivity, higher utilization of metals, and more efficient energy saving (Li, Rong, Zhang, Wang, & Li, 2020). Because of their unique structural characteristics, SANs have shown high

* Corresponding authors.
E-mail addresses: wzl@jlu.edu.cn (Z. Wang), guanjq@jlu.edu.cn (J. Guan).

https://doi.org/10.1016/j.foodchem.2023.136518
Received 23 March 2023; Received in revised form 20 May 2023; Accepted 30 May 2023
Available online 3 June 2023

electrochemical activity in various reactions and have broad application prospects. Unlike traditional nano-catalysts, the metal-carrier interaction in SANs is the most significant as the size of metal sites is reduced to atomic level (Hou et al., 2019). Therefore, adjusting local coordination conditions can improve the electronic and geometric structure of metal atoms. Particularly, the addition of some synergistic constituents can enhance catalytic property of SANs (Bai, Duan, Nan, Wang, Tang, & Guan, 2022; Han & Guan, 2022a). For example, local coordination atoms, heteroatoms and other metal atoms have been put forward to regulate local condition of single atomic sites (Gong et al., 2020).

Due to uniform active sites, high utilization of metal atoms and fast catalytic kinetics, SANs have a wide application prospect in electrochemical sensing field (Xiang, Feng, & Chen, 2020). In 2019, Fe—N—C SAN was first applied in sensing field to monitor H_2O_2 (Jiao et al., 2019). Since then, SANs have been extensively applied in different sensing fields. For example, Lyu et al. used Fe-N_x SANs to replace natural horseradish peroxidase (HRP) in enzyme-linked immunosorbent experiment, which improved the detection performance (Lyu et al., 2020). Later, they improved the sensitivity of lateral flow immunoassay (LFIA) by introducing Fe-SANs (Lyu et al., 2022). Chen et al. constructed a biosensor based on Fe-N/C SAN for the screening of alkaline phosphatase activity (Chen et al., 2020). The introduction of SANs is of great significance to electrochemical sensors. SANs-based electrochemical sensors show excellent performance in monitoring H_2O_2 in living cells, enzymes in vivo, small molecules in serum, and urine, highlighting their application potential in natural life systems and food industry (Wei, Song, et al., 2021). Up to now, there have been a few review papers related to sensing application of nano-enzymes. For example, Arshad et al. introduced the application of nano-enzymes in the field of food biomarker sensing (Arshad, Mohd-Naim, Chandrawati, Cozzolino, & Ahmed, 2022). Huang et al. reviewed the research progress of nano-enzymes in food quality and safety detection (Huang et al., 2022). Kurup et al. emphasized the application of nano-enzymes in the development of instant biosensors, and paid more attention to the development and design of sensors based on nano-enzymes (Kurup & Ahmed, 2023). However, to the best of our knowledge, there is no comprehensive review paper on the application of SANs in electrochemical monitoring of food safety and human health.

In this review, we briefly introduce the sensing mechanisms of electrochemical sensors. Subsequently, we discuss the main progress of SANs in electrochemical sensors, focusing on the detection of H_2O_2, DA, UA, glucose and other small molecular substances. Finally, we put forward the optimization strategies, application prospects and possible challenges of electrochemical sensors based on SANs. We hope that this review can provide some systematic insights for the development of SAN-based electrochemical sensors, and promote the development of related technologies, especially in the fields of food safety and human health.

2. Electrochemical sensor

There are many kinds of sensors, and the common ones mainly include strain sensors, temperature sensors and pressure sensors. Most strain sensors and temperature sensors are resistive sensors, which depend on the resistance change caused by strain or temperature stimulus (Wei, Li, et al., 2021). The resistive sensor is usually composed of a flexible elastomer substrate and a sensing assembly of solid conductive elements. The strain sensors can be used to detect large strains and subtle human movements. The development of strain sensor has become the research focus of cardiac rehabilitation (Chang, Chen, Chen, Zhu, & Guo, 2021). Flexible strain sensors have great potential in health monitoring, human movement monitoring, humanoid robots and other emerging fields. Stretchable strain sensor and temperature sensor are two important components of electronic skin and wearable electronic products (Shen et al., 2022). Pressure sensors are usually classified into four types: piezoresistive sensors, capacitive sensors, piezoelectric sensors and triboelectric sensors. The principle of pressure sensors is to convert external pressure into resistance output signals. Wearable pressure sensors show good application potential in motion detection and human–computer interaction (Jiang et al., 2023).

Compared with other sensing analysis methods, electrochemical sensors have attracted wide attention because of their highly selective and sensitive detection performance. At present, they have become one of the most widely used sensors. It is urgent to design advanced electrochemical sensing platforms for food, biological and health monitoring. Electrochemical sensors are mainly composed of recognizing elements, signal conversion system, information transmission and processing system. They can be divided into potential sensors, conductivity sensors and current sensors according to different output signals (Fig. 1). In this section, we give a brief introduction to electrochemical sensors, where electrodes can be used to sense analytes without causing damage to the detection system.

2.1. Mechanism of electrochemical sensors

Electrochemical sensors are the devices that convert chemical signals caused by the substances to electrical signals using the basic principle of electrochemical analysis and experimental technology (Amaral et al., 2022). The signal conversion system directly or indirectly converts the reaction signals on electrochemical sensors into electrical signals. Then the electrochemical signals are processed in the information transmission and processing system, so as to carry out quantitative or qualitative analysis of the target (Baranwal, Barse, Gatto, Broncova, & Kumar, 2022). Electrochemical sensors can be used to monitor the target analytes by measuring the degree of redox reactions, exhibiting high selectivity and low detection limit (Ho, Choi, Jo, Myoung, & Cho, 2021).

2.2. Enhancement mechanism of SAN-based electrochemical sensors

SANs can enhance reactivity and regulate reaction pathways through redox mediation, preferential adsorption/catalysis of reactants or intermediates, and synergies with other active centers from substrate or nearby heteroatoms. It is a key in the research of sensor interface in the field of electrical analysis (Huang, Chen, Gan, Wang, & Dong, 2019). The wide application of SANs provides some valuable inspiration for the construction of efficient electrochemical sensors. In recent years, SANs have appeared as electrode materials, showing excellent electrocatalytic performance, where the free movement of valence electrons can enhance electrochemical sensing performance (Shen, Liu, Li, & Yang, 2019). The electrons can cross the crystal lattice, so that the current can be conducted in the SANs. Therefore, the substrate in SANs with good conductivity can improve the sensitivity (Yin, Wang, Fan, Zuo, & Li, 2021).

The mechanisms of electrochemical sensing signal enhancement

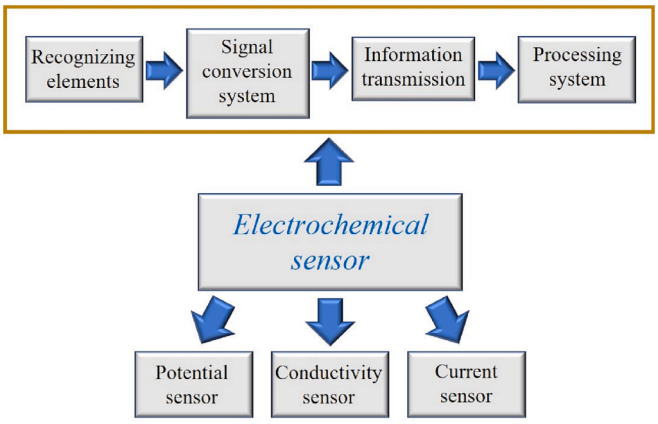


Fig. 1. Composition and classification of electrochemical sensors.

include the following four aspects: (i) suppressing charge recombination to reduce the injection of electrons from the electrode surface into the electrolyte (Kirchner & Hirsch, 2020), (ii) enhancing interfacial charge transfer to enhance the movement of electrons from sensors to redox probes by decreasing the diffusion activity of probes in the electrolyte, (iii) increasing current conduction efficiency to increase the number and migration rate of free electrons (Yang et al., 2017), and (iv) providing extra reaction sites (Liu, Huang, & Qian, 2021). SANs have obvious advantages, especially in enhancing interface charge transfer and improving current conduction efficiency. Therefore, they are good electrode materials worthy of further research (Guan, Bai, & Tang, 2021).

3. Applications of SAN-based electrochemical sensors

Electrode is the core part of electrochemical sensor, which plays a vital role in the performance. The rapid development of nanomaterials provides a new way to improve the sensitivity and selectivity of electrochemical sensors (Han & Guan, 2022b). At present, a great deal of research work has been devoted to developing electrode materials with excellent electrocatalytic activity (Liu, Zhang, Yan, & Yu, 2017). Since SANs have unique mono-dispersed metal sites and electronic structures, they can provide abundant active sites and promote charge transfer, thus improving the sensing performance.

Enzymes have excellent specificity, and thus enzyme-based sensors have excellent sensitivity and selectivity (Cui, Li, Ryabchuk, Junge, & Beller, 2018). However, natural enzymes are easily denatured and inactivated, which result in high extraction price and poor stability, seriously preventing their practical applications. Therefore, man-made nanozymes have attracted wide attention as substitutes for natural enzymes. For example, Gijare et al. modified tin oxyfluoride (FTO) substrate with reduced graphene oxide (rGO) as an enzyme-free nanozyme to detect glucose (Gijare, Chaudhari, Ekar, & Garje, 2021). Ahmed et al. proposed an electrochemical sensor for detecting UA using polypyrrole doped carbon black-Co_3O_4 nanocomposites (Ahmed, Faisal, Alsareii, & Harraz, 2022). The non-enzymatic sensors have the advantages of high sensitivity and low detection limit. Compared with natural enzymes, nanozymes have high stability, low cost and easy batch preparation. They can be applied in biosensing, catalysis, cancer therapy, environmental treatment and other fields (Qiu, Pu, Ran, Liu, Ren, & Qu, 2018). However, the activity and specificity of nanozymes are different from those of natural enzymes, which limit their applications in sensing and biomedicine (Huang, Ren, & Qu, 2019). SANs can not only provide an ideal model for the design of reasonable nanozymes at the atomic level, but also offer an appropriate platform for researching the source of enzyme-like activity (Jiao et al., 2020). SANs with good activity and stability have super-sensitive electrochemical sensing ability. Therefore, the development of SANs is helpful to the research of natural enzyme substitutes, showing a promising application foreground in the sensing of small molecular markers of major diseases. In this section, the applications of SANs in electrochemical sensors are reviewed (Table 1).

3.1. Detection of H_2O_2

H_2O_2 is significant in industrial, synthetic and biomedical fields, such as pharmacy, clinic, food, environment, mining, and textile. In living organisms, besides the well-known cytotoxicity, H_2O_2 is an important medium of biological physiology, activation of aging cells and diseases·H_2O_2 is often associated with the occurrence of cancer, Parkinson's disease (PD), Alzheimer's disease (AD), diabetes and other diseases (Winterbourn, 2018). In addition, H_2O_2 is used in food industry and regarded as an antibacterial agent. However, the residual H_2O_2 and its derived active substances can cause oxidative damage to human health (Xing, Zhang, Fu, Lorenzo, & Hao, 2022). Therefore, realizing the quantitative detection of H_2O_2 is of great significance for ensuring food safety and diagnosing physiological health level (Kornienko, Ly, Robinson, Heidary, Zhang, & Reisner, 2019).

3.1.1. Detection of H_2O_2 in vitro

The detection of H_2O_2 in vitro can lay a good foundation for its quantitative detection in cells and food (Sarma, Vatsyayan, Goswami, & Minteer, 2009). We can use SANs with peroxidase (POD) activity as substitutes for natural enzyme reduction of H_2O_2. At present, most of studies on SANs focus on atomically dispersed metal-N_x moieties embedded on carbon carrier (M—N—C) (Huang, Chen, et al., 2019). Cheng et al. prepared an Fe-based SAN by anchoring single Fe atoms onto nitrogen-doped carbon nanotubes (CNT/FeNC), showing excellent peroxidase-like activity (Fig. 2a) (Cheng et al., 2019). The CNT/FeNC SAN had the highest catalytic activity at pH value of 3.5, and had stable peroxidase-like activity in a broad temperature range. In addition, they

Table 1
Performance of SAN-based electrochemical sensors.

Sensor	Target	Linear range	LOD (nM)	Sensitivity (μA mM^{-1} cm^{-2})	Reference
CNT/FeNC	H_2O_2	0.1–100 mM	30	–	(Cheng, Li, Liu, Lin, & Du, 2019)
	glucose		20,000		
		0.1–10 mM	30		
	AA	0.1–10 μM			
SA Co-MoS_2	H_2O_2	50 nM-5.845 mM 5.845–17.241 mM	10	–	(Wang et al., 2019)
Fe-SASC/NW	H_2O_2	5.0×10^{-10}-0.5 M	46.35	–	(Ding, Lyu, et al., 2021)
Fe_3C@C/Fe—N—C	H_2O_2	1–6000 μM	260	1225	(Wei, Song, et al., 2021)
Fe SAs-N/C	H_2O_2	1–54 μM 54–764 μM 764–9664 μM	340	–	(Liang et al., 2022)
Mn-MoS_2/PGS	DA	50 pM-50 μM	0.05	–	(Lei et al., 2020)
Ni-MoS_2	DA	1 pM-1 mM	0.001	–	(Sun, Chen, et al., 2022)
A-Co-NG	UA	0.4–41950 μM	33.3 ± 0.024	301.6	(Hu et al., 2021)
Ru-Ala-C_3N_4	DA	0.06–490 μM	20	–	(Xie et al., 2021)
	UA (at the same time)	0.5–2100 μM	170		
Fe-N_5 SASC	DA	0.005–500 μM	7	–	(Bushira, Kitte, Li, Zheng, Wang, & Jin, 2022)
	UA (at the same time)	0.01–480 μM	27		
GO_x/Co-SASC	glucose	5 μM-1 mM	–	0.001	(Hou et al., 2019)
Pt_1/$Ni(OH)_2$/NG	glucose	0.01–2.18 mM	–	220.75	(Long et al., 2022)
NCA-Co	glucose	0.5 μM-6 mM	100	–	(Song et al., 2022)
NiN_4-SASCs	H_2S	–	–	–	(Pan et al., 2022)
Ni SASCs/N—C	NO	–	1.8	0.43	(Zhou et al., 2020)
Co-N_4/C	O_2	–	–	–	(Wu et al., 2020)

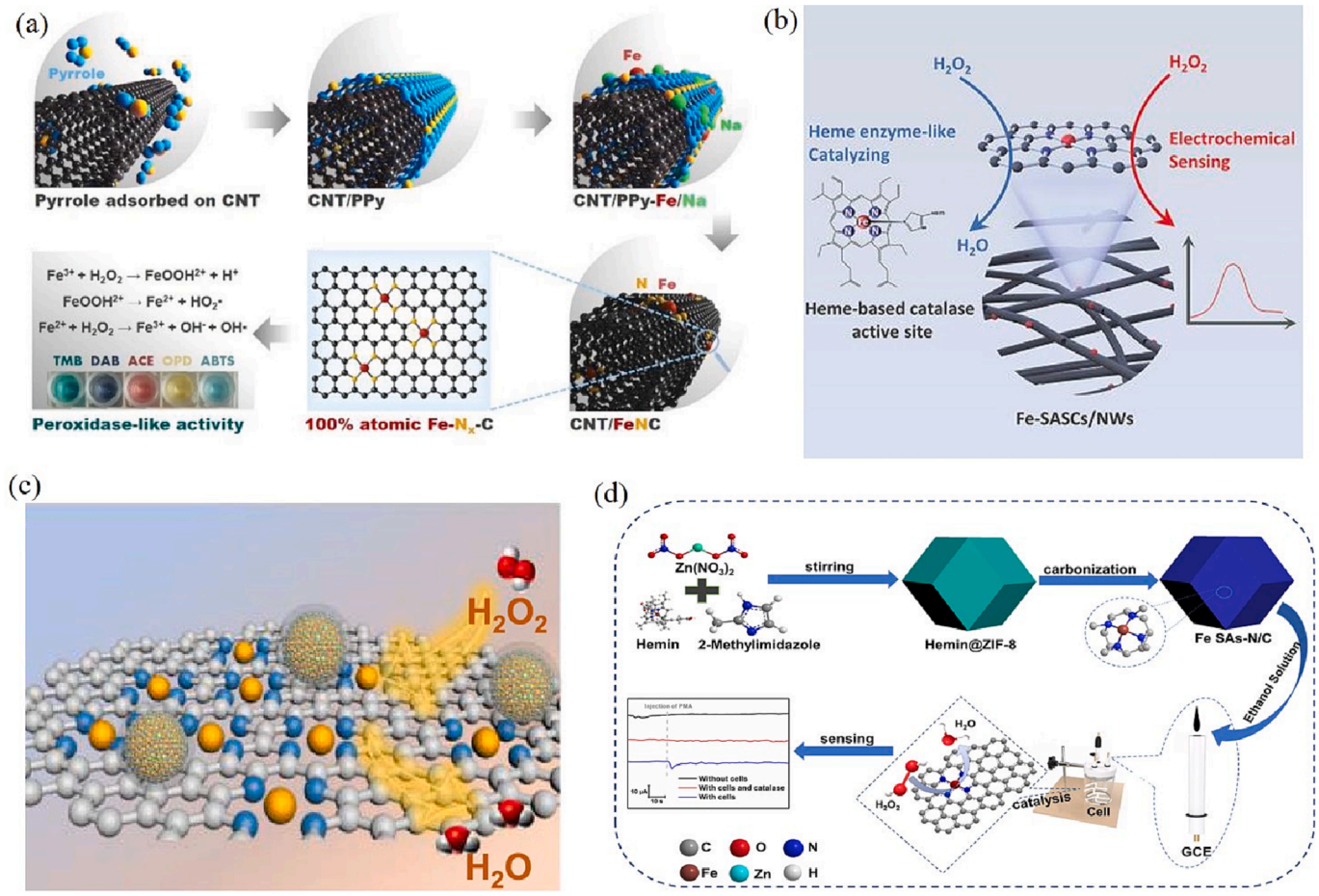


Fig. 2. (a) Synthetic illustration and catalytic mechanism of CNT-/FeNC-based SAN. (b) Mechanism diagram of H_2O_2 detection on Fe-SASC/NW (c) Schematic diagram of electrochemical sensing of H_2O_2 based on Fe_3C@C/Fe—N—C. (d) Schematic diagram of the synthesis and H_2O_2 detection of Fe SAs-N/C (a) Reproduced with permission (Cheng et al., 2019) Copyright 2019, Wiley-VCH Verlag. (b) Reproduced with permission (Ding, Lyu, et al., 2021) Copyright 2021, Wiley-VCH Verlag. (c) Reproduced with permission (Wei, Song, et al., 2021) Copyright 2021, American Chemical Society. (d) Reproduced with permission (Liang et al., 2022) Copyright 2022, American Chemical Society.

used CNT/FeNC SAN-based bioassays to detect H_2O_2 with ultra-high sensitivity, low LOD, good stability and signal reproducibility. The POD-like activity of M—N—C is due to the Fenton-like reaction (Xu et al., 2019).

Wang et al. used single-atom Co-MoS_2 (SA Co-MoS_2) as a peroxidase mimic, which had excellent activity and stability in the peroxidase-like catalytic reaction (Wang et al., 2019). The SA Co-MoS_2 can fully activate H_2O_2 and promote the subsequent peroxidase-like reaction, which depends on the strong chemisorption ability of H_2O_2 molecules on the SA Co-MoS_2. Compared with traditional electrochemical H_2O_2 sensors, SA Co-MoS_2 decorated electrode had a longer linear current response area from 50 nM to 17.241 mM, a lower limit of detection (LOD) of 10 nM, higher selectivity, and better stability. Ding et al. prepared a SAN (Fe-SASC/NW) with heme-like enzyme active sites through a Zn atom-assisted method (Ding, Lyu, et al., 2021). Heme-based catalase is one of the earliest known enzymes, which is usually designed to monitor H_2O_2 with high sensitivity and selectivity (Ding, Zhang, et al., 2021). Therefore, they developed an electrochemical sensor for H_2O_2 detection based on Fe-SASC/NW (Fig. 2b). The sensor had a broad linear monitoring range from 5.0×10^{10} M to 0.5 M and a low LOD of 46.35×10^{-9} M. The outstanding electrochemical performance was due to the structure of Fe-N_x similar to that of natural metalloproteinases. They further used the Fe-SASC/NW-based sensor to monitor the concentration of H_2O_2 in contact lenses disinfectants. The catalytic activity of Fe-SASC/NW decreased obviously after the addition of KSCN, proving that Fe-N_x sites were the main active sites.

3.1.2. *Detection of H_2O_2 in vivo*

Fe SAN-based sensors can be used to detect H_2O_2 in living cells, which provides a new route for the real-time detection. Fe-Fe_3C nanoparticles can enhance the oxygen reduction activity of single-atom Fe sites by changing the adsorption strength between single-atomic Fe sites and OH* intermediates (Sun et al., 2020). Wei et al. designed an ultrasensitive electrochemical H_2O_2 biosensor based on carbon coated Fe_3C nanoparticles coupling with Fe single atomic sites (Fig. 2c) (Wei, Song, et al., 2021). The intrinsic synergistic effect between Fe_3C@C nanocrystals and Fe single atomic sites came from the transfer of electrons from Fe_3C@C to Fe single atomic sites, which was helpful for intensive adsorption of H_2O_2 molecules on single-atom Fe sites. Compared with single-atom Fe—N—C, Fe_3C@C/Fe—N—C had higher POD-like activity and higher H_2O_2 detection sensitivity. The sensitivity was up to 1225 μA $mM^{-1} \cdot cm^{-2}$, the response was fast within 2 s, and the LOD was as low as 0.26 μM. In addition, they used Fe_3C@C/Fe—N—C to detect intracellular H_2O_2 discharged from Hela cells, showing that Fe_3C@C/Fe—N—C is a sensitive and accurate sensor. The successful demonstration of Fe_3C@C/Fe—N—C provided a novel way to improve the detection sensitivity of H_2O_2 in living cells, and gave a new inspiration for synergistic enhancement of single atomic sites for electrochemical sensing applications. In a closely related study, Liang et al. used heme as the Fe donor to fix Fe ions in zeolitic imidazolate frameworks (ZIF-8) to obtain Fe SAs-N/C, and constructed H_2O_2 electrochemical sensor (Fig. 2d) (Liang et al., 2022). Using the sensor, they successfully achieved real-time monitoring of H_2O_2 released by living MCF-7 cells. Compared

with other SAN-based electrochemical sensors, Fe SAs-N/C@GCE had a larger electrochemical detection area for H_2O_2, and lower LOD of 0.34 μM. The Fe-N_x active sites of Fe SAs-N/C were consistent with those of Fe-SASC/NW, which catalyzed H_2O_2 (equations (1)–(4)) (Lee, Liu, & Lu, 2016).

$$Fe^{2+} + H_2O_2 + H^+ \rightarrow Fe^{3+} + HO\bullet + H_2O \quad (1)$$

$$Fe^{3+} + H_2O_2 \rightarrow Fe^{2+} + HO_2\bullet + H^+ \quad (2)$$

$$H_2O_2 + H^+ \rightarrow HO_2\bullet + H_2O \quad (3)$$

$$Fe^{3+} + HO_2\bullet \rightarrow Fe^{2+} + O_2 + H^+ \quad (4)$$

3.2. Detection of DA

DA is an important neurotransmitter and plays a pivotal part in the functions of central nervous system and cardiovascular system (Pan, Kaminga, Wen, Wu, Acheampong, & Liu, 2019). Because DA can promote the growth of livestock by decreasing fat deposition and increasing protein accumulation, it is usually utilized as a "lean meat agent" to feed livestock for human consuming all over the world. However, this is illegal because long-term intake of DA residues will result in headache, chest tightness, nausea and other undesirable effects (Li et al., 2021). Moreover, abnormal DA concentration can lead to nervous system diseases, including depression, PD, AD, schizophrenia and so on. In addition, the content of DA in urine is the key diagnostic reference for catecholamine secreting tumors such as pheochromocytoma (Shukla, Aroosh, Matzafi, & Ben-Yoav, 2021). Therefore, precise DA detection is important for food industry, disease diagnosis and health monitoring.

MoS_2 is an excellent electrochemical sensing material with high specific surface area, low charge transfer resistance and high density of electronic state (Li, Wang, Xie, Liang, Hong, & Dai, 2011). The band gap of MoS_2 is limited and adjustable, and MoS_2 is an effective sensor material for DA detection, which has unique electronic characteristics (Kalantar-zadeh, Ou, Daeneke, Strano, Pumera, & Gras, 2015). Precious metal particles are usually supported on MoS_2 to construct composite materials for selective detection of DA (Sun et al., 2014). However, due to the scarcity and high price of precious metals, it is essential to seek low-cost substitutes. Up to now, MoS_2-based SANs have been successfully synthesized as electrochemical sensors to monitor DA. For example, Lei et al. prepared an ultra-sensitive electrochemical DA sensor based on Mn doped MoS_2 by an expandable two-step method (Lei et al., 2020). Compared with other defect configurations, the substitution of Mo atoms by Mn (Mn_{Mo}) in MoS_2 lattice was advantageous in energy, showing physical adsorption of DA molecules instead of chemical adsorption. The physical adsorption ensures that DA molecules can be removed after oxidation to allow other DA molecules to reach the sites. The sensor showed extremely high sensitivity, with the LOD of 50 pM in a buffer solution, 5 nM in 10% serum and 50 nM in man-made sweat. The sensor can be used to selectively detect DA with good stability due to the catalytic behavior of Mn dopant. The successful application of Mn-MoS_2 in electrochemical sensors showed that single-atom metal-doped transition metal dichalcogenides (TMDs) have unique electronic properties, which can offer a new platform to build ultra-sensitive biosensors. Sun et al. devised an ultra-sensitive DA sensor on the basis of flower-shaped MoS_2 modified by single-atom Ni (Ni-MoS_2) (Sun, Chen, et al., 2022). The large percentage of Ni active sites on the base surface of MoS_2 efficaciously improved the intrinsic conductivity and electrochemical activity. The DA sensor based on Ni-MoS_2 was able to monitor the DA concentration in PBS, bovine serum and man-made urine with superior sensitivity. The LOD can reach 1 pM in PBS, 1 pM in bovine serum and 100 pM in man-made urine. Moreover, the sensor exhibited good selectivity, repeatability and stability. The authors assembled Ni-MoS_2 into a test strip, and successfully realized the detection of DA content in blood and urine.

3.3. Detection of UA

UA exists in milk, which contributes to the dietary intake of antioxidants, ascorbic acid (AA), tocopherol, tyrosine and cysteine. Imbalance of UA level in milk may affect the flavor, and its detection can provide information about the health and metabolism of dairy cows and other mammals (Motshakeri, Phillips, & Kilmartin, 2019). Besides, UA is a metabolic product of purine alkaloids and the excessive presence in the body would cause diseases including arthritis, preeclampsia, kidney diseases and cardiovascular diseases (Zhang et al., 2019). Therefore, UA detection is important for the diagnosis of these diseases.

At present, almost all electrochemical UA sensors are on the basis of enzymes. However, enzymes are easy to inactivate, and thereby people are committed to searching for new materials for the electrochemical detection of UA (Shi et al., 2019). Hu et al. anchored high-density and island-like Co atoms on *N*-doped graphene substrate (A-Co-NG), and constructed an electrochemical bionic sensor for UA detection (Hu et al., 2021). The A-Co-NG sensor exhibited a wide detection area of 0.4–41950 μM, and a low LOD of 33.3 ± 0.024 nM. In addition, it had good stability, reproducibility, repeatability, reversibility, and selectivity to UA. The A-Co-NG sensor exhibited precise diagnosis of UA in serum and its accuracy reached 98.5%, which provided a basis for its actual application.

Furthermore, SAN-based electrochemical sensors can be used to detect UA and DA simultaneously, which are ubiquitous active molecules in human body. The abnormal level of DA or UA can lead to dysfunction of human body and cause diseases (Yang, Hu, & Li, 2019). Therefore, the concurrent monitoring of DA and UA is very important for disease diagnosis. However, due to their similar structures and electrochemical properties, simultaneous monitoring of DA and UA is still a huge challenge. Ru-based SANs can be used to simultaneously detect DA and UA, which plays an important role in promoting the development of noble metal catalysts. The high cost of noble metal catalysts has always been the main factor limiting their industrial application. Therefore, it is of great significance to develop catalysts with minimum metal loading (Zhang, Zhang, Jia, Zhang, & Han, 2021). Xie et al. synthesized a SAN (Ru-Ala-C_3N_4) with atomic Ru embedded on carbon nitride carrier as a highly sensitive electrochemical biosensor for simultaneous detection of DA and UA (Xie et al., 2021). The plentiful single-atom Ru active sites and effective electron transport ability in the Ru-Ala-C_3N_4 were conducive to the adsorption of DA and UA. The calibration curves of DA and UA were broad (0.06–490 μM and 0.5–2135 μM, respectively), and the LODs were very low (20 nM and 170 nM, respectively). In addition, the Ru-Ala-C_3N_4 sensor had excellent repeatability and stability, as well as superior selectivity, and sensitivity, which can be used to efficiently detect DA and UA in authentic biological serum specimens. In addition, graphene is a good substrate of SANs for DA/UA detection. The strong interaction between DA/UA and graphene substrate is beneficial to the electron transfer from SANs to DA/UA (Wang, Li, Tang, Lu, & Li, 2009). Bushira et al. prepared atomic Fe coordinated with five N atoms on graphene (Fe-N_5 SASC) by one-step pyrolysis, and successfully realized simultaneous detection of DA and UA (Bushira et al., 2022). Due to its unique electronic structure and ample active sites, the electrochemical sensor based on enzyme-like Fe-N_5 SASC showed good linear characteristic response within the range of 0.005–500 μM and 0.01–480 μM, and the LOD of DA and UA was 0.007 and 0.027 nM, respectively. Moreover, the biosensor based on Fe-N_5 SASC was effective in detecting DA and UA in human serum samples, and had good anti-interference capacity, stability and repeatability.

3.4. Detection of glucose

Glucose is an essential nutrient for human body, while abnormal glucose content can result in a variety of diseases (Dong et al., 2019).

Low glucose content can result in hypoglycemia and insulin shock, while high glucose content can result in diabetes if there is no treatment (Justice Babu, Sheet, Lee, & Gnana Kumar, 2018). Long-term excessive blood glucose content may even lead to serious complications, such as renal failure, blindness and heart disease (Fan et al., 2023). Therefore, it is very important to monitor the glucose in the diet and in vivo to prevent the occurrence of diabetes. Moreover, glucose is a model substrate for biomass photo-reforming, which might result in environmental pollution (Eqi et al., 2022).

In 2019, Hou et al. developed an online electrochemical system (OECS) for monitoring glucose in vivo using Co-SASC-based sensor (Hou et al., 2019). Wang et al. found that the OECS can be used for selective measurement of brain glucose in rats, and can continuously monitor glucose in micro-dialysis (Wang et al., 2016). The GO_x/Co-SASC-based OECS had sensitive, selective and stable ampere response to glucose in brain micro-dialysis, which was not interfered by other electro-active species in the brain during detection, thus monitoring the dynamics of glucose in the brain. The study provided a new way for in vivo analysis of brain chemistry, which has important significance for comprehending the molecular basis of brain function.

Due to insufficient filling of d-orbitals, small molecules can be easily absorbed on Pt surface, which can be further oxidized or reduced at a certain potential (Baranwal et al., 2022). Therefore, Pt is recognized as an efficient electrocatalyst for transforming small molecules through oxidation or reduction, which has been widely used in the detection of glucose (Amaral et al., 2022). In addition, Pt is insoluble in strong acid, strong alkali and high concentration salt medium, which makes it possible to monitor glucose under physiological conditions (Niu, Shi, Zhao, & Lan, 2016). Moreover, single Pt atoms not only are the significant active sites of glucose adsorption, but also can activate the neighboring Ni atoms, inducing more positive charges on Ni atoms. The synergistic catalysis effect and enhanced electron transfer capacity of $Pt_1/Ni(OH)_2$/NG took an important function in enhancing the electrochemical non-enzymatic catalysis and sensing of glucose (Fig. 3a) (Long et al., 2022). The $Pt_1/Ni(OH)_2$/NG sensor had a low anode peak potential of 0.48 V, high electrocatalytic activity, low oxidation potential, short response time of 4.6 s, sensitivity as high as 220.75 μA $mM^{-1}cm^{-2}$ and exceptional stability for sensing of glucose. In addition, Co-based SANs attract special attention because of non-noble metal and high catalytic activity for glucose detection (Hwang, Lee, Seo, & Chung, 2018). Song et al. synthesized NCA-Co by embedding Co atoms into nitrogen-doped carbon aerogels using biomass hydrogel as a precursor (Song et al., 2022). The prepared NCA-Co had special structural features, such as microporous imperfections and nano-folds, which can stabilize the Co single atoms (Fig. 3b). The non-enzymatic glucose sensor based on NCA-Co had a LOD of 0.1 μM, a linear scope of 0.5 μM-6 mM, fantastic stability, high selectivity and reproducibility. In addition, the NCA-Co-based sensor showed significant performance in the detection of glucose in man-made spittle and human serum samples. Further studying on clinical human serum samples found that the relative standard deviations were all below 5%. The measured results were close to those of commercial blood glucose meter. The recovery rate was between 94% and 105%, showing that the NCA-Co/GCE sensor had promising application prospect.

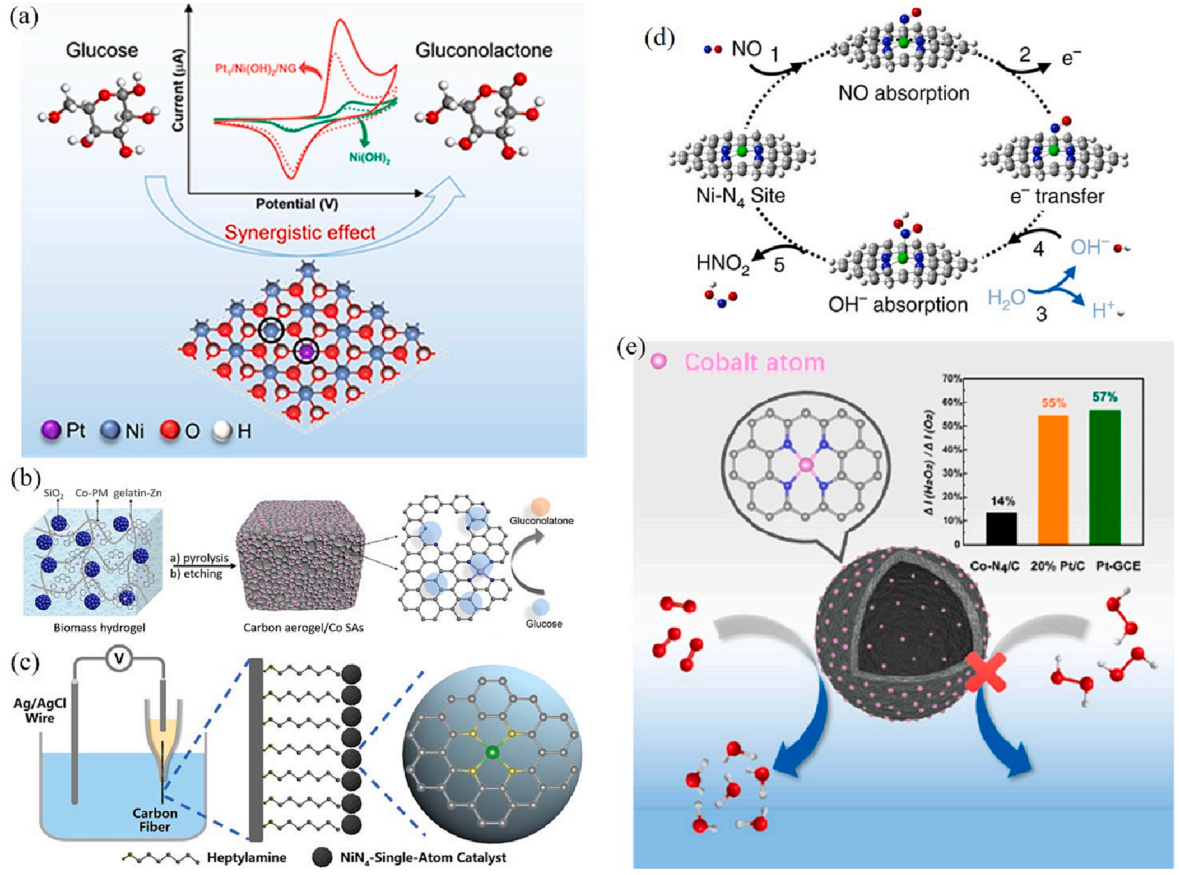


Fig. 3. (a) Mechanism of detecting glucose by $Pt_1/Ni(OH)_2$/NG (b) Schematic diagram of the synthesis and glucose detection of NCA-Co aerogels. (c) Schematic illustration of the NiN_4-SACs-GRP microsensor for H_2S sensing (d) Structure of electrocatalytic oxidation process of NO on Ni SASCs/N—C. (e) Mechanism of oxygen monitoring on Co-N_4/C. (a) Reproduced with permission (Long et al., 2022) Copyright 2022, American Chemical Society. (b) Reproduced with permission (Song et al., 2022) Copyright 2022, Elsevier. (c) Reproduced with permission (Pan et al., 2022) Copyright 2022, American Chemical Society. (d) Reproduced with permission (Zhou et al., 2020) Copyright 2020, Springer Nature. (e) Reproduced with permission (Wu et al., 2020) Copyright 2020, American Chemical Society.

3.5. Detection of other small molecular substances

H_2S has been found in many kinds of foods, including meat, eggs, fruits and vegetables. H_2S is generally regarded as a toxic gas, which does harm to human health (Wang, Leng, Wang, & Zhao, 2022). However, appropriate low concentration of H_2S has a positive impact on food. In addition, H_2S plays an important role in the central nervous system (CNS) and takes part in anti-inflammatory, anti-oxidation and anti-apoptosis processes. H_2S has also been found in human body and environment. Abnormal concentration of H_2S will endanger human health, destroy the environment and result in food safety problems (Xie, Wang, Fan, Tu, Liu, & Pu, 2023). The detection of H_2S is of great significance to neurodegenerative diseases such as PD, AD and food safety (Zivanovic et al., 2019). Pan et al. developed an electrochemical H_2S sensor with excellent precision in vivo by combining the superiorities of SANs and electrooxidation-reduction potential measurement (Fig. 3c) (Pan et al., 2022). They used a galvanic redox potentiometry (GRP) sensor to successfully quantify H_2S discharge behaviors in mouse brain under regular and PD situations, and accurately measured H_2S in vivo. GRP is a new sensing technology based on the principle of spontaneous dual polarization (Wu, Yu, & Mao, 2017). GRP sensors do not need external power supply support, avoiding the film effect on adjacent neurons (Yu et al., 2020). More importantly, it reduces the accumulation of products on the electrode surface and the passivation of reaction sites. Therefore, compared with current sensors, the GRP sensor based on NiN_4-SASCs (abbreviated as NiN_4-SASCs-GRP) had a wider detection scope of H_2S concentration, better sensing stability, and stronger anti-interference ability of physiological disturbance.

NO is the first gas found to have regulatory effect in human body and plays an important role in many physiological and pathological processes (Xiao, Wu, Hao, Zhang, Yu, & Mao, 2017). Real-time monitoring of NO in vivo plays an important role in monitoring nerve transmission, inflammatory reaction, cardiovascular system, and the occurrence and development of cancer (Li, Qi, et al., 2020). Zhou et al. developed an electrochemical sensor based on Ni-based SASCs for detecting NO in living cell surroundings (Fig. 3d) (Zhou et al., 2020). They anchored Ni single atoms onto nitrogen-doped hollow carbon spheres (Ni SASCs/N—C), which can promote the electrochemical oxidation of NO and realize the true-time sensing of NO in living cell surroundings. Ni SACs/N—C with dispersed Ni-N_4 catalytic sites was a reliable stretchable electrochemical sensing material, and therefore, they used Ni SASCs/N—C to construct a flexible tensile sensor, which had supernal biocompatibility, high mechanical tensile tolerance and high sensitivity of 430.6nA μM^{-1} cm^{-2}. It can selectively and sensitively monitor NO dynamics in cells in real time under the stimulation of drugs and stretching. Ni remained in single-atom dispersion after NO adsorption, while the binder Nafion on the sensor surface could well restrain the current response to nitrite, which was the primary disturbance to NO detection (Li, Xie, Gao, & Li, 2015).

Like food and water, oxygen is one of the most fundamental elements of human health (Wang, Hu, Mi, Yan, & Zhao, 2021). Therefore, it is of great significance to detect the oxygen concentration in the body. Oxygen monitoring is generally based on electrocatalytic four-electron oxygen reduction reaction (ORR) mechanism (Chang, Batchelor-McAuley, & Compton, 2020). Wu et al. restricted Co single atoms in *N*-doped hollow carbon spheres to synthesize a Co-N_4/C catalyst (Wu et al., 2020). The tolerance of Co-N_4/C to H_2O_2 when catalyzing four-electron ORR was obviously higher than that of Pt in neutral medium. In the application of intracorporeal oxygen sensing, the activation of H_2O_2 was prevented at Co-N_4 sites, which was due to the weak adsorption interaction between H_2O_2 and Co atoms (Fig. 3e). Co-N_4 SASC had high resistance to other interfering substances in vivo, and possessed excellent selective O_2 sensing ability in vivo, which is superior to Pt electrocatalysts.

4. Optimization strategies of SAN-based electrochemical sensors

At present, various electrochemical sensors based on SANs have been developed. However, there are many factors that affect the performance and practical applications of SAN-based electrochemical sensors, such as easy aggregation and low load of single-atom metals, single detection ability and complex detection process, poor stability of electrode, and poor applicability to complex detection environments (Iwase, Nakanishi, Miyayama, & Kamiya, 2020). To improve the detection performance of SANs-based electrochemical sensors, it is necessary to further optimize the preparation process, applicability, stability, detection process, and detection capability. In this section, we will introduce some optimization strategies for SAN-based electrochemical sensors.

4.1. Improving the electrochemical activity of SANs

Isolated metal single atoms are the main active sites for electrochemical detection, but the load content of metal in SANs is usually low, resulting in relatively low activity. However, due to the large surface free energy of single metal atoms, increasing metal loading would easily lead to the agglomeration to form large clusters, resulting in the decrease of catalytic activity. So far, controllable synthesis of SANs is still challenging (Ji, Chen, Wang, Zhang, Wang, & Li, 2020a). However, reasonable design and structural regulation can improve the metal loading density of SANs. In addition, the activity of SANs can be improved by adjusting the electronic structure of active sites, constructing diatomic metal active sites, and introducing unsaturated coordination or defective sites on the carrier surface. The ways of regulating electron structure include constructing planar conjugate structure, forming conductive composite material, and doping guest molecule (Xiao, Wang, & Guan, 2022). In addition, the electrochemical performance of SANs can be also improved by designing substrates with high conductivity, excellent chemical stability and high surface area to volume ratio.

4.2. Improving the stability and applicability of the sensors

For cheap and stable recognition of target analytes, biomimetic recognition components such as molecularly imprinted polymers (MIPs) and aptamers can be used in conjunction with SANs. Introducing conductive MIPs can significantly improve the sensitivity and selectivity of electrochemical sensors (Wang, Liu, Zhu, & Tian, 2023). In addition, the SAN modifier has poor dispersion and is easy to fall off the electrode surface, which affects the stability and repeatability of the sensor. In order to obtain a long-term stable electrochemical sensing interface, a very stable self-assembled interface is important. For example, replacing the traditional Au-S self-assembled interface with Au—C—C bonds can improve the stability of the sensor (Wang et al., 2023). In addition, the fabrication of thin films, and the cross-linking of materials can stabilize SANs on the electrode surface. Furthermore, developing new detection technology can improve monitoring sensitivity and adaptability to complicated environment (Fu, Ding, & D'Alessandro, 2023). It is feasible to further enhance the suitability of the sensor by combining electrochemical sensor and optical sensor to construct a dual sensor to minimize false positive signals.

4.3. Broadening the application prospect of sensors

Wearable devices are an important breakthrough in the development of sensors. They can be used to analyze real-time physiological data in a non-invasive/minimally invasive process, accurate detection of vital signs including heart rate, body temperature and blood pressure, and help to monitor the individual health status (Gao et al., 2023). The detection of sweat metabolites can non-invasively provide biochemical information of human health status, thus reducing the pressure of invasive blood testing. The sensor of sweat metabolites based on

wearable technology has achieved some research results in non-invasive and personalized health monitoring (Das, Nag, & Banerjee, 2023). SANs have better electrochemical performance and biocompatibility than nanomaterials. Therefore, the application of SANs in wearable electrochemical sensors is more conducive to the comprehensive monitoring of human physiological information and timely monitoring of health conditions.

With the popularity of smart phones, electrochemical sensors that can interface with smart phones for detection will make up for the shortage of fast field detection and become more and more important in the future (Faham, Salimi, & Ghavami, 2023). Therefore, it is possible to integrate wireless data transfer devices on electrochemical sensors, and develop smartphone applications for visualizing. At present, some sweat metabolite sensors based on nanomaterial wearable technology have been combined with smart phones (Cheng et al., 2021). For example, Wang et al. developed a portable ascorbic acid detection system, which can be used to detect the level of ascorbic acid in human sweat (Wang, Pan, et al., 2022). They combined the sensor system with a smart phone through an application-specific integrated circuit with Bluetooth 5.0 function, which can accurately monitor the ascorbic acid level in sweat (Fig. 4a). Cheng et al. designed a wireless, battery-free and flexible integrated patch for real-time detection of human sweating cortisol (Cheng et al., 2021). The near field communication (NFC) module on the near field communication patch can realize wireless power collection and data interaction with smart phones (Fig. 4b). Ciui et al. reported a new fully integrated wearable bandage and microneedle electrochemical sensing platform, which was used to detect tyrosinase (TYR) on the skin surface and subcutaneous tissues for potential melanoma screening (Ciui et al., 2018). They connected wearable sensors to ultralight flexible electronic boards, which can wirelessly transmit data to mobile devices (Fig. 4c). In addition, electrochemical sensors can be combined with silicon integrated circuit components with complex electronic functions. Signal processing can reduce the influence of signal noise, so as to accurately evaluate the physiological state of human body. Portability, flexibility, visualization and wearability are the key characteristics of emerging electrochemical sensors. The application of SANs to emerging electrochemical sensors can improve the performance of sensors and further broaden the application prospect.

4.4. *Improving the multiple detection ability of the sensors*

The most reported electrochemical sensors are composed of two or more mixed materials to promote the properties. Hybrid materials can solve the problem of multiple detection capability in the applications of practical environment (Pathiraja, Bonner, & Obare, 2023). Therefore, preparing electrochemical sensors based on multiple SANs can improve the ability of multiple detections. Reasonably designed electrochemical sensors based on multiple SANs are promising for simultaneous detection of different small molecules. Such multiple detections can save more resources and improve monitoring efficiency. In addition, sensor arrays can be assembled to detect different analytes, which can improve the multiple detection ability. Increasing the density of the arrays is beneficial to more complete and faster detection (Rocha, Hasimoto, & Santhiago, 2023).

5. Conclusions and perspectives

In recent years, SANs occupy a significant position in the field of electrochemical analysis because of their high catalytic efficiency, good stability and high metal utilization. In this paper, we reviewed the

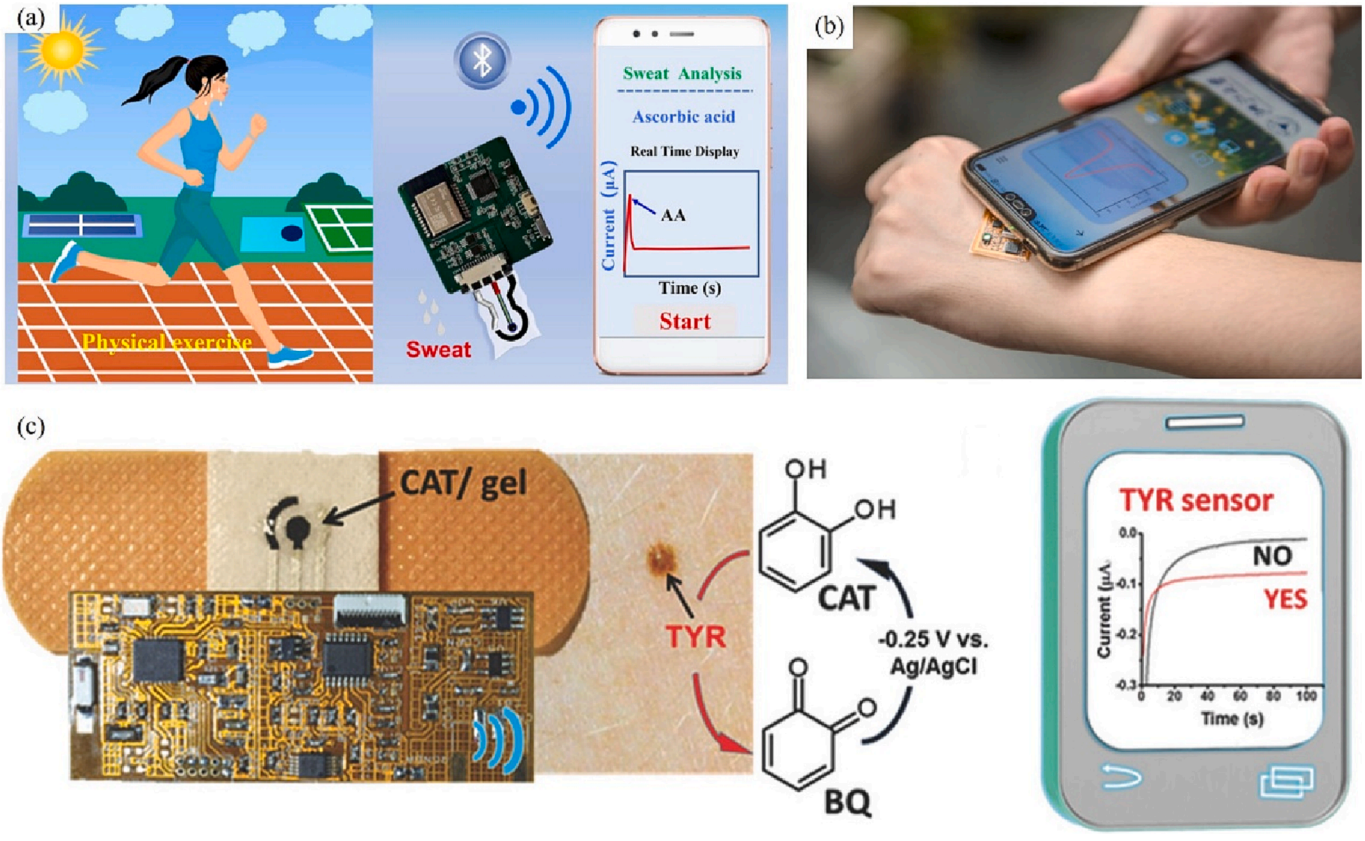


Fig. 4. (a) Schematic diagram of sweat monitoring of ascorbic acid detection system and its integration with smartphone. (b) An image of in situ detection of sweat cortisol with smartphone. (c) TYR sensing program based on bandage electrochemical sensor and ampere data wirelessly transmitted to smartphone. (a) Reproduced with permission (Wang, Pan, et al., 2022) Copyright 2022, Academic Press Inc. (b) Reproduced with permission (Cheng et al., 2021) Copyright 2021, Elsevier. (c) Reproduced with permission (Ciui et al., 2018) Copyright 2018, John Wiley and Sons Ltd.

sensing mechanisms and applications of SAN-based electrochemical sensors in food safety and health monitoring. Different synthesis strategies would affect the morphology and structure of SANs, thus influencing their electrochemical properties. Therefore, the controllable synthesis of SANs is the key to improve the electrochemical performance. Nowadays, atomic level characterization technologies for identifying the atomic structure of active sites have been rapidly developed, which is beneficial to the controllable synthesis and further design of SANs. In addition, understanding the detection mechanism of SANs is very important for the applications. In situ characterization methods can be used to analyze the electrocatalytic process of SANs, such as in situ transmission electron microscope (TEM), X-ray photoelectron spectroscopy (XPS) and X-ray absorption spectrum (XAS). Moreover, the in situ characterization technologies can be used to monitor the dynamic changes of reaction intermediates and help to understand the structure–activity relationship for electrochemical sensing. However, the current in situ characterization methods are still in the early stage of development, and sometimes they can't meet the actual needs. Therefore, it is important to further explore advanced in situ characterization and computational modeling methods for the further development of SAN-based electrochemical sensors.

SANs not only show excellent electrocatalytic performance, but also show high stability because their catalytic active sites are immobilized by adjacent ligands. The SAN-based electrochemical sensors have high sensitivity, low LOD, good stability, good reproducibility and strong anti-interference ability. These sensors realize simple, stable and even quantitative analysis of chemical signals in living cell environment. The introduction of SANs brings great possibilities for wide applications of electrochemical sensors in biology, biomedicine, biotechnology, clinical and medical diagnosis, environmental and health monitoring and food industry. Moreover, the introduction of SANs provides more possibilities for the intelligent application of electrochemical sensors. We believe that with continuous efforts, SAN-based electrochemical sensors will be successfully combined with smart phones to realize intelligence, and to be widely used in real life in the future.

CRediT authorship contribution statement

Jingru Sun: Data curation, Investigation, Writing – original draft, Writing – review & editing. **Zhenlu Wang:** Supervision. **Jingqi Guan:** Conceptualization, Supervision, Resources, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Acknowledgments

This work was supported by the National Natural Science Foundation of China (No. 22075099), the Natural Science Foundation of Jilin Province (No. 20220101051JC), and the Education Department of Jilin Province (No. JJKH20220967KJ, No. JJKH20220968CY).

References

Ahmed, J., Faisal, M., Alsareii, S. A., & Harraz, F. A. (2022). Highly sensitive and selective non-enzymatic uric acid electrochemical sensor based on novel polypyrrole-carbon black-Co_3O_4 nanocomposite. *Advanced Composites and Hybrid Materials, 5*(2), 920–933. https://doi.org/10.1007/s42114-021-00391-1

Amaral, E. M. F., de Andrade, J. C. B., de Freitas, L. B., Teixeira, G. T. L., do Nascimento, J. P. L., Gelamo, R. V., & Moreto, J. A. (2022). Electrochemical Sensors and Biosensors: Their Basic Working Principles and Some Applications. *Revista Virtual de Quimica*, 1–18. https://doi.org/10.21577/1984-6835.20220112

Arshad, F., Mohd-Naim, N. F., Chandrawati, R., Cozzolino, D., & Ahmed, M. U. (2022). Nanozyme-based sensors for detection of food biomarkers: A review. *RSC Advances, 12*(40), 26160–26175. https://doi.org/10.1039/D2RA04444G

Bai, X., Duan, Z., Nan, B., Wang, L., Tang, T., & Guan, J. (2022). Unveiling the active sites of ultrathin Co-Fe layered double hydroxides for the oxygen evolution reaction. *Chinese Journal of Catalysis, 43*(8), 2240–2248. https://doi.org/10.1016/s1872-2067(21)64033-0

Baranwal, J., Barse, B., Gatto, G., Broncova, G., & Kumar, A. (2022). Electrochemical Sensors and Their Applications: A Review. *Chemosensors, 10*(9), 363. https://doi.org/10.3390/chemosensors10090363

Bushira, F. A., Kitte, S. A., Li, H., Zheng, L., Wang, P., & Jin, Y. (2022). Enzyme-like Fe-N_5 single atom catalyst for simultaneous electrochemical detection of dopamine and uric acid. *Journal of Electroanalytical Chemistry, 904*, Article 115956. https://doi.org/10.1016/j.jelechem.2021.115956

Chang, X., Batchelor-McAuley, C., & Compton, R. G. (2020). Hydrogen peroxide reduction on single platinum nanoparticles. *Chemical Science, 11*(17), 4416–4421. https://doi.org/10.1039/D0SC00379D

Chang, X., Chen, L., Chen, J., Zhu, Y., & Guo, Z. (2021). Advances in transparent and stretchable strain sensors. *Advanced Composites and Hybrid Materials, 4*(3), 435–450. https://doi.org/10.1007/s42114-021-00292-3

Chen, Q., Li, S., Liu, Y., Zhang, X., Tang, Y., Chai, H., & Huang, Y. (2020). Size-controllable Fe-N/C single-atom nanozyme with exceptional oxidase-like activity for sensitive detection of alkaline phosphatase. *Sensors and Actuators B: Chemical, 305*, Article 127511. https://doi.org/10.1016/j.snb.2019.127511

Cheng, C., Li, X., Xu, G., Lu, Y., Low, S. S., Liu, G., … Liu, Q. (2021). Battery-free, wireless, and flexible electrochemical patch for in situ analysis of sweat cortisol via near field communication. *Biosensors and Bioelectronics, 172*, Article 112782. https://doi.org/10.1016/j.bios.2020.112782

Cheng, N., Li, J. C., Liu, D., Lin, Y., & Du, D. (2019). Single-atom nanozyme based on nanoengineered Fe-N-C catalyst with superior peroxidase-like activity for ultrasensitive bioassays. *Small, 15*(48), 1901485. https://doi.org/10.1002/smll.201901485

Ciui, B., Martin, A., Mishra, R. K., Brunetti, B., Nakagawa, T., Dawkins, T. J., … Wang, J. (2018). Wearable Wireless Tyrosinase Bandage and Microneedle Sensors: Toward Melanoma Screening. *Advanced Healthcare Materials, 7*(7), 1701264. https://doi.org/10.1002/adhm.201701264

Cui, X., Li, W., Ryabchuk, P., Junge, K., & Beller, M. (2018). Bridging homogeneous and heterogeneous catalysis by heterogeneous single-metal-site catalysts. *Nature Catalysis, 1*(6), 385–397. https://doi.org/10.1038/s41929-018-0090-9

Das, R., Nag, S., & Banerjee, P. (2023). Electrochemical Nanosensors for Sensitization of Sweat Metabolites: From Concept Mapping to Personalized Health Monitoring. *Molecules, 28*(3), 1259. https://doi.org/10.3390/molecules28031259

Ding, S., Lyu, Z., Fang, L., Li, T., Zhu, W., Li, S., … Lin, Y. (2021). Single-Atomic Site Catalyst with Heme Enzymes-Like Active Sites for Electrochemical Sensing of Hydrogen Peroxide. *Small, 17*(25), 2100664. https://doi.org/10.1002/smll.202100664

Ding, S., Zhang, N., Lyu, Z., Zhu, W., Chang, Y.-C., Hu, X., … Lin, Y. (2021). Protein-based nanomaterials and nanosystems for biomedical applications: A review. *Materials Today, 43*, 166–184. https://doi.org/10.1016/j.mattod.2020.11.015

Dong, Q., Wang, X., Liu, H., Ryu, H., Zhao, J., Li, B., & Lei, Y. (2019). Heterogeneous Iridium Oxide/Gold Nanocluster for Non-enzymatic Glucose Sensing and pH Probing. *Engineered Science*. https://doi.org/10.30919/es8d512

Eqi, M., Shi, C., Xie, J., Kang, F., Qi, H., Tan, X., … Guo, J. (2022). Synergetic effect of Ni-Au bimetal nanoparticles on urchin-like TiO_2 for hydrogen and arabinose co-production by glucose photoreforming. *Advanced Composites and Hybrid Materials, 6*(1). https://doi.org/10.1007/s42114-022-00580-6

Faham, S., Salimi, A., & Ghavami, R. (2023). Electrochemical-based remote biomarker monitoring: Toward Internet of Wearable Things in telemedicine. *Talanta, 253*, Article 123892. https://doi.org/10.1016/j.talanta.2022.123892

Fan, M., Zhu, S., Zhang, Q., Wang, X., Zhang, L., Chang, Z., & Chong, R. (2023). Sensitive photoelectrochemical sensing of glucose using hematite decorated with NiAl-layered double hydroxides. *Food Chemistry, 405*, Article 134883. https://doi.org/10.1016/j.foodchem.2022.134883

Fu, X., Ding, B., & D'Alessandro, D. (2023). Fabrication strategies for metal-organic framework electrochemical biosensors and their applications. *Coordination Chemistry Reviews, 475*, Article 214814. https://doi.org/10.1016/j.ccr.2022.214814

Gao, F., Liu, C., Zhang, L., Liu, T., Wang, Z., Song, Z., … Xue, N. (2023). Wearable and flexible electrochemical sensors for sweat analysis: A review. *Microsyst Nanoeng, 9*(1), 1. https://doi.org/10.1038/s41378-022-00443-6

Gijare, M., Chaudhari, S., Ekar, S., & Garje, A. (2021). Reduced Graphene Oxide Based Electrochemical Nonenzymatic Human Serum Glucose Sensor. *ES Materials & Manufacturing*. https://doi.org/10.30919/esmm5f486

Gong, L., Zhang, H., Wang, Y., Luo, E., Li, K., Gao, L., … Ge, J. (2020). Bridge bonded oxygen ligands between approximated FeN_4 sites confer catalysts with high ORR performance. *Angewandte Chemie, 132*(33), 14027–14032. https://doi.org/10.1002/anie.202004534

Guan, J., Bai, X., & Tang, T. (2021). Recent progress and prospect of carbon-free single-site catalysts for the hydrogen and oxygen evolution reactions. *Nano Research, 15*(2), 818–837. https://doi.org/10.1007/s12274-021-3680-9

Hamukwaya, S. L., Zhao, Z., Hao, H., Abo-Dief, H. M., Abualnaja, K. M., Alanazi, A. K., … Guo, Z. (2022). Enhanced photocatalytic performance for hydrogen production and carbon dioxide reduction by a mesoporous single-crystal-like TiO_2 composite catalyst. *Advanced Composites and Hybrid Materials*. https://doi.org/10.1007/s42114-022-00545-9

Han, J., & Guan, J. (2022a). A macro library for monatomic catalysts. *Chinese Journal of Catalysis, 44*, 1–3. https://doi.org/10.1016/S1872-2067(22)64153-6

Han, J., & Guan, J. (2022b). Multicomponent transition metal oxides and (oxy) hydroxides for oxygen evolution. *Nano Research, 16*, 1913–1966. https://doi.org/10.1007/s12274-022-4874-7

Ho, D. H., Choi, Y. Y., Jo, S. B., Myoung, J. M., & Cho, J. H. (2021). Sensing with MXenes: Progress and Prospects. *Advanced Materials, 33*(47), e2005846.

Hou, H., Mao, J., Han, Y., Wu, F., Zhang, M., Wang, D., … Li, Y. (2019). Single-atom electrocatalysis: A new approach to in vivo electrochemical biosensing. *Science China Chemistry, 62*(12), 1720–1724. https://doi.org/10.1007/s11426-019-9605-0

Hu, F. X., Hu, T., Chen, S., Wang, D., Rao, Q., Liu, Y., … Li, C. M. (2021). Single-atom cobalt-based electrochemical biomimetic uric acid sensor with wide linear range and ultralow detection limit. *Nano-Micro Letters, 13*(1), 7. https://doi.org/10.1007/s40820-020-00536-9

Huang, L., Chen, J., Gan, L., Wang, J., & Dong, S. (2019). Single-atom nanozymes. *Science. Advances, 5*(5), eaav5490. https://doi.org/10.1126/sciadv.aav5490

Huang, Y., Mu, X., Wang, J., Wang, Y., Xie, J., Ying, R., & Su, E. (2022). The recent development of nanozymes for food quality and safety detection. *Journal of Materials Chemistry B, 10*(9), 1359–1368. https://doi.org/10.1039/D1TB02667D

Huang, Y., Ren, J., & Qu, X. (2019). Nanozymes: Classification, catalytic mechanisms, activity regulation, and applications. *Chemical Reviews, 119*(6), 4357–4412. https://doi.org/10.1021/acs.chemrev.8b00672

Hwang, D.-W., Lee, S., Seo, M., & Chung, T. D. (2018). Recent advances in electrochemical non-enzymatic glucose sensors-a review. *Analytica Chimica Acta, 1033*, 1–34. https://doi.org/10.1016/j.aca.2018.05.051

Iwase, K., Nakanishi, S., Miyayama, M., & Kamiya, K. (2020). Rational Molecular Design of Electrocatalysts Based on Single-Atom Modified Covalent Organic Frameworks for Efficient Oxygen Reduction Reaction. *ACS Applied Energy Materials, 3*(2), 1644–1652. https://doi.org/10.1021/acsaem.9b02141

Ji, S., Chen, Y., Wang, X., Zhang, Z., Wang, D., & Li, Y. (2020). Chemical Synthesis of Single Atomic Site Catalysts. *Chem Rev, 120*(21), 11900–11955. https://doi.org/10.1021/acs.chemrev.9b00818

Jiang, D., Lian, M., Xu, M., Sun, Q., Xu, B. B., Thabet, H. K., … Guo, Z. (2023). Advances in triboelectric nanogenerator technology-applications in self-powered sensors, Internet of things, biomedicine, and blue energy. *Advanced Composites and Hybrid Materials, 6*(2). https://doi.org/10.1007/s42114-023-00632-5

Jiao, L., Xu, W., Yan, H., Wu, Y., Liu, C., Du, D., … Zhu, C. (2019). Fe-N-C Single-Atom Nanozymes for the Intracellular Hydrogen Peroxide Detection. *Analytical Chemistry, 91*(18), 11994–11999. https://doi.org/10.1021/acs.analchem.9b02901

Jiao, L., Yan, H., Wu, Y., Gu, W., Zhu, C., Du, D., & Lin, Y. (2020). When nanozymes meet single-atom catalysis. *Angewandte Chemie, 132*(7), 2585–2596. https://doi.org/10.1002/anie.201905645

Justice Babu, K., Sheet, S., Lee, Y. S., & Gnana Kumar, G. (2018). Three-dimensional dendrite Cu-Co/reduced graphene oxide architectures on a disposable pencil graphite electrode as an electrochemical sensor for nonenzymatic glucose detection. *ACS Sustainable Chemistry & Engineering, 6*(2), 1909–1918. https://doi.org/10.1021/acssuschemeng.7b03314

Kalambate, P. K., Rao, Z., Wu, J., Shen, Y., Boddula, R., & Huang, Y. (2020). Electrochemical (bio) sensors go green. *Biosensors and Bioelectronics, 163*, Article 112270. https://doi.org/10.1016/j.bios.2020.112270

Kalantar-zadeh, K., Ou, J. Z., Daeneke, T., Strano, M. S., Pumera, M., & Gras, S. L. (2015). Two-dimensional transition metal dichalcogenides in biosystems. *Advanced Functional Materials, 25*(32), 5086–5099. https://doi.org/10.1002/adfm.201500891

Kirchner, E.-M., & Hirsch, T. (2020). Recent developments in carbon-based two-dimensional materials: Synthesis and modification aspects for electrochemical sensors. *Microchimica Acta, 187*(8), 441. https://doi.org/10.1007/s00604-020-04415-3

Kornienko, N., Ly, K. H., Robinson, W. E., Heidary, N., Zhang, J. Z., & Reisner, E. (2019). Advancing techniques for investigating the enzyme-electrode interface. *Accounts of Chemical Research, 52*(5), 1439–1448. https://doi.org/10.1021/acs.accounts.9b00087

Kurup, C. P., & Ahmed, M. U. (2023). Nanozymes towards Personalized Diagnostics: A Recent Progress in Biosensing. *Biosensors, 13*(4), 461. https://www.mdpi.com/2079-6374/13/4/461.

Lee, K.-T., Liu, D.-M., & Lu, S.-Y. (2016). $SnFe_2O_4$ Nanocrystals as Highly Efficient Catalysts for Hydrogen-Peroxide Sensing. *Chemistry - A European Journal, 22*(31), 10877–10883. https://doi.org/10.1002/chem.201504881

Lei, Y., Butler, D., Lucking, M. C., Zhang, F., Xia, T., Fujisawa, K., … Terrones, H. (2020). Single-atom doping of MoS_2 with manganese enables ultrasensitive detection of dopamine: Experimental and computational approach. *Science Advances, 6*(32), eabcc4250. https://doi.org/10.1126/sciadv.abc4250

Lei, Y., Zhang, Y., Yuan, L., & Li, J. (2022). Biochar-supported Cu nanocluster as an electrochemical ultrasensitive interface for ractopamine sensing. *Food Chemistry: X, 15*, Article 100404. https://doi.org/10.1016/j.fochx.2022.100404

Li, J., Xie, J., Gao, L., & Li, C. M. (2015). Au Nanoparticles-3D Graphene Hydrogel Nanocomposite To Boost Synergistically in Situ Detection Sensitivity toward Cell-Released Nitric Oxide. *ACS Applied Materials and Interfaces, 7*(4), 2726–2734. https://doi.org/10.1021/am5077777

Li, R., Qi, H., Ma, Y., Deng, Y., Liu, S., Jie, Y., … Wheatley, L. (2020). A flexible and physically transient electrochemical sensor for real-time wireless nitric oxide monitoring. *Nature Communications, 11*(1), 3207. https://doi.org/10.1038/s41467-020-17008-8

Li, X., Rong, H., Zhang, J., Wang, D., & Li, Y. (2020). Modulating the local coordination environment of single-atom catalysts for enhanced catalytic performance. *Nano Research, 13*(7), 1842–1855. https://doi.org/10.1007/s12274-020-2755-3

Li, Y., Wang, H., Xie, L., Liang, Y., Hong, G., & Dai, H. (2011). MoS_2 nanoparticles grown on graphene: An advanced catalyst for the hydrogen evolution reaction. *Journal of the American Chemical Society, 133*(19), 7296–7299. https://doi.org/10.1021/ja201269b

Li, Z., Zhang, X., Huang, X., Zou, X., Shi, J., Xu, Y., … Zhai, X. (2021). Hypha-templated synthesis of carbon/ZnO microfiber for dopamine sensing in pork. *Food Chemistry, 335*, Article 127646. https://doi.org/10.1016/j.foodchem.2020.127646

Liang, Y., Zhao, P., Zheng, J., Chen, Y., Liu, Y., Zheng, J., … Hou, C. (2022). Fe Single-Atom Electrochemical Sensors for H_2O_2 Produced by Living Cells. *ACS Applied Nano Materials, 5*(8), 11852–11863. https://doi.org/10.1021/acsanm.2c02853

Liu, H., Zhang, L., Yan, M., & Yu, J. (2017). Carbon nanostructures in biology and medicine. *Journal of Materials Chemistry B, 5*(32), 6437–6450. https://doi.org/10.1039/c7tb00891k

Liu, X., Huang, L., & Qian, K. (2021). Nanomaterial-Based Electrochemical Sensors: Mechanism, Preparation, and Application in Biomedicine. *Advanced NanoBiomed Research, 1*(6), 2000104. https://doi.org/10.1002/elan.202200228

Long, B., Zhao, Y., Cao, P., Wei, W., Mo, Y., Liu, J., … Zeng, M.-H. (2022). Single-Atom Pt Boosting Electrochemical Nonenzymatic Glucose Sensing on Ni $(OH)_2$/N-Doped Graphene. *Analytical Chemistry, 94*(4), 1919–1924. https://doi.org/10.1021/acs.analchem.1c04912

Lyu, Z., Ding, S., Tieu, P., Fang, L., Li, X., Li, T., … Lin, Y. (2022). Single-Atomic Site Catalyst Enhanced Lateral Flow Immunoassay for Point-of-Care Detection of Herbicide. *Research, 2022*, 9823290. https://doi.org/10.34133/2022/9823290

Lyu, Z., Ding, S., Zhang, N., Zhou, Y., Cheng, N., Wang, M., … Lin, Y. (2020). Single-Atom Nanozymes Linked Immunosorbent Assay for Sensitive Detection of Abeta 1–40: A Biomarker of Alzheimer's Disease. *Research, 2020*, 4724505. https://doi.org/10.34133/2020/4724505

Motshakeri, M., Phillips, A. R. J., & Kilmartin, P. A. (2019). Application of cyclic voltammetry to analyse uric acid and reducing agents in commercial milks. *Food Chemistry, 293*, 23–31. https://doi.org/10.1016/j.foodchem.2019.04.071

Niu, X., Shi, Q., Zhu, W., Liu, D., Tian, H., Fu, S., … Du, D. (2019). Unprecedented peroxidase-mimicking activity of single-atom nanozyme with atomically dispersed Fe-N_x moieties hosted by MOF derived porous carbon. *Biosensors and Bioelectronics, 142*, Article 111495. https://doi.org/10.1016/j.bios.2019.111495

Niu, X. H., Shi, L. B., Zhao, H. L., & Lan, M. B. (2016). Advanced strategies for improving the analytical performance of Pt-based nonenzymatic electrochemical glucose sensors: A minireview. *Analytical Methods, 8*(8), 1755–1764. https://doi.org/10.1039/C5AY03181H

Pan, C., Wu, F., Mao, J., Wu, W., Zhao, G., Ji, W., … Mao, L. (2022). Highly Stable and Selective Sensing of Hydrogen Sulfide in Living Mouse Brain with NiN_4 Single-Atom Catalyst-Based Galvanic Redox Potentiometry. *Journal of the American Chemical Society, 144*(32), 14678–14686. https://doi.org/10.1021/jacs.2c04695

Pan, X., Kaminga, A. C., Wen, S. W., Wu, X., Acheampong, K., & Liu, A. (2019). Dopamine and dopamine receptors in Alzheimer's disease: A systematic review and network meta-analysis. *Frontiers in Aging Neuroscience, 11*, 175. https://doi.org/10.3389/fnagi.2019.00175

Pathiraja, G., Bonner, C. D. J., & Obare, S. O. (2023). Recent Advances of Enzyme-Free Electrochemical Sensors for Flexible Electronics in the Detection of Organophosphorus Compounds: A Review. *Sensors, 23*(3), 1226. https://doi.org/10.3390/s23031226

Ping, D., Yi, F., Zhang, G., Wu, S., Fang, S., Hu, K., … Guo, Z. (2023). NH_4Cl-assisted preparation of single Ni sites anchored carbon nanosheet catalysts for highly efficient carbon dioxide electroreduction. *Journal of Materials Science & Technology, 142*, 1–9. https://doi.org/10.1016/j.jmst.2022.10.006

Qiu, H., Pu, F., Ran, X., Liu, C., Ren, J., & Qu, X. (2018). Nanozyme as artificial receptor with multiple readouts for pattern recognition. *Analytical Chemistry, 90*(20), 11775–11779. https://doi.org/10.1021/acs.analchem.8b03807

Rocha, J. F., Hasimoto, L. H., & Santhiago, M. (2023). Recent progress and future perspectives of polydopamine nanofilms toward functional electrochemical sensors. *Analytical and Bioanalytical Chemistry, 1–18*. https://doi.org/10.1007/s00216-023-04522-z

Sarma, A. K., Vatsyayan, P., Goswami, P., & Minteer, S. D. (2009). Recent advances in material science for developing enzyme electrodes. *Biosensors and Bioelectronics, 24*(8), 2313–2322. https://doi.org/10.1016/j.bios.2008.09.026

Shen, C., Liu, S., Li, X., & Yang, M. (2019). Electrochemical detection of circulating tumor cells based on DNA generated electrochemical current and rolling circle amplification. *Analytical Chemistry, 91*(18), 11614–11619. https://doi.org/10.1021/acs.analchem.9b01897

Shen, Y., Yang, W., Hu, F., Zheng, X., Zheng, Y., Liu, H., … Chen, K. (2022). Ultrasensitive wearable strain sensor for promising application in cardiac rehabilitation. *Advanced Composites and Hybrid Materials, 6*(1). https://doi.org/10.1007/s42114-022-00610-3

Shi, Z., Li, X., Yu, L., Wu, X., Wu, J., Guo, C., & Li, C. M. (2019). Atomic matching catalysis to realize a highly selective and sensitive biomimetic uric acid sensor. *Biosensors and Bioelectronics, 141*, Article 111421. https://doi.org/10.1016/j.bios.2019.111421

Shukla, R. P., Aroosh, M., Matzafi, A., & Ben-Yoav, H. (2021). Partially functional electrode modifications for rapid detection of dopamine in urine. *Advanced Functional Materials, 31*(17), 2004146. https://doi.org/10.1002/adfm.202004146

Song, Y., He, T., Zhang, Y., Yin, C., Chen, Y., Liu, Q., … Chen, S. (2022). Cobalt single atom sites in carbon aerogels for ultrasensitive enzyme-free electrochemical detection of glucose. *Journal of Electroanalytical Chemistry, 906*, Article 116024. https://doi.org/10.1016/j.jelechem.2022.116024

Sun, H., Chao, J., Zuo, X., Su, S., Liu, X., Yuwen, L., … Wang, L. (2014). Gold nanoparticle-decorated MoS_2 nanosheets for simultaneous detection of ascorbic acid,

dopamine and uric acid. *RSC Advances, 4*(52), 27625–27629. https://doi.org/10.1039/c4ra04046e

Sun, X., Chen, C., Xiong, C., Zhang, C., Zheng, X., Wang, J., … Wu, Y. (2022). Surface modification of MoS_2 nanosheets by single Ni atom for ultrasensitive dopamine detection. *Nano Research, 16*, 917–924. https://doi.org/10.1007/s12274-022-4802-8

Sun, X., Wei, P., Gu, S., Zhang, J., Jiang, Z., Wan, J., … Fang, C. (2020). Atomic-level Fe-N-C coupled with Fe_3C-Fe nanocomposites in carbon matrixes as high-efficiency bifunctional oxygen catalysts. *Small, 16*(6), 1906057. https://doi.org/10.1002/adma.201806312

Sun, Z., Zhang, Y., Guo, S., Shi, J., Shi, C., Qu, K., … Guo, Z. (2022). Confining FeNi nanoparticles in biomass-derived carbon for effectively photo-Fenton catalytic reaction for polluted water treatment. *Advanced Composites and Hybrid Materials, 5*(2), 1566–1581. https://doi.org/10.1007/s42114-022-00477-4

Wang, B., Leng, J., Wang, X., & Zhao, W. (2022). Reversible AIE-active fluorescent probe with a large emission peak shift for ratiometric detection of food freshness indicator H_2S. *Food Chemistry, 386*, Article 132768. https://doi.org/10.1016/j.foodchem.2022.132768

Wang, L., Pan, L., Han, X., Ha, M. N., Li, K., Yu, H., … Wang, H. (2022). A portable ascorbic acid in sweat analysis system based on highly crystalline conductive nickel-based metal-organic framework (Ni-MOF). *Journal of Colloid and Interface Science, 616*, 326–337. https://doi.org/10.1016/j.jcis.2022.02.058

Wang, S., Liu, Y., Zhu, A., & Tian, Y. (2023). In Vivo Electrochemical Biosensors: Recent Advances in Molecular Design, Electrode Materials, and Electrochemical Devices. *Analytical Chemistry, 95*(1), 388–406. https://doi.org/10.1021/acs.analchem.2c04541

Wang, X., Li, Q., Xu, J., Wu, S., Xiao, T., Hao, J., … Mao, L. (2016). Rational Design of Bioelectrochemically Multifunctional Film with Oxidase, Ferrocene, and Graphene Oxide for Development of in Vivo Electrochemical Biosensors. *Analytical Chemistry, 88*(11), 5885–5891. https://doi.org/10.1021/acs.analchem.6b00720

Wang, Y., Hu, F.-L., Mi, Y., Yan, C., & Zhao, S. (2021). Single-metal-atom catalysts: An emerging platform for electrocatalytic oxygen reduction. *Chemical Engineering Journal, 406*, Article 127135. https://doi.org/10.1016/j.cej.2020.127135

Wang, Y., Li, Y., Tang, L., Lu, J., & Li, J. (2009). Application of graphene-modified electrode for selective detection of dopamine. *Electrochemistry Communications, 11*(4), 889–892. https://doi.org/10.1016/j.elecom.2009.02.013

Wang, Y., Qi, K., Yu, S., Jia, G., Cheng, Z., Zheng, L., … Zhao, J. (2019). Revealing the intrinsic peroxidase-like catalytic mechanism of heterogeneous single-atom Co-MoS_2. *Nano-Micro Letters, 11*(102), 102. https://doi.org/10.1007/s40820-019-0324-7

Wei, H., Li, A., Kong, D., Li, Z., Cui, D., Li, T., … Guo, Z. (2021). Polypyrrole/reduced graphene aerogel film for wearable piezoresisitic sensors with high sensing performances. *Advanced Composites and Hybrid Materials, 4*(1), 86–95. https://doi.org/10.1007/s42114-020-00201-0

Wei, X., Song, S., Song, W., Xu, W., Jiao, L., Luo, X., … Gu, W. (2021). Fe_3C-assisted single atomic Fe sites for sensitive electrochemical biosensing. *Analytical Chemistry, 93*(12), 5334–5342. https://doi.org/10.1021/acs.analchem.1c00635

Winterbourn, C. C. (2018). Biological production, detection, and fate of hydrogen peroxide. *Antioxidants & Redox Signaling, 29*(6), 541–551. https://doi.org/10.1089/ars.2017.7425

Wu, F., Pan, C., He, C.-T., Han, Y., Ma, W., Wei, H., … Yu, P. (2020). Single-atom Co-N_4 electrocatalyst enabling four-electron oxygen reduction with enhanced hydrogen peroxide tolerance for selective sensing. *Journal of the American Chemical Society, 142*(39), 16861–16867. https://doi.org/10.1021/jacs.0c07790

Wu, F., Yu, P., & Mao, L. (2017). Self-powered electrochemical systems as neurochemical sensors: Toward self-triggered in vivo analysis of brain chemistry. *Chemical Society Reviews, 46*(10), 2692–2704. https://doi.org/10.1039/C7CS00148G

Wu, M., Jing, T., Tian, J., Qi, H., Shi, D., Zhao, C., … Guo, Z. (2022). Synergistic effect of silver plasmon resonance and p-n heterojunction enhanced photoelectrochemical aptasensing platform for detecting chloramphenicol. *Advanced Composites and Hybrid Materials, 5*(3), 2247–2259. https://doi.org/10.1007/s42114-021-00377-z

Xiang, H., Feng, W., & Chen, Y. (2020). Single-atom catalysts in catalytic biomedicine. *Advanced Materials, 32*(8), 1905994. https://doi.org/10.1002/adma.201905994

Xiao, L., Wang, Z., & Guan, J. (2022). 2D MOFs and their derivatives for electrocatalytic applications: Recent advances and new challenges. *Coordination Chemistry Reviews, 472*, Article 214777. https://doi.org/10.1016/j.ccr.2022.214777

Xiao, T., Wu, F., Hao, J., Zhang, M., Yu, P., & Mao, L. (2017). In vivo analysis with electrochemical sensors and biosensors. *Analytical Chemistry, 89*(1), 300–313. https://doi.org/10.1021/acs.analchem.6b04308

Xie, L., Wang, R., Fan, C., Tu, Y., Liu, G., & Pu, S. (2023). Mitochondria-targeted fluorescent probe with long wavelength emission for detecting H_2S and its application in foodstuff, water and living cells. *Food Chemistry, 410*, Article 135411. https://doi.org/10.1016/j.foodchem.2023.135411

Xie, X., Wang, D. P., Guo, C., Liu, Y., Rao, Q., Lou, F., … Yang, H. B. (2021). Single-atom ruthenium biomimetic enzyme for simultaneous electrochemical detection of dopamine and uric acid. *Analytical Chemistry, 93*(11), 4916–4923. https://doi.org/10.1021/acs.analchem.0c05191

Xing, L., Zhang, W., Fu, L., Lorenzo, J. M., & Hao, Y. (2022). Fabrication and application of electrochemical sensor for analyzing hydrogen peroxide in food system and biological samples. *Food Chemistry, 385*, Article 132555. https://doi.org/10.1016/j.foodchem.2022.132555

Xu, B., Wang, H., Wang, W., Gao, L., Li, S., Pan, X., … Liu, H. (2019). A Single-Atom Nanozyme for Wound Disinfection Applications. *Angewandte Chemie International Edition, 58*(15), 4911–4916. https://doi.org/10.1002/anie.201813994

Yang, J., Hu, Y., & Li, Y. (2019). Molecularly imprinted polymer-decorated signal on-off ratiometric electrochemical sensor for selective and robust dopamine detection. *Biosensors and Bioelectronics, 135*, 224–230. https://doi.org/10.1016/j.bios.2019.03.054

Yang, T., Yu, R., Yan, Y., Zeng, H., Luo, S., Liu, N., … Li, W. (2018). A review of ratiometric electrochemical sensors: From design schemes to future prospects. *Sensors and Actuators B: Chemical, 274*, 501–516. https://doi.org/10.1016/j.snb.2018.07.138

Yang, X., Gan, H., Tian, Y., Peng, L., Xu, N., Chen, J., … Liu, F. (2017). Fast identification of the conduction-type of nanomaterials by field emission technique. *Scientific Reports, 7*(1), 13057. https://doi.org/10.1038/s41598-017-12741-5

Ye, C., Zhang, N., Wang, D., & Li, Y. (2020). Single atomic site catalysts: Synthesis, characterization, and applications. *Chemical Communications, 56*(56), 7687–7697. https://doi.org/10.1039/d0cc03221b

Yin, F., Wang, F., Fan, C., Zuo, X., & Li, Q. (2021). Biosensors based on DNA logic gates. *View, 2*(2), 20200038. https://doi.org/10.1016/j.aca.2017.08.001

Yu, P., Wei, H., Zhong, P., Xue, Y., Wu, F., Liu, Y., … Mao, L. (2020). Single-Carbon-Fiber-Powered Microsensor for In Vivo Neurochemical Sensing with High Neuronal Compatibility. *Angewandte Chemie International Edition, 59*(50), 22652–22658. https://doi.org/10.1002/anie.202010195

Zhang, H., Zhang, T., Jia, Y., Zhang, J., & Han, Y. (2021). Single-Atom Ruthenium Catalytic Sites for Acetylene Hydrochlorination. *The Journal of Physical Chemistry Letters, 12*(30), 7350–7356. https://doi.org/10.1021/acs.jpclett.1c01779

Zhang, R., Gao, S. J., Zhu, C. Y., Sun, Y., Liu, X. L., Zhao, M. M., & Wang, C. H. (2019). Characterization of a novel alkaline Arxula adeninivorans urate oxidase expressed in Escherichia coli and its application in reducing uric acid content of food. *Food Chemistry, 293*, 254–262. https://doi.org/10.1016/j.foodchem.2019.04.112

Zhou, M., Jiang, Y., Wang, G., Wu, W., Chen, W., Yu, P., … Mao, L. (2020). Single-atom Ni-N_4 provides a robust cellular NO sensor. *Nature Communications, 11*(1), 3188. https://doi.org/10.1038/s41467-020-17018-6

Zivanovic, J., Kouroussis, E., Kohl, J. B., Adhikari, B., Bursac, B., Schott-Roux, S., … Jung, Y. (2019). Selective persulfide detection reveals evolutionarily conserved antiaging effects of S-sulfhydration. *Cell Metabolism, 30*(6), 1152–1170. https://doi.org/10.1016/j.cmet.2019.10.007