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Advancing healthcare applications: wearable sensors utilizing metal–organic frameworks

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Recent advancements in wearable sensor technologies have sparked a revolution in healthcare, enabling real-time monitoring and diagnostics. Metal–organic frameworks (MOFs) have emerged as a promising class of materials in developing wearable sensors due to their unique properties, including high surface area, tunable porosity, and exceptional adsorption capacity. This review overviews the state-of-the-art MOF-based wearable sensors for healthcare applications. It explores their fabrication methods, sensing mechanisms, and applications in various medical fields, such as disease detection, physiological monitoring, and drug delivery. Additionally, we discuss the challenges and prospects of integrating MOFs into wearable devices to enhance their performance and utility in the healthcare domain.

Introduction

Wearable sensors have witnessed tremendous growth and popularity in healthcare due to their potential to revolutionize patient monitoring and personalized medicine.^{1–3} Metal–organic frameworks (MOFs) are hybrid materials with intriguing

properties that make them suitable for sensor applications.^{4–8} This review focuses on recent developments in MOF-based wearable sensors for healthcare, aiming to explore their potential to address critical medical challenges.

Metal–organic frameworks (MOFs) have gained significant attention in wearable sensor fabrication due to their exceptional properties and versatile applications.^{9–12} MOFs are hybrid materials of metal ions coordinated with organic linkers, resulting in a three-dimensional porous structure. This unique architecture gives MOFs an incredibly high surface area, which can be precisely tailored by varying the metal ions and organic linkers used in their synthesis.^{13–16} By tuning the parameters, two-dimensional metal–organic frameworks have recently attracted interest in various fields

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with a specific focus on their potential applications in the energy and healthcare fields.

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including wearable devices. The favorable properties of these two-dimensional materials such as large surface area and tunable properties have intrigued the researchers in the field of wearable sensors.^{17–20}

One of the primary reasons why MOFs appeal to wearable sensors is their tunable porosity, allowing them to adsorb and desorb target molecules selectively. This property makes MOFs well-suited for sensing various analytes, including gases, liquids, and biomolecules.^{21–24} MOFs offer high sensitivity and selectivity, making them excellent candidates for detecting even trace amounts of specific substances.

In the context of wearable sensors, MOFs provide several advantages. First and foremost, their integration into wearable substrates is relatively straightforward. MOFs can be synthesized on flexible materials or coated onto wearable devices, allowing lightweight and unobtrusive sensors to be developed.^{25–28} This feature is crucial in healthcare applications, where patients prefer non-invasive and comfortable monitoring devices.

The fabrication methods for MOF-based wearable sensors vary depending on the specific application and desired properties. Standard synthesis techniques include solvothermal, hydrothermal, and microwave-assisted methods.^{29–31} These methods enable the controlled growth of MOFs, ensuring uniformity and stability in the final sensor device.

Furthermore, researchers have explored different approaches to functionalize MOFs for specific sensing applications. By modifying the surface chemistry of MOFs or introducing functional groups, sensor selectivity can be fine-tuned to target particular analytes or biomarkers. For instance, MOFs can be engineered to selectively capture glucose molecules in diabetes monitoring or detect volatile organic compounds indicative of certain diseases.^{32–36} The exceptional porosity of MOFs also allows for efficient drug loading and release, making them promising candidates for wearable drug delivery systems.^{37–39} MOFs can serve as drug carriers, delivering therapeutics in a controlled manner to the wearer, thus improving treatment efficacy and reducing side effects.

Despite the numerous advantages, there are some challenges associated with MOF-based wearable sensor fabrication. One primary concern is the stability of MOFs under real-world conditions. MOFs can be sensitive to moisture, temperature fluctuations, and chemical environments, affecting long-term performance. Researchers are actively working on strategies to improve MOF stability and develop protective coatings to enhance durability. Another challenge lies in ensuring the biocompatibility of MOFs when used for medical applications. While many MOFs are safe, their potential toxicity or immune response must be thoroughly investigated before deploying them in wearable healthcare devices.^{40–42}

Moreover, MOFs have emerged as a promising class of materials for wearable sensor fabrication, offering unique properties such as tunable porosity, high surface area, and exceptional sensing capabilities. Their integration into wearable substrates allows for the development of unobtrusive and sensitive sensors for various healthcare applications, including disease detection, physiological monitoring, and drug delivery.^{43–47} Despite some challenges, ongoing research in MOFs holds great promise for revolutionizing healthcare by enabling personalized, real-time monitoring and diagnostics with the help of wearable sensors.

MOFs in wearable sensor fabrication

Metal-organic frameworks (MOFs) have gained significant attention recently due to their unique structural properties and vast applications, including wearable sensors. MOFs are a class of highly ordered, porous materials constructed from metal ions (or clusters) and organic ligands. Their tunable structures and surface functionalities make them ideal candidates for sensing various analytes in wearable devices.^{48–52} This article delves into the synthesis and fabrication methods of MOFs for wearable sensors, focusing on solvothermal, hydrothermal, and microwave-assisted techniques and strategies to integrate MOFs onto flexible and wearable substrates.



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Synthesis methods of MOFs for wearable sensors

Solvothermal method

The solvothermal method involves the reaction of metal salts and organic ligands in a solvent under elevated temperature and pressure conditions. This process allows for precise MOF size, morphology, and crystallinity control. A schematic illustration of the solvothermal method is shown in Fig. 1a. Solvothermal synthesis provides a high yield of MOFs with well-defined structures, making it a popular choice for wearable sensor applications. The reaction parameters such as temperature, pressure, reaction time, and choice of solvent can influence the final properties of the MOF.^{53–59}

Hydrothermal method

Hydrothermal synthesis is similar to the solvothermal method but operates at lower temperatures and pressures. The process occurs in an aqueous environment, where the metal salts and ligands react under controlled hydrothermal conditions. This technique is advantageous for producing MOFs on a larger scale and can be easily scaled up for the industrial production of wearable sensors. An illustration of the hydrothermal method is shown in Fig. 1b. Hydrothermal synthesis also allows for incorporating various functional groups into the MOF structure, enhancing the sensor's selectivity and sensitivity.^{60–65}

Microwave-assisted method

Microwave-assisted synthesis is a relatively newer technique that offers rapid and efficient MOF formation. It involves exposing the reaction mixture to microwave irradiation, significantly accelerating the chemical reaction and reducing the synthesis time. This method provides better nucleation and crystal growth control, resulting in highly crystalline MOFs with improved sensor performance. A schematic representation of microwave-assisted synthesis is shown in Fig. 1d. Microwave-assisted synthesis is particularly suitable for the on-demand fabrication of wearable sensors, as it reduces production time and energy consumption.^{66–70}

Sonochemical method

The sonochemical method also called ultrasound-assisted synthesis has advantages over conventional methods. The synthesis relies on the ultrasound-induced cavitation to induce chemical reactions. The process involves quick dispersion of the solutes and increases the reaction speed improving the efficiency and shortening the synthesis time. The method produces uniform crystals with size comparatively smaller than the conventional methods like solvothermal and hydrothermal. An illustration representing the process of sonochemical-based synthesis of MOFs is shown in Fig. 1c.^{71–77}

Vapor phase synthesis method

The vapor phase synthesis method involves the formation of metal–organic frameworks through the use of less solvents or solventless synthesis. It is more suitable for developing thin films and more favored in industrial device fabrication. The process involves the deposition of MOFs through vaporized metal precursors and linkers on the substrate. The growth of the films depends on the substrate orientation. An illustration of MOF synthesis through the vapor phase method is shown in Fig. 1e. The process is favourable for preparing thin films for wearable devices at an industrial level. Some types of the vapor phase synthesis include chemical vapor deposition, atomic layer deposition and pulsed laser ablation (Table 1).^{78–83}

Integration of MOFs onto flexible and wearable substrates

Inkjet printing

Inkjet printing is a popular technique for integrating MOFs onto flexible substrates.^{84–86} The MOF ink, containing dispersed MOF particles in a solvent, is ejected through a nozzle and deposited onto the substrate in a controlled pattern. The inkjet printing process is shown in Fig. 2b. This method allows for precise deposition, creating customized sensor arrays with different MOFs for selective sensing of multiple analytes. Inkjet printing is cost-effective, scalable, and compatible with many substrates, making it ideal for wearable sensor fabrication.^{87–91}

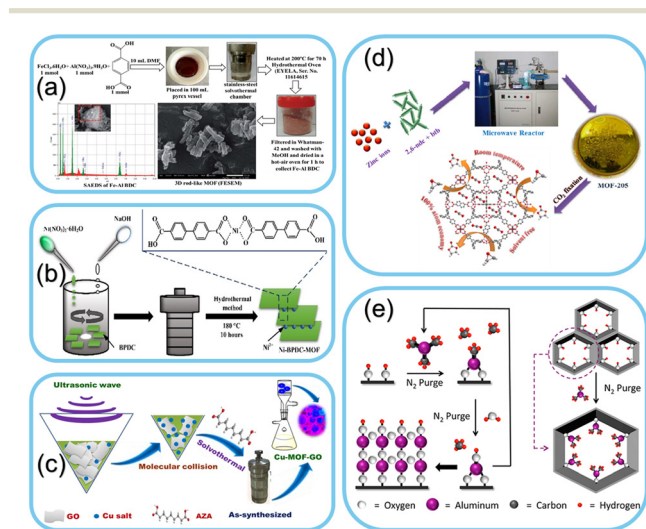


Fig. 1 Common methods involved in the synthesis of MOFs: a) Solvothermal method. Reproduced from ref. 57 with permission from The Royal Society of Chemistry, copyright 2022. b) Hydrothermal method. Reproduced from ref. 65 with permission from MDPI, copyright 2022. c) Sonochemical method. Reproduced from ref. 72 with permission from American Chemical Society, copyright 2022. d) Microwave-assisted method. Reproduced from ref. 67 with permission from American Chemical Society, copyright 2016. e) Vapor phase synthesis method. Reproduced from ref. 78 with permission from American Chemical Society, copyright 2013.



Table 1 Advantages and disadvantages of synthesis methods of MOFs

Synthesis method	Advantages	Disadvantages
Solvothermal method	Controlled nucleation growth High crystallinity Wide temperature range	Long reaction time Large amounts of solvent are required
Hydrothermal method	Low cost Large-scale preparation Controlled nucleation and growth	Long reaction time High energy consumption
Microwave-assisted method	Short reaction time Simple and energy efficient High purity	Reaction solvent requirements are limited Isolation of single crystals is difficult
Sonochemical method	Small and uniform particles Short reaction process Homogeneous particle size and morphology	Ultrasound waves hinder formation of large crystals
Vapor phase synthesis method	Use less solvents Large-scale synthesis	Substrate dependent nucleation and growth Suitable for thin films

Drop-casting

Drop-casting is a straightforward method for MOF integration on wearable substrates. In this approach, a solution containing MOF particles is directly dropped or cast onto the substrate and allowed to dry. The deposited MOF layer adheres to the substrate surface, forming a thin film that can be used as a sensing element. An illustration of the drop-casting process is shown in Fig. 2a. Drop-casting is suitable for proof-of-concept experiments and rapid prototyping of wearable sensors due to its ease of use and minimal equipment requirements.^{92–97}

Electrospinning

Electrospinning is a versatile technique for integrating MOFs into wearable sensor platforms. It involves the electrostatic deposition of MOF nanofibers onto flexible substrates. The resulting fibrous structure enhances the active surface area

of the sensor, leading to improved sensitivity and response times. Electrospinning also allows for combining MOFs with other nano-materials, such as carbon nanotubes or graphene, further enhancing sensor performance. The process of electrospinning is shown in Fig. 2c.^{98–103}

Layer-by-layer assembly

Layer-by-layer assembly involves the sequential deposition of MOF layers and other functional materials onto the substrate. This approach enables precise control over the MOF thickness and the incorporation of additional functionalities, such as polymers or enzymes, for targeted sensing applications. An illustration of layer-by-layer assembly is shown in Fig. 2d. Layer-by-layer assembly can be performed using various techniques, including dip-coating, spin-coating, or spray-coating, offering flexibility in sensor design (Table 2).^{104–110}

Sensing mechanisms

The evolution of wearable technology has revolutionized our lives, making it possible to monitor our health, environment, and surroundings with unprecedented ease and precision. One of the key advancements in this domain is the utilization of metal–organic frameworks (MOFs) as sensing materials in wearable devices. MOFs are highly porous materials composed of metal ions or clusters coordinated with organic ligands. Their unique structural properties make them ideal candidates for diverse sensing applications, including chemical, physical, and biological sensing.^{111–115} In this article, we delve into the sensing mechanisms employed by MOF-based wearable sensors, highlighting specific examples of their utilization as gas sensors, biosensors, and pH sensors.

Chemical sensing mechanisms

Gas sensors

MOFs possess a high surface area and tunable pore sizes, providing an exceptional gas adsorption and detection

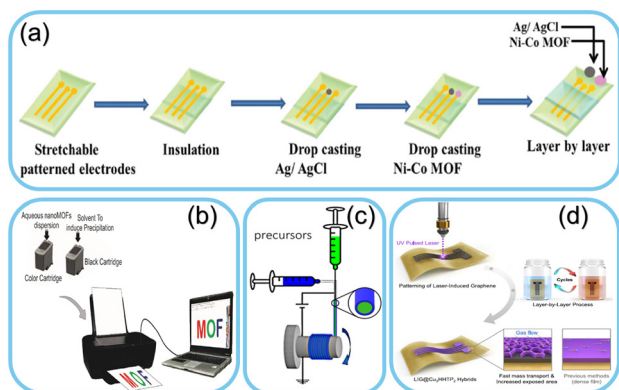


Fig. 2 Schematics of different fabrication technologies involved in wearable sensors. a) Drop casting method. Reproduced from ref. 97 with permission from The Royal Society of Chemistry, copyright, 2022. b) Inkjet printing. Reproduced from ref. 89 with permission from American Chemical Society, copyright 2015. c) Electrospinning. Reproduced from ref. 103 with permission from American Chemical Society, copyright 2021. d) Layer by layer assembly. Reproduced from ref. 110 with permission from Springer Nature, copyright 2023.



Table 2 Comparison of different fabrication techniques involved in wearable sensors

Fabrication method	Advantages	Disadvantages
Inkjet printing	Simple and fast fabrication process	Customized ink jet printers are required
Drop-casting	Allows mass production Simple and low cost No wastage of materials	Nozzle clogging Limitations in large area coverage Poor uniformity Film thickness is difficult to control
Electrospinning	Simple, scalable and cost-effective Fabricates fiber diameters from a few nm to several microns	Toxic solvents Jet instability
Layer-by-layer assembly	Good uniformity Control of layer thickness Large area coverage	Wastage of materials Limits in adhesion to the substrate

platform.^{116–119} For instance, a MOF composed of zinc ions and 2-methylimidazole ligands has been employed to detect volatile organic compounds (VOCs) like benzene, toluene, and xylene. These VOCs are prevalent indoor air pollutants that can cause health issues upon prolonged exposure.^{120–124} Ali *et al.* reported the fabrication of a MOF-polymer mixed flexible membrane for detecting hydrogen sulfide, as shown in Fig. 3a. The prepared MOF-5 has a higher surface area of 621 m² g⁻¹ and 643 m² g⁻¹ and a larger pore size with the number density of MOF-5 being 2.46×10^{28} atoms per m³ which enhanced the energy transport. The presence of MOF-5 in the membrane matrix improves the transportation of H₂S acidic protons across the membrane and throughout the open porosity of the MOF structure. The developed gas sensor showed high sensitivity, low power consumption and flexibility at room temperature.¹²⁵ Metal-organic frameworks have been reported as sensor materials for gas sensors under varying humidity. In another study, five types of MOF-based sensors were tested for nitrogen gas, and the fabricated

sensor is shown in Fig. 3b.¹²⁶ The adsorption of specific gas molecules onto the MOF surface alters its electrical conductivity, leading to a measurable change in resistance. Another study reported developing dual-function metal-organic framework-based wearable fibres for NO₂ sensors. The developed sensor showed an ultralow detection limit due to the presence of a gas sensitive MOF and high specific capacitance demonstrating its potential application for wearable devices.¹²⁷ By integrating this MOF into a wearable sensor, individuals can now monitor their indoor air quality in real time, allowing timely intervention and improved health outcomes.

pH sensors

MOFs can be engineered to exhibit pH-responsive behaviour due to protonatable functional groups in their organic linkers.^{128–130} A prime example is the utilization of UiO-66, a zirconium-based MOF, which undergoes structural changes in response to varying pH levels. These structural changes significantly alter the MOF's optical properties, making it an effective pH sensor.^{131–133} When incorporated into wearable devices, such pH-sensitive MOFs can continuously monitor physiological parameters like sweat pH, offering valuable insights into an individual's health status and hydration levels.

Physical sensing mechanisms

Strain and pressure sensors

The mechanical flexibility of MOFs makes them suitable candidates for strain and pressure-sensing applications. When subjected to external mechanical forces, MOFs can undergo reversible deformations, influencing their electrical conductivity or optical properties.^{134–138} A MOF-based strain sensor can be incorporated into wearable textiles to monitor body movements or detect potential injuries during physical activities. An ultrasensitive, anti-jamming and durable sensor was developed by Pan *et al.* They developed a metal-organic framework-based strain sensor with accurate signal detection and noise-screening capability. The developed sensor easily differentiated between muscle hyperplasia from subtle swaying and other vigorous activities. The fabricated sensor is shown in Fig. 4.¹³⁹ In another study, 3D-printed

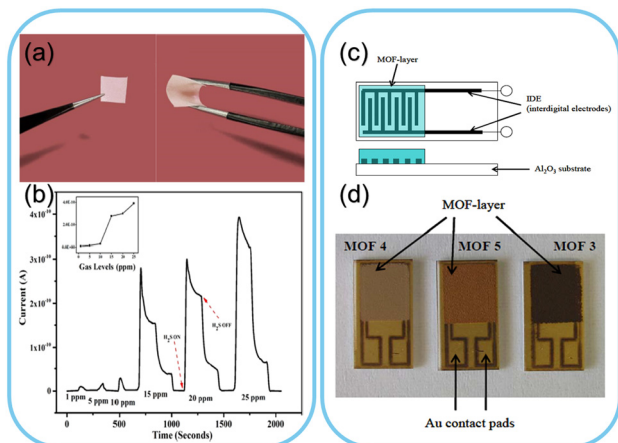


Fig. 3 Gas sensors based on MOFs. a) MOF-5 based nanocomposite membrane. b) Electrical current response of the MOF-5 nanocomposite as a function of time and H₂S concentration measured at room temperature. Inset: Response for the corresponding gas concentration. Reproduced from ref. 125 with permission from American Chemical Society, copyright 2021. c) Systematic view and d) schematic view of the developed MOF-based gas sensor. Reproduced from ref. 126 with permission from MDPI, copyright 2009.



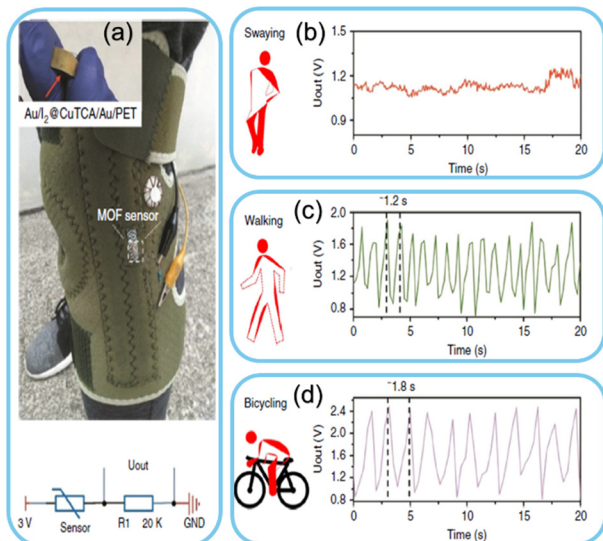


Fig. 4 Strain sensor based on MOFs. a) Schematic of a developed Cu-based MOF integrated with an intelligent kneecap. The sensor's output signal under b) leg swaying, c) walking and d) bicycling. Reproduced from ref. 139 with permission from Springer Nature, copyright 2018.

colourimetric and mechanical sensors based on MOFs were developed. The developed device produced a colour change in the presence of acidic components and showed high sensitivity to mechanical deformation and various body movements.¹⁴⁰ Another study fabricated a wearable self-powered pressure sensor based on ZIF-8, a zinc-based metal-organic framework. The prepared triboelectric nanogenerator is a wearable biomotion sensor that detects body movements with high sensitivity.¹⁴¹ This real-time feedback can help individuals optimize their exercise routines and avoid overexertion.

Temperature sensors

The thermal responsiveness of certain MOFs allows them to serve as temperature sensors. When exposed to varying temperatures, the MOF lattice undergoes structural changes that lead to detectable electrical conductivity or thermal emissivity alterations.^{142–146} A thermometer based on a lanthanide metal-organic framework is reported with good sensitivity in the wide temperature range of 4 to 290 K.¹⁴⁷ Another study reported the development of a multimode temperature sensor with high resolution demonstrated by temperature mapping.¹⁴⁸ Integrating these MOFs into wearable devices enables precise temperature monitoring, which is crucial for healthcare, sports, and environmental monitoring applications.

Biological sensing mechanisms

Biosensors

The versatility of MOFs enables their functionalization with biomolecules, such as enzymes, antibodies, or nucleic acids, enabling the development of highly sensitive and specific

biosensors.^{149–154} For example, a MOF-based biosensor functionalized with glucose oxidase can detect glucose levels in sweat or interstitial fluids, providing non-invasive glucose monitoring for individuals with diabetes.¹⁵⁵ Creatine kinase, a cardiac biomarker widely used to diagnose myocardial infarction accurately, can be detected using MOFs with high sensitivity and selectivity (Fig. 5b).¹⁵⁶ The immobilized biomolecules interact selectively with target analytes, triggering detectable changes in the MOF's properties, such as its optical absorbance or electrical impedance. By incorporating these MOF-based biosensors into wearable devices, real-time health monitoring and disease management become feasible for users.

Furthermore, MOF-based wearable sensors represent a remarkable leap in sensing technology, offering a wide range of chemical, physical, and biological applications. Their unique structural properties, high surface area, and tunability enable precise detection and monitoring of various analytes, making them invaluable tools for healthcare, environmental monitoring, and beyond.^{157–160} Wang *et al.* reported a copper metal-organic framework sensor for sensing ascorbate in sweat. The developed sensor showed high selectivity for ascorbate. The sensing performance of the developed sensor is shown in Fig. 5a.¹⁶¹ A bimetallic metal-organic framework-based sensor was designed for detecting glucose from sweat during dancing. As shown in Fig. 5c, the wearable glucose sensor showed high sensitivity, repeatability, reproducibility, long-term stability and a low detection limit while monitoring sweat glucose levels

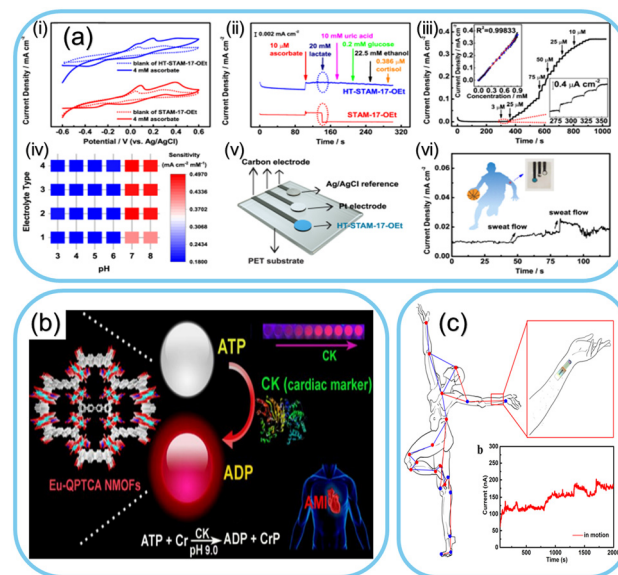


Fig. 5 Biosensors based on MOFs. a) Ascorbate sensor based on a MOF: (i)–(iii) current response for ascorbate, Inset of (iii) shows corresponding calibration curve of amperometric response (iv) sensitivity in different electrolytes, (v) and (vi) fabricated sensor and data collection. Reproduced from ref. 161 with permission from Springer Nature, copyright 2023. b) Schematic representation of cardiac biomarker sensing by a lanthanide MOF. Reproduced from ref. 156 with permission from American Chemical Society, copyright 2019. c) Schematic diagram of a dancer dancing with a MOF-based glucose monitor and the corresponding response signal. Reproduced from ref. 162 with permission from Springer Nature, copyright 2023.



during dancing.¹⁶² As researchers continue to explore novel MOF materials and functionalization techniques, the potential of wearable sensors to enhance our lives and well-being is bound to grow further, paving the way for a more thoughtful and healthier future.

Healthcare applications

Disease detection

MOF-based sensors have demonstrated tremendous potential in identifying diseases such as diabetes, cancer, and infectious diseases at their nascent stages, enabling timely interventions and improving patient outcomes.^{163–167} This review delves into the fascinating world of MOF-based sensors. It analyses the specific MOFs utilized, the target biomarkers they detect, and their exceptional sensitivity and selectivity in revolutionizing disease diagnosis.

Understanding MOFs and their sensing mechanism.

Metal–organic frameworks (MOFs) are a class of crystalline materials composed of metal ions or clusters linked by organic ligands. Their unique structural properties include a high surface area and tunable porosity, making them ideal for various applications, including gas storage, separation, and catalysis.^{168–172} More recently, scientists have harnessed the exceptional characteristics of MOFs to develop ultrasensitive sensors for disease detection.

MOF-based sensors operate on the principle of host–guest interactions. When the target biomarkers specific to a particular disease interact with the MOF's porous framework, they induce a change in the sensor's physical properties, such as electrical conductivity, fluorescence, or mass, allowing for precise and real-time detection.^{173–177}

Early detection of diabetes. Diabetes, a metabolic disorder affecting millions worldwide, requires early detection for effective management. MOF-based sensors have emerged as a promising tool for monitoring blood glucose levels non-invasively. By functionalizing the MOF surface with glucose-binding molecules, these sensors can detect even minute changes in glucose concentrations.^{178–180} A non-invasive flexible electrode material based on bimetallic metal–organic frameworks was fabricated by Zha *et al.* for glucose sensing and micro supercapacitors. The developed sensor exhibits high glucose sensitivity and high energy density. The intelligent sensing system with an integrated micro supercapacitor could accurately measure sweat glucose in real time.¹⁸¹ Another group prepared a non-invasive electrochemical glucose sensor that accurately detects glucose from sweat. The bimetallic-based glucose sensor showed excellent sensitivity and high stretchability and stability. The fabricated sensor is illustrated in Fig. 6a.¹⁸² In another study, a bimetallic MOF-based electrochemical sweat sensor was reported to monitor glucose levels from sweat continuously. The flexible sensor showed high sensitivity and stability and can be attached to the skin for continuous glucose monitoring for one day. The high-performance wearable sensor is shown in Fig. 6b.⁹⁷ This advance in technology offers diabetic patients a convenient and

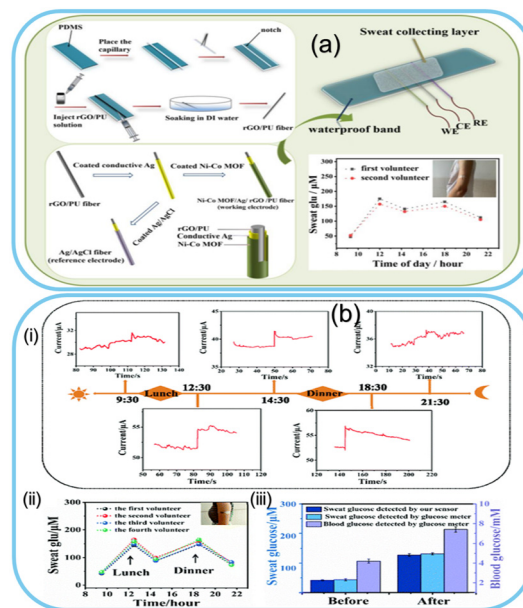


Fig. 6 Wearable glucose sensor based on MOFs. a) Highly stretchable wearable Ni-Co MOF-based nanocomposite fibre for sweat glucose detection. Reproduced from ref. 182 with permission from American Chemical Society, copyright 2021. b) NCAP film-based wearable sweat sensor: (i) and (ii) real-time monitoring of glucose, (iii) comparison of the developed sensor with a commercial glucose meter. Reproduced from ref. 97 with permission from The Royal Society of Chemistry, copyright 2022.

pain-free alternative to traditional blood glucose monitoring methods.

Unveiling cancer biomarkers. Cancer, a complex and heterogeneous disease, demands early diagnosis for successful treatment outcomes. MOF-based sensors have revolutionized cancer diagnostics by detecting specific biomarkers associated with different types of cancer. Functionalizing MOFs with antibodies or aptamers enables them to recognize and bind to cancer-specific biomolecules. This leads to early and accurate detection of cancerous cells or circulating tumour markers in bodily fluids.^{183–187} A CuBTC metal–organic framework-based composite was developed to detect ovarian cancer biomarkers. Due to the synergistic effect between the composite materials, the developed sensor showed excellent electrochemical performance and high practicability.¹⁸⁸ Another study reported a Ni-hermin MOF, which mimics an enzyme for colourimetric cancer cell detection. The developed nanocomposite with folic acid as a recognition element was used for the colourimetric assay for direct cancer cell detection.¹⁸⁹ Consequently, this technology holds tremendous promise in enhancing cancer screening and patient survival rates.

Combating infectious diseases. Infectious diseases remain a significant global health challenge, necessitating rapid and accurate diagnostics. MOF-based sensors offer an innovative approach to detect infectious agents such as bacteria, viruses, and parasites.^{190–192} A fluorescence molecularly imprinted sensor based on a metal–organic framework was developed to detect the virus accurately. The



developed sensor showed high selectivity and specificity.¹⁹³ Another luminescence-based biosensor based on an Fe-MOF was developed for common pathogens. The biosensor was able to detect *P. aeruginosa* and *E. coli*.¹⁹⁴ Another study reported the optical detection of *E. coli* using a terbium-based MOF with high sensitivity and specificity.¹⁹⁵ The high selectivity of MOFs allows them to be tailored to target distinct biomarkers associated with specific pathogens. As a result, MOF-based sensors provide a reliable and efficient means of early diagnosis, crucial for timely treatment and containment of infectious disease outbreaks.

Sensitivity and selectivity advantages. One of the most remarkable attributes of MOF-based sensors is their exceptional sensitivity and selectivity. The high surface area and tunable porosity of MOFs enable efficient capture and concentration of target biomolecules, ensuring that even trace amounts of disease-related markers can be detected. Moreover, MOFs can be engineered to be highly selective, accurately distinguishing between similar biomolecules and reducing the likelihood of false-positive results.^{196–200}

Physiological monitoring

These innovative sensors offer a revolutionary approach to physiological monitoring, enabling real-time tracking of vital signs such as heart rate, body temperature, and blood pressure.^{201–206} This article explores the significance of MOF-based wearable sensors and their potential to transform how we monitor and manage our health.

Understanding MOF-based wearable sensors

Metal-organic frameworks (MOFs) are porous materials of metal ions connected by organic linkers. Their unique structure gives them an exceptionally high surface area and tunable properties, making them ideal candidates for various applications, including gas storage, catalysis, and sensing.^{207–209}

In the context of wearable sensors, MOFs have gained attention due to their ability to adsorb and interact with specific molecules, including gases and biomolecules.^{210–212} This property opens up new possibilities for non-invasive physiological monitoring. High-performance electronic devices for monitoring physiological changes are developed. A study reported the development of a wearable sensor based on zirconium-based metal-organic frameworks for arterial pulse monitoring. The developed device is based on the piezoelectric performance of the nanocomposites, and the results revealed high sensitivity for pulse monitoring as shown in Fig. 7a.²¹³ Another group developed a breath sensor based on HKUST-1 MOF and MoS₂ for monitoring respiratory disorders. The developed sensor was efficient in various breaths and showed fast response time and excellent stability. The prepared device is shown in Fig. 7b.²¹⁴ Researchers have harnessed the versatility of MOFs to develop wearable sensors that can capture and detect biomarkers indicative of an individual's health status. An

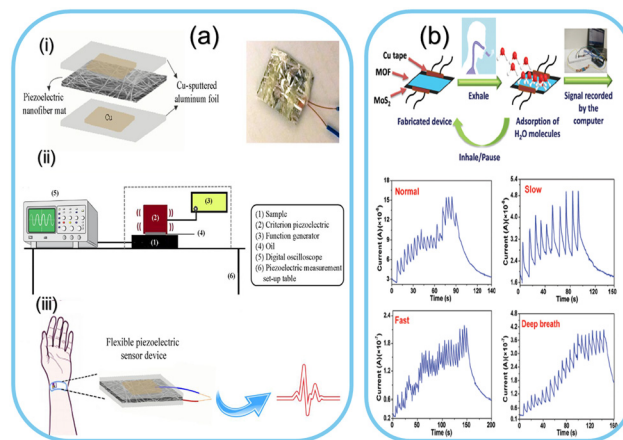


Fig. 7 Physiological monitoring systems based on MOFs. a) Artery pulse monitoring. Schematic of (i) sensor assembly, (ii) set-up, (iii) recording of the artery pulse signal. Reproduced from ref. 213 with permission from American Chemical Society, copyright 2020. b) Fabricated breath sensor and current response showing different types of breath. Reproduced from ref. 214 with permission from The Royal Society of Chemistry, copyright 2020.

illustration representing the advantages and applications is shown in Fig. 8.

Advantages of MOF-based wearable sensors

Non-invasiveness

MOF-based wearable sensors offer a non-invasive alternative to traditional methods of vital sign monitoring. Unlike invasive techniques requiring needles or catheters, MOF-based sensors can be easily integrated into everyday accessories like wristbands or clothing, minimizing discomfort and promoting continuous monitoring.^{215–217}

Real-time monitoring

MOFs' high sensitivity and selectivity enable real-time monitoring of various biomarkers. This capability is crucial for promptly

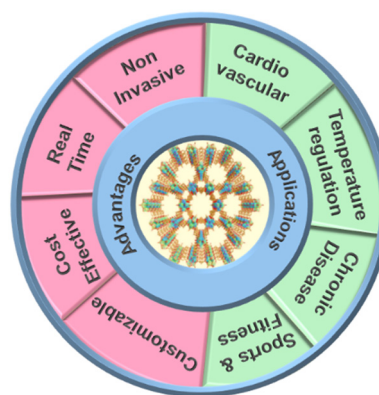


Fig. 8 Schematic illustration of advantages and applications of MOF-based wearable sensors.



detecting fluctuations in vital signs, allowing for timely intervention and better management of health conditions.^{218–220}

Customizability

Researchers can design MOFs with tailored properties to target specific biomarkers. This customizability allows the development of wearable sensors optimized for monitoring various health parameters, making them versatile tools for personalized healthcare.^{221,222}

Cost-effectiveness

Compared to some conventional medical monitoring techniques, MOF-based wearable sensors can be produced relatively cheaply. This cost-effectiveness makes them more accessible to a broader population, potentially improving healthcare outcomes across different socio-economic backgrounds.²²³

Applications of MOF-based wearable sensors

Cardiovascular health monitoring

MOF-based wearable sensors can detect and track heart rate and blood pressure, providing valuable insights into an individual's cardiovascular health. Continuous monitoring of these vital signs can aid in identifying irregularities, helping to prevent serious complications such as heart attacks or strokes.^{224,225}

Temperature regulation

Monitoring body temperature is vital for detecting fever or hypothermia, which can indicate various infections or illnesses. MOF-based sensors can offer accurate and continuous body temperature tracking, making them essential for fever surveillance and patient care.^{226,227}

Chronic disease management

Patients with chronic conditions like diabetes or hypertension can benefit significantly from MOF-based wearable sensors. These devices can help individuals manage their conditions more effectively by providing real-time data on blood glucose levels or blood pressure fluctuations.^{228,229}

Sports and fitness

Athletes and fitness enthusiasts can utilize MOF-based wearable sensors to monitor their performance and physical exertion levels during workouts. These sensors can track heart rate, providing valuable information to optimize training routines and avoid overexertion.^{230–233}

Drug delivery

MOFs are highly versatile and tunable structures of metal ions or clusters coordinated with organic linkers. Their

unique properties, including high porosity, large surface area, and customizable chemical structures, have garnered immense interest for applications in various fields, including drug delivery.^{234–237} In this article, we will explore how MOFs are revolutionizing drug delivery systems, particularly in the context of wearable devices, offering unprecedented opportunities for personalized and precise medication administration.

The versatility of MOFs in drug delivery

MOFs are renowned for their extraordinary flexibility in design, allowing researchers to tailor their properties to suit specific drug delivery needs. The most critical property of drug carriers is the biocompatibility of the material. The tunable properties of MOFs favors producing a system with high biocompatibility and biodegradability.^{238–241} By selecting appropriate metal ions and organic linkers, MOFs can be engineered to possess desired pore sizes and surface functionalities. These characteristics enable MOFs to encapsulate a wide range of drug molecules, including small molecules, proteins, peptides, and nucleic acids. Moreover, MOFs can protect drugs from degradation and undesirable environmental interactions, ensuring their stability and bioavailability during delivery.^{242–246} However, continued research is needed to determine the long-term safety of MOF-based wearable devices.

Controlled drug release mechanisms

One of the most significant advantages of utilizing MOFs as drug carriers is their ability to control drug release rates. MOFs can be engineered to have stimuli-responsive behaviours triggered by environmental cues such as temperature, pH, light, or specific chemical signals. This responsiveness allows for precise on-demand drug release, maximizing therapeutic efficacy while minimizing potential side effects.^{247–250} Yang *et al.* developed an insulin delivery system depending on the blood glucose level. The enzyme-

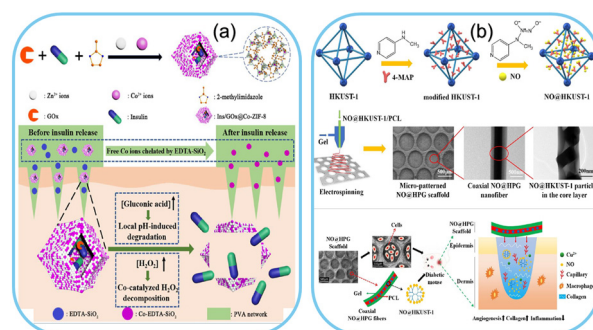


Fig. 9 MOF-based drug delivery systems. Schematic representation of a) MOF-based microneedles for glucose-mediated transdermal insulin delivery. Reproduced from ref. 251 with permission from American Chemical Society, copyright 2020. b) Cu-based MOF for NO release for enhanced diabetic wound healing. Reproduced from ref. 252 with permission from American Chemical Society, copyright 2020.



loaded drug delivery system was designed for pain-free insulin delivery through stimuli-responsive microneedles. The schematic illustration of drug release is shown in Fig. 9a.²⁵¹ Another study reported the development of MOFs as a controllable drug delivery system for nitric oxide. The developed drug delivery system releases NO for accelerating diabetic wound healing as shown in Fig. 9b.²⁵² Wearable devices equipped with MOF-based drug delivery systems can be programmed to release medications at specific times or in response to physiological indicators, making them ideal for treating chronic conditions or managing acute symptoms efficiently.

Integration with wearable devices

Integrating MOFs into wearable devices marks a significant advancement in drug delivery technology. Wearable devices, such as smartwatches, patches, or implants, offer continuous monitoring and personalized care, enabling real-time feedback and adjustment of drug dosages.^{253–257} MOFs, as drug carriers in these devices, ensure that the right amount of medication is delivered at the right time, enhancing treatment outcomes and patient compliance. Additionally, the portability and unobtrusiveness of wearable devices make them an attractive option for patients, facilitating seamless drug administration and management of chronic conditions.

Advantages of MOF-based smart drug delivery systems

a. Improved patient adherence

MOF-based wearable drug delivery systems enable a more consistent and automated drug administration process, reducing the chances of missed doses and promoting patient adherence to treatment regimens.²⁵⁸

b. Enhanced therapeutic efficacy

The controlled and targeted drug release offered by MOFs ensures that medications reach their intended site of action in optimal concentrations, enhancing therapeutic efficacy while reducing the risk of systemic side effects.^{259,260}

c. Reduced healthcare burden

With precise drug dosing and improved patient compliance, MOF-based intelligent drug delivery systems can potentially reduce hospital admissions and emergency room visits, alleviating the burden on healthcare systems.²⁶¹

d. Personalized medicine

MOFs' tunable nature allows for personalized drug delivery strategies, tailoring treatments to individual patient needs to be based on their unique physiological profiles and disease characteristics.²⁶²

Challenges and future prospects

a. Stability in harsh environments

MOFs may experience degradation due to moisture, chemicals, or other harsh environmental conditions. Researchers need to develop strategies to enhance the stability of MOFs under real-world operating conditions.

b. Scalability and cost-effectiveness

Large-scale synthesis of MOFs at an affordable cost remains challenging. Researchers are exploring novel synthesis methods and scalable production techniques to make MOFs more commercially viable.

c. Selectivity and cross-sensitivity

Achieving high selectivity and avoiding cross-sensitivity to other compounds are critical for accurate and reliable sensing. Continued research is necessary to improve the selectivity of MOF-based sensors (Fig. 10).

Conclusion

Metal–organic frameworks have emerged as a promising class of materials in developing wearable sensors for healthcare applications. The unique properties of MOFs offer opportunities for highly sensitive and selective sensing and intelligent drug delivery. While challenges remain, ongoing research and innovation hold tremendous potential for advancing MOF-based wearable sensors and revolutionizing healthcare monitoring and diagnostics. As technology evolves, these sensors may become integral to personalized medicine, leading to improved patient outcomes and enhanced quality of life.

Data availability

All required data can be found within the main manuscript file.

Code availability

Not applicable.



Fig. 10 Schematic illustration of challenges in MOF-based wearable systems.



Author contributions

P. N. Blessy Rebecca: conceptualization, investigation, methodology, writing – original draft; D. Durgalakshmi: conceptualization, investigation, methodology; S. Balakumar: conceptualization, validation, review; R. Ajay Rakkesh: investigation, supervision, review & editing, conceptualization.

Conflicts of interest

The authors declare that they have no conflict of interest.

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