

Progress in the Application of MOF-based SERS Sensors in Biomedicine

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Abstract— In order to create lattices with a highly structured periodic porous network structure centered on metal ions or metal ion clusters, MOF compounds bind organic ligands. Because of its many benefits, MOFs are employed in many industries, such as gas storage, catalysis, adsorption, and separation. The utilization of MOFs in SERS substrate can effectively tackle the problem of substrate nanoparticle aggregation while simultaneously enhancing the sensitivity of SERS analysis. The most prominent characteristics of MOFs are their maximal permeability and interior surface area. When utilized in gas separation, the pore widths enable molecules to be selectively separated based on their size and form. Clarifying the application of metal organic framework conductivity in SERS detection is the aim of this work. The use of MOFs in the creation of sensing materials has various benefits. These include complex structures involving "multiple metals and organic linkers, conformationally flexible linkers and geometrically adaptable inorganic building blocks, and unique and highly adjustable physicochemical and structural properties like consistent porosity and adjustable pore diameter." Finally, fresh perspectives on the properties, structure, and stability of these materials will spur their advancement for specialized uses in energy storage, manufacturing, medicine delivery, electronics, and environmental remediation. As a result, MOFs have a promising future across numerous industries.

Keywords— MOF, Metal organic framework, Conductivity of organic metal, SERS detection, Drug monitoring, microneedles, sensor, flexible electronic devise.

I. INTRODUCTION

1.1 Metal-organic frameworks (MOFs) and their unique properties

1.1.1 Overview:

Coordinate bonds make up "Metal Organic Frameworks (MOFs)," a type of materials that are crystalline in nature. These linkages exist between metal cations and the organic, multidentate particles. Many scientists and engineers have become interested in MOFs during the past few years. One of the characteristics of MOFs is their huge surface area and incredibly large pores. The MOFs continue to be the best options for use in gas storage and catalysis because of these exceptional and distinctive qualities. Younis et al., (2021) studied that the excellent chemical and thermal stability are a critical feature for MOFs used in hostile environments (Younis et al., 2021). Although researches of Annamalai et al., (2022) have vehemently argued that it is impractical to fully control every parameter of a chemical reaction, the planned production of MOFs likewise necessitates total control over the materials

and instruments to be employed. False the claim that a sizable series of solids were produced during the planned synthesis of IRMOFs based on MOF-5 (Annamalai et al., 2022).

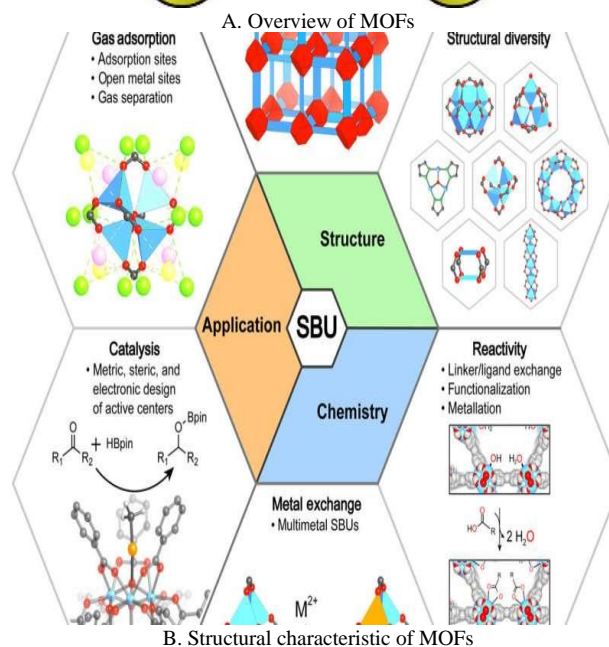
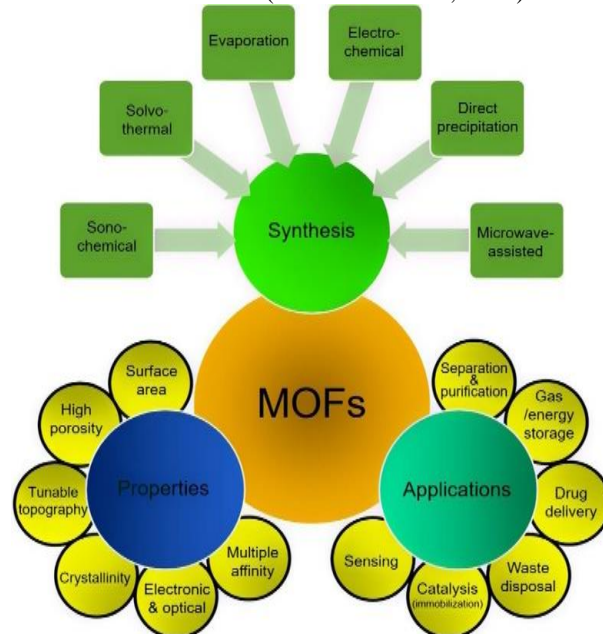


Figure 1: Part A of this figure provides an overview of MOFs, whereas Part B explains their structural characteristics.

Sources: (Bilal et al, 2019)

1.1.2 Properties:

The greatest characteristic of MOFs is their exceptionally high porosity and internal surface area. Because of this, they work especially well in applications where adsorption and gas storage are involved. For uses in gas separation, the pore diameters enable the selective separation of molecules according to size and form. This characteristic is essential for customizing MOFs for particular uses, such as offering analytes unique binding sites (Saraci et al., 2020). There are practically infinite combinations of metal ions and organic linkers that can be used to create MOF structures. The exact composition of MOFs has a significant impact on their stability, which can vary greatly (Agafonov et al., 2022). Certain MOFs that include plasmonic metals can function as SERS substrates straight away.

These MOFs have the ability to improve Raman signals via both electromagnetic and chemical enhancement processes (Saeb et al., 2021). Because MOFs are porous, molecules can be concentrated inside of them, raising the local concentration of analytes and boosting the SERS signal. The MOFs' structure and chemical functionality can be adjusted to interact with specified analytes in certain ways (Mandal et al., 2021).

discharged into the “air, soil, and water, environmental monitoring is necessary.” Certain pollutants have the ability to endure for an extended period and spread across vast areas of soil until they come into contact with water supplies (Javaid et al, 2021). Electronic security systems come in a variety of forms and are used to protect the country, homes, elderly people, infants, banks, mobile devices, and more. There are security concerns even for farmers.

1.2.1 Environmental Sensing sector:

Sensors are vital for tracking the environment since they provide information that is needed to comprehend and safeguard our natural resources. By detecting pollutants including CO₂, NO_x, and particulate matter, sensors assist nations and communities in enhancing public health and adhering to environmental laws. In order to provide safe drinking water, preserve the health of ecosystems, and oversee wastewater treatment, sensors keep an eye on pH, turbidity, dissolved oxygen, and other parameters. Sensors are essential for conservation efforts because they detect animal movements, keep an eye on environments, and aid in the study of biodiversity. Sensors are essential for weather forecasting and climate research because they can monitor temperature, humidity, barometric pressure, and other variables (Ullo & Sinha, 2020)

1.2.2 Healthcare sector

Healthcare sensor is anticipated that rising life expectancy and declining birth rates would result in a sizable ageing population in the near future, placing a heavy burden on these nations' socioeconomic structures. For the benefit of senior healthcare and wellbeing, it is crucial to create affordable, user-friendly systems (Tyagi et al., 2020).

Sensors in healthcare offer a variety of applications that enhance patient care and make new medical technology possible. Smartwatches and fitness trackers, for example, use sensors to track blood oxygen levels, heart rate, and activity levels. Medical equipment uses a variety of sensors, such as blood pressure sensors and glucose monitors for diabetes, to identify and track illnesses. Temperature, pressure, and flow sensors make guarantee that industrial processes run within predetermined parameters, which improves efficiency and safety. These sensors are what power the efficiency and safety of industrial operations. Mamdiwar et al, (2021) studied that reduced downtime and maintenance expenses are achieved by using vibration sensors and other diagnostic instruments to anticipate equipment breakdowns before they occur. Additionally given is a survey of textile-based sensors that may find application in wearable technology. Lastly, the ability of several communication technologies to work together (Mamdiwar et al., 2021).

1.2.3 Security sector

There are reports that pests and weeds have developed chemical resistance, necessitating the use of additional pesticides and herbicides. This translates into increased expenses for farmers, increased harm to the environment, and a rise in health issues. It is outside the purview of this essay to cover every security concern and sensor (Jacob Rodrigues, 2020). The essay has been condensed to just a few security applications, including industrial, personal, home, and national

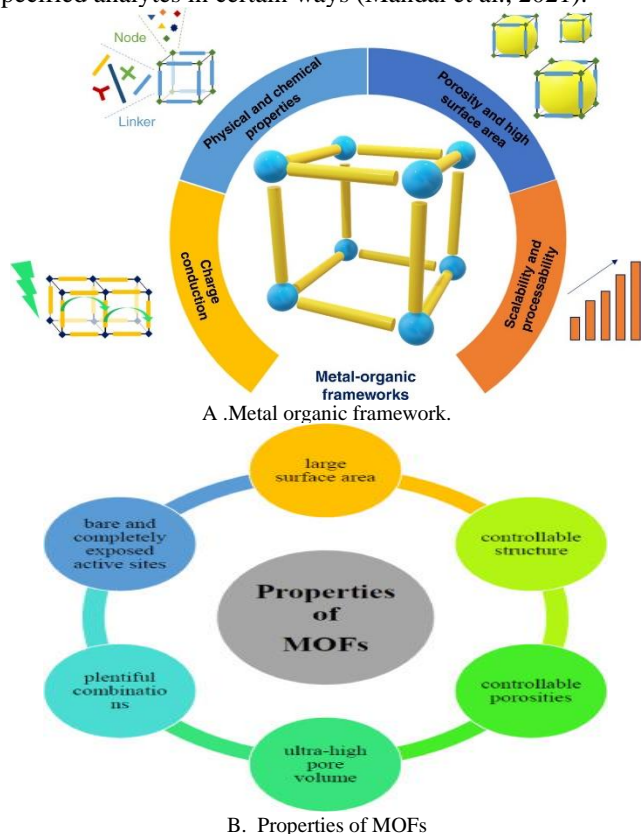


Figure 2: Figure A and B explain the metal organic framework and properties of MOFs.

Source: (Baumann et al, 2019)

1.2 Importance of sensors in various fields

In order to safeguard the environment and the general people from harmful substances and diseases that may be

cybersecurity. Sensing hardware and software, ranging from simple to complex, is used to protect people, property, financial institutions, and private information against threats.

In addition to home security applications, motion sensors are also useful in the industrial sector. They are frequently used on assembly lines to monitor the quantity of goods produced or to turn off potentially harmful equipment when someone is detected to be too close to it (Haghi et al., 2020). Motion sensors

are also used by a variety of businesses to manage ATM displays, based on whether someone is spotted in a room, and operate certain parking meters and automatic ticket gates. One of the most crucial electronic security devices is a radar sensor. An electronic signal is sent by a radar, bouncing off objects and returning to the receiver for further examination (Mamun, & Yuce, 2020).

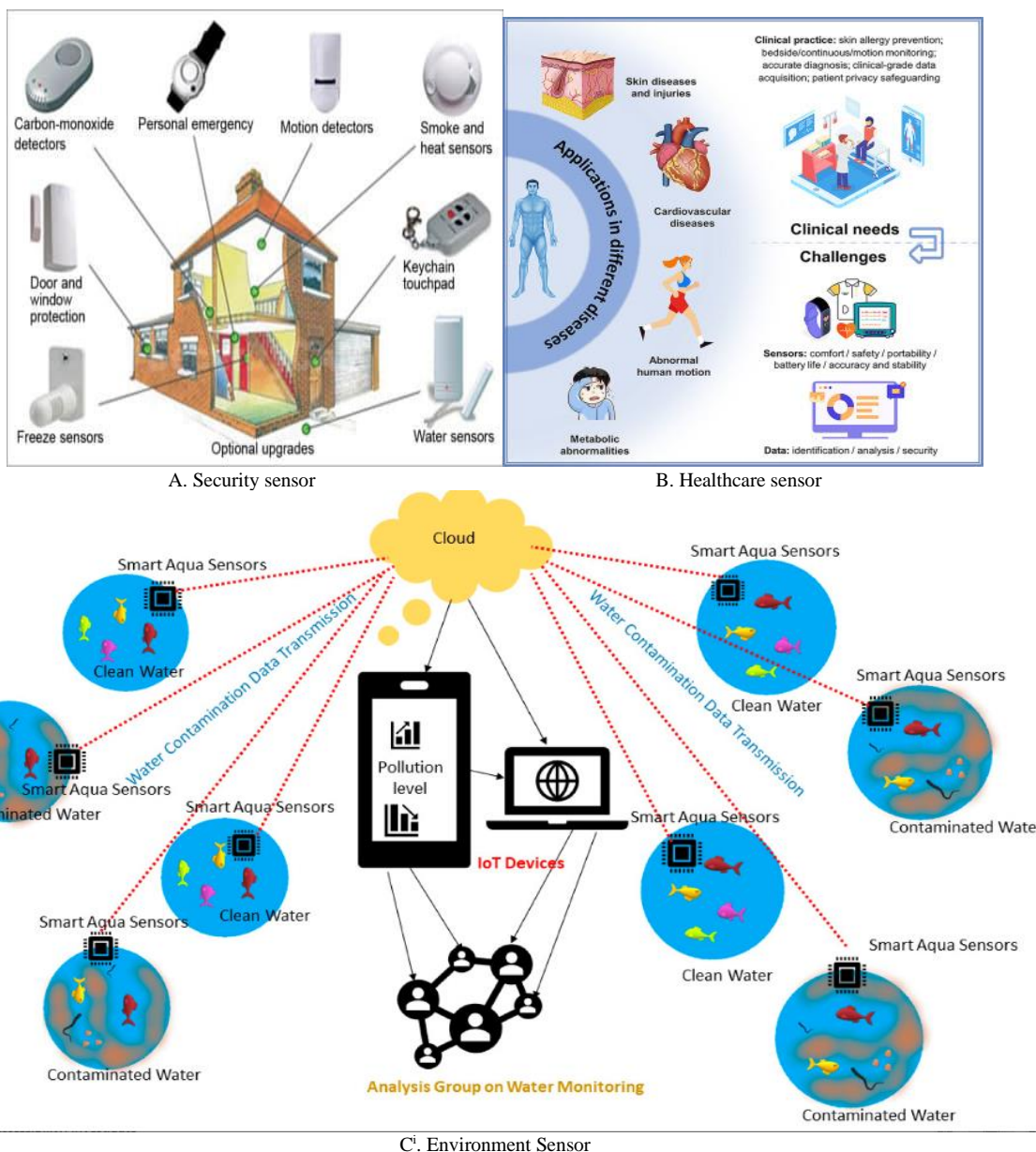


Figure 3: This figure explains the security sensor in part A, the healthcare sensor in part B, and the environment sensor in part C. Source: A. (Ullo & Sinha, 2020), B. (Tao et al, 2023), C. (CD-Team, 2019).

1.3 MOFs functionalization capabilities.

The oxidation of organic molecules is catalyzed heterogeneously by metal–organic frameworks. In the chemical industry, oxidation processes are vital for the production of numerous important chemicals. Heterogeneous catalysts with a range of supports are gaining popularity due to their exceptional

and reasonably priced ability to speed up chemical processes. Additionally, they reduce the amount of chemicals used in industry, making them environmentally beneficial. It is without a doubt the best option to select for the organic synthesis process due to the peculiarities. Because of the special structure of metal-organic frameworks, oxidation processes involving

alkanes like fluorene, adamantane, ethylbenzene, diphenylmethane, and alkenes as well as many other organic compounds can be effectively catalyzed (Zhang et al., 2022). Because of their remarkable structural diversity, porosity, and tunability, potential MOFs materials are excellent choices for a variety of applications. Most people agree that micro and nanoscale materials are an important subset of nanomaterials and a rapidly expanding field. As catalysts, nanomaterials show exceptional characteristics, such as a high aspect ratio (Zhang et al., 2022).

TABLE 1: surface area, adjustable pore diameters, and functionalization potential of sensor.

MOF Type	Surface area	Tunable pore sizes	Functionalization groups	References
ZIF-8	1500 M ² /g	11 Å	CH ₃ , NH ₂	(Kim, 2016)
MOF-5 (IRMOF-1)	4000 M ² /g	15 Å	Benzenes and amine group	(Li et al., 2023)
HKUST-1 (Cu-BTC)	1800 M ² /g	10 Å	Pyridine, Imidazole	(Zaman, 2017)
MIL-101 (Cr)	4000 M ² /g	25 Å	SO ₃ H ₃ , NH ₂	(Do-Young Hong, 2009)
MIL-53 (Al)	1500 M ² /g	8 Å	Carboxyl and hydroxyl group	(Do et al., 2011)

The many sensor MOFs are described in this table along with their large surface area, adjustable pore diameters, and functionalization potential.

On the other hand, by preserving the structural design and topology stability, several structural and functional variations might be easily accomplished during synthesis or post-synthesis adjustments. The development of reticular chemistry is an essential component for the production and use of MOFs (Ahmadi et al., 2022). For basic advantages and uses in drug and enzyme administration, sensing, heterogeneous catalysis, gas storage and separation, and biomedical imaging, MOF materials have been investigated. Currently, multiple functionalization approaches, such as post-synthetic modification, are being used by researchers for MOFs. These modifications can be accepted by forming organic ligands and/or metal clusters inside the pores with functional ligands encircling important molecules. These strategies make MOFs a perfect structure for combining materials that have been functionally created (Yuan et al, 2022).

II. METAL-ORGANIC FRAMEWORKS MATERIAL IN SERS SENSOR

Surface-improving a type of "molecular fingerprint spectrum known as Raman spectroscopy (SERS)" shows that the peak intensity is proportional to the molecule concentration and that the frequency variation is associated with specific molecular vibration information (Qin et al., 2023).

MOFs belong to the subclass of coordination networks, which in turn belong to the subclass of coordination polymers, as per the official language approved by IUPAC on Batten et al. (2013). MOFs are characterized by remarkably high specific surface areas (Zhang et al., 2021). This large surface area is crucial for increasing sensor sensitivity because it provides

more active sites for interaction with analyte molecules (He et al., 2021). The organic synthesis benefits from the active site's confinement since it shields the catalyst from other reactive species. The large surface area provided by MOFs' small footprint is one of its advantages (Olorunyomi et al., 2021).

This technique involves controlling the nucleation and development of MOF crystals by gradually adding or varying one or more reactants or additives (Jiao & Jiang, 2023). The majority of the time, solve thermal techniques are used to generate MOFs at high pressure and temperature. These methods yield cleaner outcomes and are quicker and less expensive (Chronopoulos et al., 2022).

By altering the metal ions or organic ligands utilized in their synthesis, MOFs' pores can be made to operate differently and have a different size (Kirlikovali et al., 2022). Beyond just providing protection, MOFs exhibit great promise. The primary element necessary for it to function as an efficient catalyst is its porous designed system. Similarly, because they are corrosive and challenging to separate and dispose of, these porous solid catalysts play a critical role in replacing homogeneous catalysts used in the liquid-phase manufacturing process of bulk and fine chemicals, which represent a risk to the environment. When a catalyst is employed in a reaction, the rate at which the product forms depend on the surface area that is available.

Consequently, the higher the throughput, the more surface area that is accessible to the reactants (Wang et al., 2022). There are other physical characteristics than surface area that influence how much adsorption and catalytic reaction occur. The catalyst material's or support's pore structure is equally significant, even though it adds to the surface area overall. This is because the distribution of pore sizes in a particular catalyst preparation may prevent large reactant molecules from accessing some internal surface area and may also limit the rate of conversion to products by obstructing the diffusion of reactants and products throughout the porous medium (Xu & Hu, 2023).

2.1 Types of MOFs in SERS

MOFs can be categorized into a number of groups based on the components that make up each group (Qian et al., 2021). It should be mentioned that certain MOFs have the ability to independently function as SERS substrates and provide additional SERS improvement. Without the help of other reinforcing materials, the SERS enhancement results of MOFs were first reported in "MIL-100 (Al), MIL-100 (Cr), and MIL-101 (Cr). The charge transfer effect between the adsorbed molecules and metal oxide clusters in MOFs was primarily responsible for the SERS effect of MOFs." Reviewing the most recent developments in the burgeoning field of MOFs-based SERS research is very desirable, as is the continued proliferation of MOFs-based SERS substrate creation. Moreover, MOFs were used as molecularly selective SERS substrates, a feature that was difficult to achieve with conventional SERS substrates devoid of functionalization. To achieve the objectives, the metal center, carbon bonds and shell topology of MOF-based SERS devices were optimized in this work. The phenomena of MOFs exhibiting selective SERS enhancement was attributed to the combined influence of many

resonances, such as charge transfer resonance, molecule resonance, and inter-band resonance.

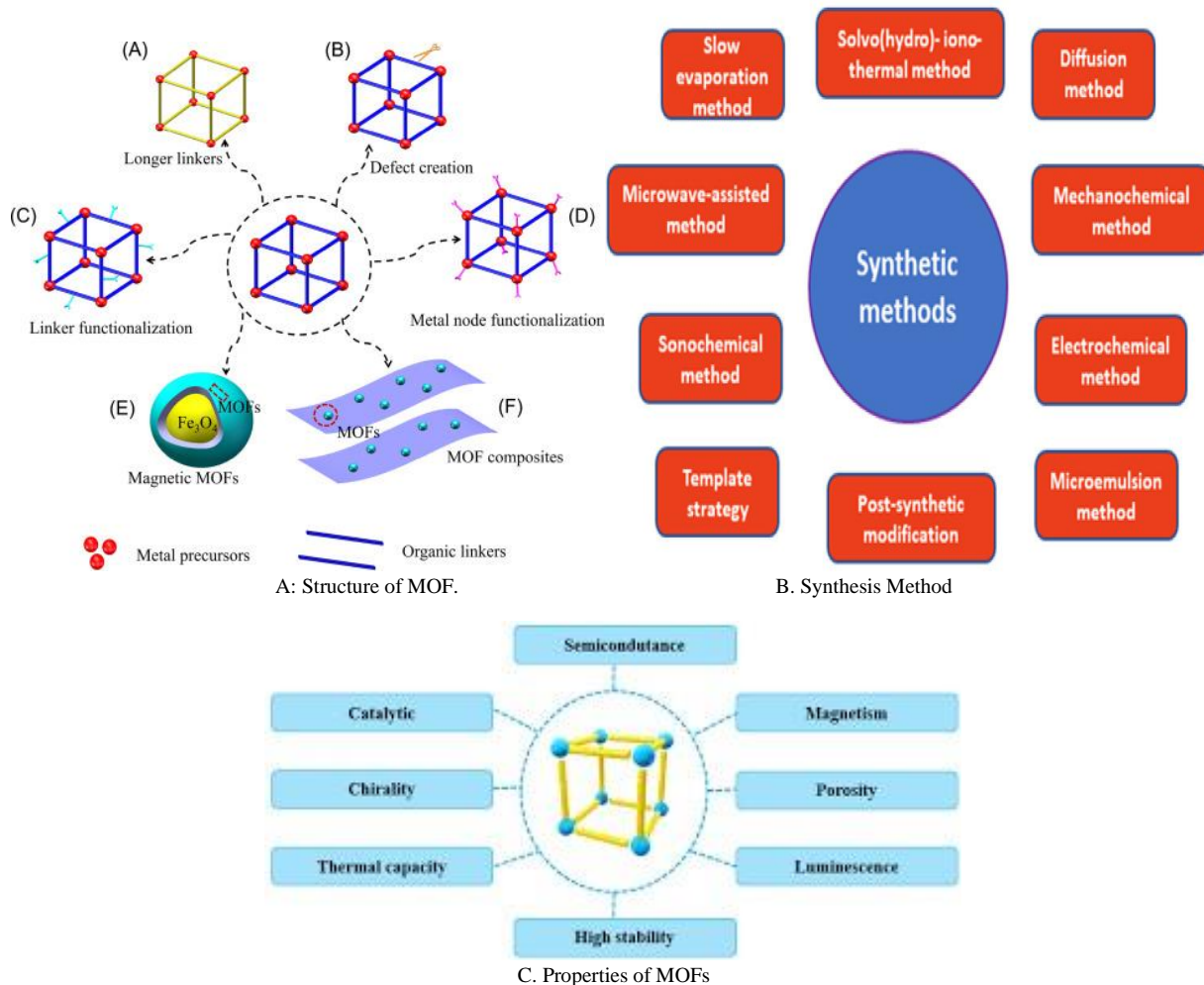


Figure 4: This figure explains the structure of MOFs in part A, synthesis method in part B, and the properties in part C. (A: (Kitagawa, 2014), B: (Raptopoulou, 2021), C: (Kitagawa, 2014))

2.1.1. Zeolitic Imidazolate Frameworks

“Frameworks of Zeolitic Imidazolates (ZIFs) imidazole with various elements and valence electrons are used to form zeolitic imidazolate functional frameworks.” Because of its performance, the ZIF-8 material is discussed above other ZIF materials. “ZIFs are utilized as a network to create innovative MOF composites because of their enormous pore size and exceptional chemical and thermal resilience.”

2.1.2. Porous Coordination Networks (PCNs)

“Porous coordination networks are composed of stereo-octahedron materials having a three-dimensional hole-cage-hole topology” (Ajdari et al, 2022).

2.1.3. Materials Institute Lavoisier (MIL)

“Different elements with valence electrons and an organic atom with two carboxylic functional groups are used to make MOFs. Under external stimulation, MIL MOFs' pore size arrangement could be freely changed” (Sriram et al., 2022).

2.1.4. Porous Coordination Polymers (PCPs)

“Transition metal ions serve as the SBU and carboxylic acid, pyridine, and its derivatives as the PBU in the synthesis of porous coordination polymer materials. In order to detect

organic vapors, Hirai and colleagues immobilized PCP Zn (NO₂-ip)(bpy) on the surface of QCM.” When it comes to heterogeneous catalysis and biomacromolecule separation, PCPs are exceptional (Raptopoulou, 2021).

2.2 Fabrication of MOF substrate for SERS Sensor

Plasmonic nanoparticles are included, the MOF material is synthesized, and the final sensor is assembled in order to fabricate MOF substrates for SERS sensors. In addition to increasing the sensitivity of SERS analysis, MOF-based SERS substrate can address the issue of substrate nanoparticle aggregation. The type of metal ion used in the MOF structure has a big impact on its functionality, porosity, and chemical stability. These include gas separation and storage, heterogeneous catalysis, photovoltaics, photocatalysis, chemical applications, biomass conversion, and biomedical applications (Bhattacharai et al, 2021). Its use as a MOF catalyst in chemical production has been covered in a number of articles. As may be clearly seen from the reading materials, MOFs have certain qualities that make them particularly desirable for use as catalysts (Mallakpour et al., 2021). Examples of reactions that

use MOFs as catalysts or support catalysts are the diversity of organic conversions (Shinde et al., 2021).

TABLE 2: The various MOF kinds and their uses with varying capacities, current densities, energy densities, power densities, and capacitance retention are explained in this table.

No	Type	Specific capacities	Current density	Energy density	Power density	Capacitance retention	References
1	Zeolitic Imidazolate Frameworks (ZIF-8)	450-500 F g ⁻¹	1-2 A g ⁻¹	200-300 Wh Kg ⁻¹	1000-2000 W Kg ⁻¹	90-95 %	(Sharma & Chand, 2023)
2	Porous Coordination Networks (PCNs)	400-450 F g ⁻¹	1-2 A g ⁻¹	180-250 Wh Kg ⁻¹	800-1500 W Kg ⁻¹	88-93 %	(Wang, 2019)
3	Materials Institute Lavoisier (MIL)	500-550 F g ⁻¹	2-4 A g ⁻¹	250-350 Wh Kg ⁻¹	1500-2500 W Kg ⁻¹	85 %	(Negin Khosroshahi et al., 2023)
4	Porous Coordination Polymers (PCPs)	350-400 F g ⁻¹	1-3 A g ⁻¹	180-220 Wh Kg ⁻¹	800-1500 W Kg ⁻¹	85.90 %	(Mayra Sánchez-Serratos, 2016)

TABLE 3: The fabrication of different MOF substrates for SERS sensors.

MOF Type	Synthesis Method	Functionalization	Characteristics	Applications
ZIF-8	Solvothermal	Ag or Au nanoparticles impregnation	Good chemical stability, homogeneous pore structure, and large surface area	Detection of organic molecules and biomolecules
MIL-101(Cr)	Hydrothermal	Au nanoparticles impregnation	Large pore size, high surface area, and thermal stability	Environmental monitoring and pollutant detection
HKUST-1	Solvothermal	Ag nanoparticles impregnation	High porosity, good thermal stability, and easy functionalization	Detection of aromatic compounds and pesticides
MOF-5	Solvothermal	Ag nanoparticles impregnation	High porosity, good chemical stability, and large surface area	Detection of gases and volatile organic compounds
PCN-222	Solvothermal	In-situ growth of Ag or Au nanoparticles	Large pores, high stability, and strong light absorption	Detection of biomolecules and catalytic reactions

For the purpose of identifying and measuring the “physical, chemical, or biological characteristics” of the environment, objects, or systems, sensing technologies are indispensable. A sensor is a device that converts a physical stimulus - such as light, temperature or chemical composition - into a quantity that can be measured and processed - an electrical signal.

Pei et al., (2021) studied that predictive and preventive maintenance are two advantages of deploying sensors and sensing technology. They not only make sure that measurement data is transferred more quickly, but they also improve accuracy, which boosts asset health and process control. A new generation of sensors can transmit both weirdly and wirelessly, offering a constant stream of real-time data from processes and assets. This gives executives a more comprehensive understanding of a process facility (Pei et al., 2021). Sensor-enabled businesses are more agile, secure, and connected than ever. Processes are kept active and run as efficiently as possible with the use of real-time feedback and data analytics services. The sophisticated and intelligent sensors of today are the product of continuous advancements in sensing technology. As opposed to traditional analogue sensors that lack any active parts, smart sensors have electrical circuits that enable them to collect data as digital measurements and outputs. These sensors have many sensing devices installed on a signal converter, along with embedded CPU units (Min, et al., 2021).

The process of transforming the detected interaction into a signal that can be measured, usually an electrical signal, is known as transduction. These transform material quantities into signals that are electrical. Optical sensors are frequently employed in the measurement of chemical compositions and interactions because they are capable of detecting changes in light properties such as intensity, wavelength, or polarization.

These produce an electrical output by converting mechanical changes like displacement, stress, or strain. These adapt to chemical stimuli by changing the electrical properties of the sensor in response to the presence of a particular chemical (Nenov & Yordanov, 2022).

The detected phenomenon must frequently be processed in order for the electrical signal the sensor produced to be of any use. In order to increase the electrical signal's detectability and suitability for additional processing, it strengthens it. Interpreting the sensor data using models and algorithms, which may entail statistical analysis, pattern recognition, or other techniques to transform the raw data into knowledge that may be put to use. The processed data is displayed in a format that is helpful, such as a graph, an alert signal, a numerical readout, or direct input into a control system for automatic responses, in the final phase known as the output (Algami et al., 2021). For instance, an optical or ionization-based sensing device interacts with smoke detector particles in the air. Smoke alters the ionization or optical characteristics, which alters the circuit's current flow (El-Sheimy & Youssef, 2020).

2.3 Mechanism of MOF in SERS

Recently, there has been a lot of interest in creating somewhat aperiodic frameworks to intentionally induce heterogeneities and vacancies in building blocks in order to fully realize the promise of MOF chemistry (Abdelkareem et al, 2022). The reaction time is mostly determined by the analyte's rate of diffusion to the interaction site, which is correlated with the MOFs' pore sizes and particle sizes (Gheorghe et al., 2021).

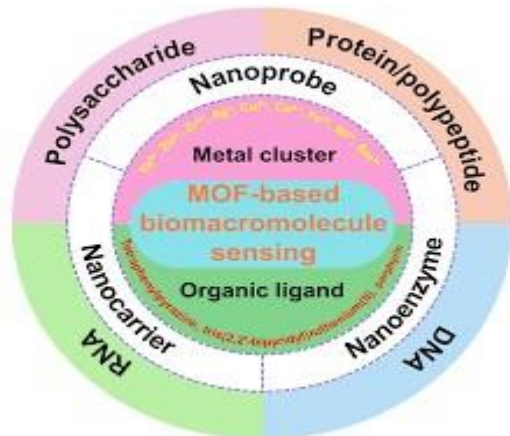
Alterations to the MOF composition to fortify metal-linker bonds, and the capacity to reversibly reorganize following the elimination or insertion of μ3-OH groups (Kajal et al. 2022). Even with the enormous advancements in MOF-based sensing

material design to date, significant research is still needed to address the primary present constraints before sensors with industrial significance and practical applications can be developed. First off, selectivity is typically low. Many MOF-sensing techniques involve a signal loss in reaction to the analyte's contact; these "turn-off" sensors are also susceptible to other interference, which further reduces signal and raises LOD. Furthermore, some MOFs continue to have the issue of having relatively low stability when operating (Nangare et al., 2023).

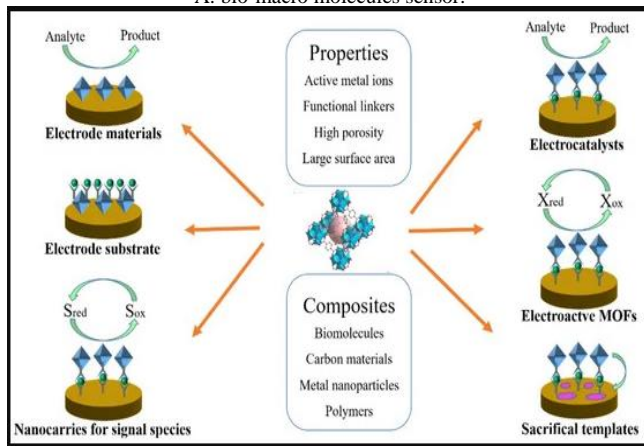
necessary when the concentrations of contaminants often vary slowly (Tian et al., 2021).

Because of their large surface area and atomic metal sites, MOFs are a good option for electrocatalysts in sensor, particularly those involved in energy-related processes. MOFs have been widely employed as an electrocatalyst for oxygen reduction reactions, gas reduction from carbonic acid, and water splitting up to now. The sensor converts any type of energy into electrical energy. It's a transducer that can detect and recognize specific environmental cues. Certain characteristics are necessary for an ideal sensor in order for it to function reliably and effectively. When designing and choosing sensors, certain general parameters are frequently looked for, although the specifics can change based on the application (Yuan et al., 2022).

Stable sensors do not significantly drift in readings even after prolonged use or exposure to environmental stressors such temperature changes, humidity, or chemical exposure. For applications that call for precise measurements, it is indispensable (Gai et al, 2022). Passive sensors, such as thermocouples, piezoelectric sensors, and photodiodes, produce their signals without the need for external energy. We refer to these kinds of sensors as self-generating sensors (Liu & Liu, 2021). Certain qualities, like "range, drift, calibration, sensitivity, selectivity, linearity, high resolution, repeatability, repeatability," and reaction time, are essential for a perfect sensor (Dutta et al., 2021). Due to a multitude of uses, including space, defense, and security, industrial and automotive manufacture, medical diagnosis and treatment, food and environmental quality monitoring, and space and automobile manufacturing, sensor technology advancements have gained significant importance (Manjakkal et al., 2020).



A. bio-macro molecules sensor.



B. Electrical sensor

Figure 5: Metal-Organic Frameworks for bio-macro molecules sensor and Electrical sensor.

Source: (Chang et al., 2022).

A sensor is an apparatus that receives a signal or stimulus and reacts to it. Researchers typically focus on achieving a few of these ideal traits while ignoring the others. One reason for this is that, if an ideal sensor can be made for every given gas, it is a very challenging operation. However, real-world uses typically don't call for sensors to have every ideal feature at once. For instance, a sensor device tracking a component's concentration in an industrial process doesn't require a detection limit at the ppb level, albeit it would be preferable to have a response time of a few seconds or less. Environmental monitoring applications can tolerate a few-minute reaction time, but significantly higher detection limit requirements are

TABLE 4: Type of ideal sensor, such as sensitivity, selectivity, and stability

NO	Type of sensor	Sensitivity	Selectivity	Stability
1	Chemical sensor	Low chemical species concentrations lead to high sensitivity.	High selectivity attained by using particular receptors	Variations in the environment lead to a high stability ratio.
2	Biological sensor	Elevated susceptibility to biological agents	Extremely high biological recognition selectivity	Ratio of moderate to high stability
3	Optical sensor	Light intensity-related high sensitivity	Selectivity attained by means of the target material.	High stability ratio
4	Gas sensor	Incredibly sensitive to find minute quantities	selectively using particular gases	High stability ratio in a range of environmental circumstances
5	Temperature sensor	High susceptibility to minute variations in temperature	Selectivity because they are a universal thermometer	Elevated stability ratio to guarantee precise temperature

Wearable technology devices are appliances that the user can customize to suit their needs. They can be used to measure fitness and wellness metrics or even the end-user's locations (Wang et al., 2020). Usually, the devices have movement sensing and surveillance software installed. New innovations that use synchronized sim cards with users' mobile devices to communicate messages and photos have surfaced recently. These devices are meant to promote customer convenience and give users instant access to information when they need it. The acceptance of wearable sensors by regular users has been greatly aided by their use in the military and medical facilities. Its ability to simplify the process and save costs within the private company has also encouraged its acceptance and manufacturers widespread use by other businesses (Xiao et al., 2022).



Figure 6: This figure explains the Wearable medical and healthcare devices and wearable electrochemical sensors for various regions of the body. Source: (Rong et al., 2021)

Wearable sensors may offer cutting-edge solutions to problems in healthcare. Certain wearable sensors, such as those for continuous physiological monitoring and weight management, are intended for use in the treatment of illnesses and health management. Wearable sensors are also used in patient and illness management. Thus, treatment decisions may be directly impacted by wearable apps. On the other hand, wearable technology, especially in outpatient recovery outside of medical institutions, can improve overall healthcare results while minimizing treatment expenditure (Sharma et al, 2023). The copious volumes of data generated by wearable sensors present a challenge as well as an opportunity for researchers who may someday incorporate more AI techniques into them. Most wearable sensors are still in the prototype stage. To increase the feasibility and functionality of wearable sensors for operational usage, issues with user acceptance, security, morality, and big datasets must be addressed. Thus, my target audience for this study will be those who are being watched over by wearing sensors on their wristwatches, as I will be reviewing wearable sensors applications in the healthcare industry (Pal et al., 2022).

III. APPLICATION OF MOF IN SERS BIOSENSOR

MOFs are widely used in a variety of applications, including medication delivery, environmental protection, adsorbents, supercapacitors, catalysts, and sensors. The spectrum of applications for typical MOFs is limited by their weak electrical conductivity and stability. The use of MOFs for the removal of chlorpyrifos has the benefits of high porosity and adjustable pore size. The abstract makes no mention of disadvantages. The large surface area and tunable porosity of MOFs make them ideal for water filtration (Younas et al. 2020).

3.1 MOF based SERS for drug detection.

A method that shows promise for the quick, accurate, and selective detection of pharmaceuticals is MOF-based SERS. In addition to these conventional domains, MOFs-based materials for SERS sensing have garnered significant interest from scholars and made impressive progress. For instance, the excellent molecular adsorption and aggregation of noble metal and MOF materials results in an effective hotspot area as well as the separation of target and contaminants to limit monitoring interference. More precisely, the cost of the substrate can be significantly decreased by using various MOF materials themselves as an improved substrate for SERS application. identifying drug residues in soil and water to evaluate the efficacy of cleanup activities and the state of environmental pollution. keeping an eye on patients' therapeutic medication levels to guarantee correct dosage and adherence to treatment plans. developing machine learning and other advanced data processing methods to increase detection accuracy and facilitate the interpretation of complex SERS spectra.

3.1.1 MOF based SERS for detection of agricultural residues.

SERS is becoming more and more popular in agricultural applications, such as quality assessment of agricultural products, crop growth monitoring, plant seed screening, and safety control of food varieties, including fruit and vegetable. This is due to the growing demand for online food quality and safety inspection. It is imperative to have a thorough awareness of the latest developments in SERS-based sensor research and application in these areas. Additionally, practical tasks are addressed from various angles, and the characteristics of various SERS-based sensors and their applications in agriculture and related fields are discussed. Important discoveries and conclusions in comparison to many conventional approaches, SERS-based sensors demonstrate unique advantages in terms of detection throughput, cost, efficiency, universality, automation, and portability. Currently, scientists are working to create sophisticated SERS sensing methods for the agricultural industry by using contemporary technologies such as artificial intelligence, machine learning, mobile communication, nanomaterial/nanostructure fabrication, and machine learning (Liu et al., 2022).

According to a study by Xuan et al. (2022), it is important to use scientific technologies in the field of agriculture to identify toxins in food in order to prevent issues with food safety and safeguard public health (Kamal et al., 2023). First, their paper explains how different synthesis techniques affect the characteristics of MOFs. The uses and workings of MOFs-based sensors for different toxin detection are then compiled

and examined (Xuan et al. 2022). However, because the principles of widely used synthesis methods are unclear, the successful fabrication of MOFs with acceptable sensitivity, selectivity, and detection limit remains a huge problem. Having a thorough grasp of the mechanics underpinning the synthesis methods is crucial, as the MOFs used have a significant influence on how effective they are at detecting toxins (Xuan et al. 2020). The metal ions are bridged with different organic ligands in a typical MOF production method to generate crystalline structures with forms that include "tetrahedral, octahedral, cubic, pyramidal, linear, square planar, and trigonal bi-pyramidal (Kamal et al., 2023)." varied metal centers, organic linkers, and solvent combinations can result in varied MOF topologies and food toxin detection capabilities. Commonly utilized techniques that have gained popularity recently include "solvothermal, sonochemistry, microwave-assisted synthesis, and mechanochemistry (Kamal et al., 2023)."

3.1.2 MOF based SERS for detection of antibiotics residues

As veterinary medications, antibiotics have significantly improved the prevention and treatment of disease in the animal breeding sector. Antibiotic abuse during animal feeding frequently results in the buildup of antibiotics in animal food, which when taken by people could have a major negative impact on public health. One of the main concerns for food safety worldwide these days is antibiotic residues in food. To safeguard consumers from consuming tainted goods, quick and reliable analytical methods for identifying these residues must be put into place. Conventional analytical techniques necessitate costly equipment, complex operations, and time-consuming sample preparation. In contrast, SERS offers significantly improved target detection and outstanding sensitivity.

Many antibiotics used to treat bacterial infections and prescriptions used to treat high blood pressure, or hypertension, are examples of treatments that don't need to be monitored. Treatments are considered effective if an infection gets better with an antibiotic or if taking the recommended blood pressure medicine lowers blood pressure (Vandenhoute et al., 2023). Because SERS can offer an ultrasensitive fingerprint spectrum for the quick and noninvasive detection of trace analytes, it has emerged as a viable alternative analytical technique for detecting antibiotic residues. Although SERS is seen to be a promising technique for single-molecule detection, a significant flaw in its use for trace analysis is that it is unable to distinguish target molecules from intricate sample matrices. Researchers have therefore assessed particular target capture medium to investigate the potential of SERS in terms of selectivity in order to get around the Non specificity of SERS in antibiotic detection (Liang et al., 2021).

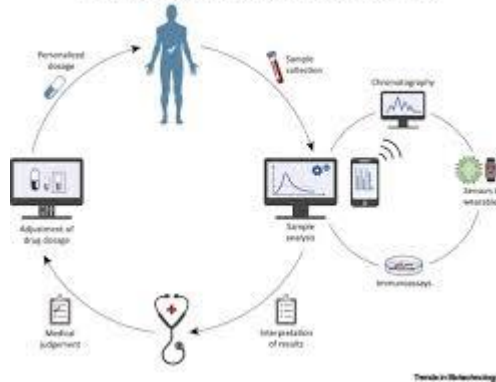
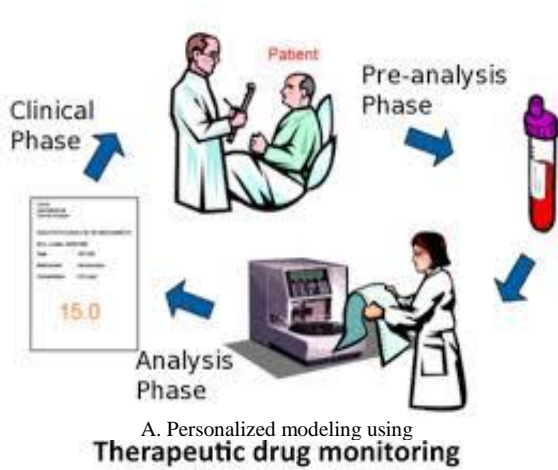
MOFs were investigated by Yang et al. (2021) as "Luminescent Sensors for Environmental Pollutants" (Yang et al. 2021). MOFs are employed in photoluminescence-based biological imaging and sensing. Lanthanides found in metallic clusters are used by a sizable portion of luminous MOFs (Marimuthu et al. 2022). Because MOFs have a large surface area, they can be used in conjunction with SERS to detect traces of antibiotics. Certain antibiotic compounds can be adsorbed selectively onto MOFs thanks to their adjustable pore diameters

and functional groups. keeping an eye on the amount of antibiotic residue in foods like meat, milk, and eggs to make sure it stays within safe bounds. Keeping an eye on the concentration of antibiotics in biological samples to guarantee proper dosage and avoid antibiotic resistance. Subsequent investigations may concentrate on surmounting these obstacles by creating more resilient and consistent MOF-based SERS substrates, investigating novel MOF materials, and combining the technology with transportable sensing devices for field usage. With great promise to improve food safety, MOF-based SERS is a promising method for the sensitive, fast, and selective detection of antibiotic residues (Marimuthu et al. 2022).

3.1.3 MOF based SERS for detection of therapeutic drug

The goal of therapeutic drug monitoring is to keep the blood concentration of a medicine roughly constant by timing the measurement of certain medications and/or the breakdown products of those drugs. A "therapeutic index," which is a ratio between a medication's toxic and therapeutic doses, is often limited for certain of the medications that are subject to monitoring. Different bodily mechanisms begin the process of eliminating a drug as soon as it enters the body. The half-life of a drug is the length of time it takes the body to cut the drug concentration in half from its original value. A medication typically takes five half-lives to entirely exit the body (Liang et al., 2021). To maintain the drug's therapeutic concentration in the body, a person usually needs to take a dose of the medication at regular intervals. For certain medications, it takes more than just administering the prescribed dosage to maintain this constant condition. Depending on age, general health and genetic makeup, each person absorbs, metabolizes, uses, and eliminates drugs at different rates. Other drugs you may be taking in addition to the drug that has to be motioned may interfere and increase or reduce the drug's concentration in the bloodstream. Another name for this is a drug-drug interaction (Marimuthu et al. 2022).

Not every medicine needs to be monitored therapeutically. The majority of medications can be provided in accordance with predetermined dose schedules and have a broad therapeutic index. Although the efficacy of these therapies has been assessed, dosing does not necessitate monitoring medication levels in the blood. Therapeutic drug monitoring adapts to and tracks these shifts. It helps to tailor a dose to meet the individual needs of a patient by detecting when a patient does not take their prescription as directed on a regular basis and the impact of drug interactions, which can result in drug concentrations that are greater or lower than anticipated at a particular dosage.



Source 7: A. (You, 2011).

B. (Ates, 2020)

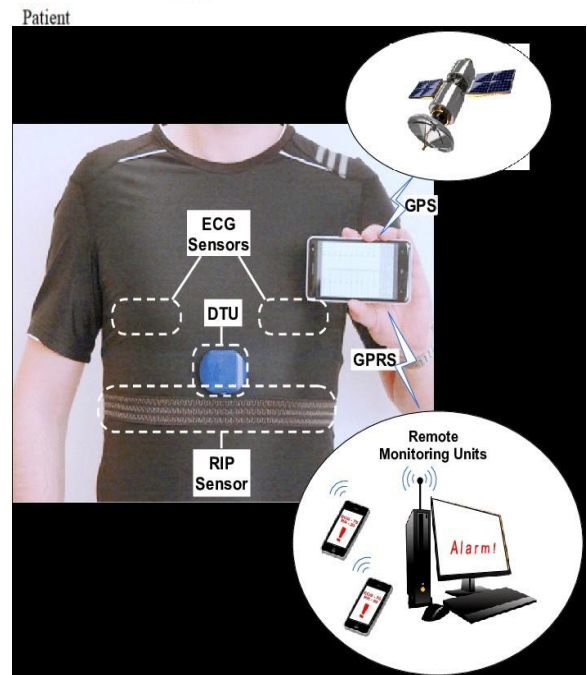
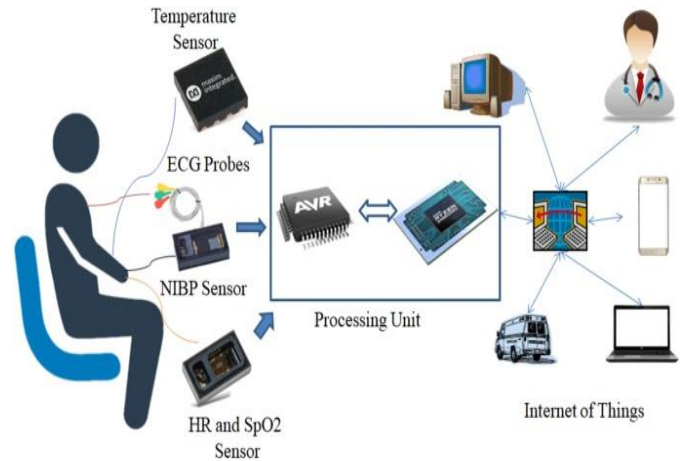


Figure 5: MOF-based physiological monitoring devices. “a) Artery pulse observation. b) wireless physiological parameters monitoring system.”
Source: (Kullayappa et al., 2023)

3.2 MOF-base SERS for biology and life analysis

There are now more opportunities for biological and life science analysis thanks to the integration of MOFs with SERS. By combining the sensitivity and specificity of SERS with the large surface area and tunability of MOFs, the combined method creates effective instruments for the detection and examination of biological chemicals and living forms (Qin et al., 2023).

3.2.1 Physiological monitoring (body fluids, exhaled air physiological indicators)

Physiological monitoring systems evaluate several facets of “human performance and either take corrective action or notify the user to take action.” Furthermore, MOFs have become a potential class of materials with unique features like high surface area, variable porosity, and outstanding sensing capabilities that can be used to fabricate wearable sensors. The development of discreet and sensitive sensors for a range of

healthcare applications, such as medication delivery, physiological monitoring, and illness detection, is made possible by their integration onto wearable substrates (Mamdiwar et al., 2021).

Based on the nanocomposites' piezoelectric performance, the devised apparatus demonstrated good sensitivity for pulse monitoring (Fig. 5a). A different team created a breath sensor for respiratory disease monitoring based on HKUST-1 MOF and MoS₂. The created sensor demonstrated good stability, a quick response time, and efficiency in a range of breathes. Figure 5b depicts the ready device. Because of MOFs' adaptability, scientists have created wearable sensors that can identify and collect indicators related to a person's health (Mamdiwar et al., 2021).

3.2.2 Monitoring of bacteria and pathogens

Food security, environmental safety, and public health all depend on the monitoring of bacteria and diseases. The health of humans is seriously threatened by bacterial illnesses. The goal of developing antibacterial agents is to stop the growth of bacteria, stop them from forming biofilms, and kill them. Metal organic framework (MOF)-based materials have garnered a lot of interest lately for a range of antibacterial applications because of their high specific surface area, high enzyme-like activity, and continuous release of metal ions. Zhang et al., (2022) examined the development of MOFs as antibacterial agents in the recent past, with an emphasis on preparation techniques, basic antibacterial mechanisms, and tactics to strengthen their antibacterial effects. In order to offer potential study avenues in this area, a number of prospects pertaining to MOFs for antibacterial applications are finally put out (Zhang et al., 2022).

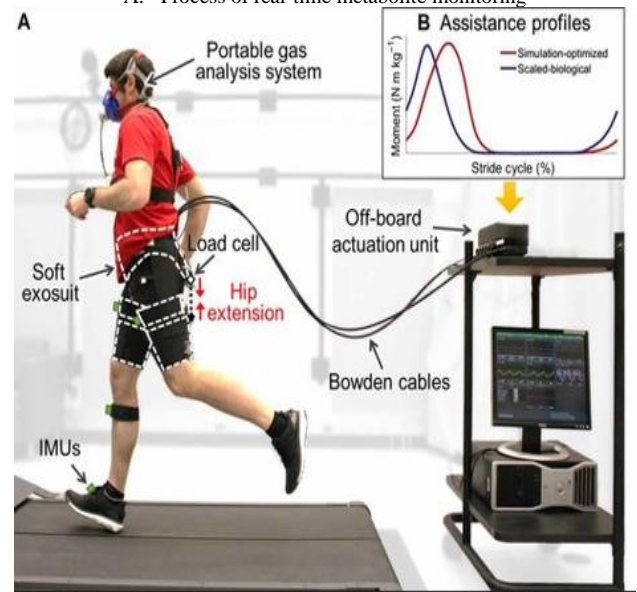
Keeping an eye out for microorganisms in food goods to stop foodborne illness outbreaks. early pathogen identification in clinical specimens. Because MOFs can recognize and capture bacteria, they can help in the diagnosis of infectious disorders. Even at low pathogen concentrations, MOFs' large surface area and porosity enable the capture of pathogens. MOFs can be applied to optical and electrochemical sensing platforms, among others (Zhang et al., 2022).

3.2.3 Metabolic analysis

An important strategy for providing the right medication and diet is prescribing and monitoring. Blood analyses that are intrusive and episodic, frequently necessitating in-person "visits to medical facilities, labor-intensive sample preparation and storage, and delicate instrumentation, are the foundation of the current gold standards in medical evaluation and metabolic testing. The current COVID-19 pandemic is out of control worldwide, so there is a critical need to develop wearable and telemedicine sensors to track people's health and facilitate prompt intervention in home and community-based settings (Mamdiwar et al., 2021)."



A. Process of real-time metabolite monitoring



B. measure metabolism level

Figure 8: Part A of this figure explains how to monitor metabolites in real time, while Part B describes how to assess metabolism using sensors.

From blood analysis to wearable sweat studies, there is a lot of promise for continuous, non-invasive monitoring of physiological indicators that are vital to human health. Unfortunately, "currently reported wearable electrochemical sensors primarily focus on a limited number of analytes, such as electrolytes, glucose, and lactate, due to the lack of a suitable continuous monitoring strategy beyond ion-selective and enzymatic electrodes or direct oxidation of electroactive molecules." Therefore, the majority of nutrients and metabolites in sweat that are clinically significant are rarely studied and are invisible to current wearable sensing devices. Furthermore, the majority of wearable biosensors on the market today require strenuous exercise in order to detect sweat; this method has limited sweat durations and poor sensing accuracy.

The biosensor is comprised of graphene electrodes that are capable of being regenerate in situ multiple times. Precision nutrition applications may be facilitated by metabolite monitoring for the early detection of aberrant health conditions (Zhang et al.,2022).

3.3. Food detection

Foodborne infections have become a global public health concern in the modern era due to the increasing number of cases. Many toxins detection approaches, including innovative sensing technologies like luminescent, electrochemical, colorimetric, and SERS methods, have recently been developed in order to realize the rapid detection of toxins and ensure food safety (Javaid et al., 2021). There are many different types of sensors, and the design and choice of sensing materials used in the sensors is what mostly determines its selectivity, sensitivity, stability, and cost. MOFs are porous hybrid nanoparticles made by bonding carbon bonds to metal ions or cluster centers. When it comes to detecting toxins in food, MOFs have a lot of practical applications. Here, their various structures and functionalities, tunable compositions, and porosities are crucial (Mamdiwar et al., 2021).

Several MOFs have been developed and synthesized so far to detect toxins in food. However, the successful preparation of

MOFs with high sensitivity, selectivity and detection limit remains a major challenge due to the lack of principles of widely used synthesis methods. The review by Xuan et al. (2022) provides an overview of the efficient techniques to guarantee food safety monitoring, as well as the regulated synthesis and characteristics of MOFs that are advantageous for quickly identifying toxins in food. The uses and workings of MOFs-based sensors for different toxin detection are next examined. There is also discussion of prospective prospects, difficulties, and future perspectives (Xuan et al., 2022).

According to research by Shen et al. (2022), stable MOFs under a range of environmental circumstances are essential for outdoor and industrial uses. Innovative synthesis techniques that lessen their negative effects on the environment, like using water as a solvent or using more sustainable, renewable sources for organic linkers, were investigated by Palakollu et al. (2022). the identification and creation of novel MOF structures using organic linkers and as-yet-undiscovered metals. MOF-based sensors for environmental or food quality monitoring in smart packaging applications. These avenues of research not only tackle the current obstacles in MOF-based sensor technology but also open up new possibilities for creative uses (Palakollu, 2022).

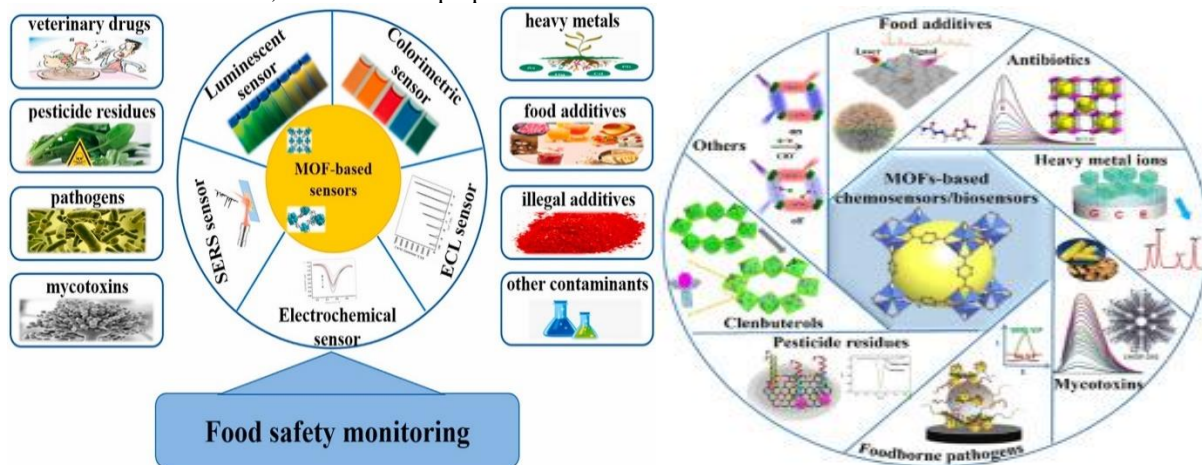


Figure 9: A) MOF Based sensor food safety monitoring. Source: A) Cheng et al, 2021) B) (Zhang et al, 2021)



Figure: Synthesis of MOFs in the detection food toxins

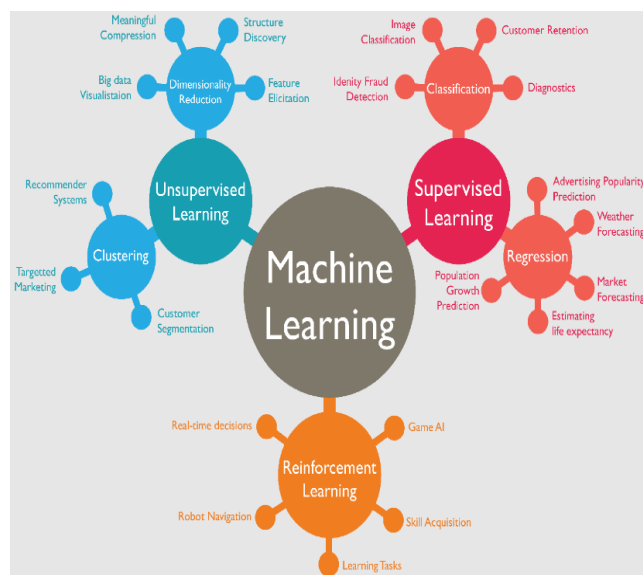
3.4 Pollutant Detection

An essential component of environmental monitoring is pollutant detection, which has become increasingly sensitive and effective thanks to technological developments. Since the beginning of industrialization, the primary concern for humans has been the identification and removal of dangerous pollutants from environmental supplies (Vandehaute et al., 2023). The prompt detection and catalytic transformation of nitroaromatics, which are frequently used as building blocks for explosives and colors, are crucial for environmental science and technology. As a result of worldwide industrialization, nitroaromatics pose serious environmental risks and have been detected in significant amounts in the effluents of several chemical enterprises. Consequently, there has been a great deal of work focused on their quick detection and catalytic conversion to safer entities (Javaid et al, 2021).

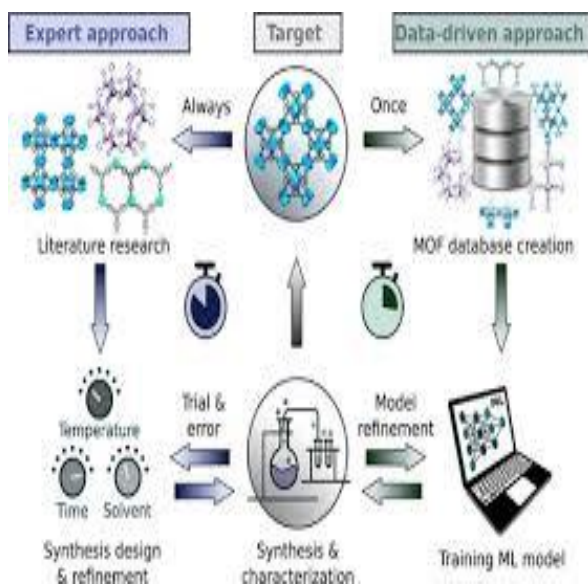
Different metals can be used to catalyze the conversion of nitro groups to amine moieties, depending on the type of reducing agent. MOFs have been a major asset to catalytic processes and reactions in recent years due to their unique catalytic capabilities, which make them attractive to utilize. However, as its optimization has been reliant on cost-effectiveness and recyclability, this has proven to be an obstacle (Yuan et al., 2022). It has been examined and discussed how far MOFs and NMOFs structures have come, as well as how they can be used to convert nitroaromatics into compounds that are beneficial in green surroundings. Study of Ahmadi et al. (2023) studied that, MOFs were seen from a particular perspective as extremely porous materials with a high specific surface area that may be used for nitroaromatic sensing, adsorption, and catalytic conversion (Ahmadi et al, 2023).

3.5 Machine learning

The emergence of ML has been aided by advancements in computational technologies, such as improved data management, retrieval, and storage, in addition to the availability of new and more potent ML algorithms. Large amounts of precise data are made available by new experimental and computational techniques, which is crucial for machine learning applications. Meanwhile, advancements in supercomputing capacities and high-throughput computational workflow managers take place (Yuan et al., 2022).



A. Screening of MOFs by machine learning.



B. Machine learning potentials for MOFs frameworks

Source: A. (Borboudakis, 2017) B. (Vandenhoute et al., 2023)

In materials science, machine learning (ML) has been used for a variety of tasks, such as predicting the properties of polymers, classifying zeolite structures, finding new drugs, identifying peptides as antibacterial agents, designing homogenous catalysts from various ligands, or determining the biological effects of nanoparticles. Comparatively speaking to polymers or zeolites, MOFs are a relatively new class of materials. ML has recently been applied to the field of MOFs in order to identify which materials are best for a given purpose among those that already exist, to find new and better materials from nearly infinite possible structures, and to identify correlations in the data obtained from molecular simulations of MOFs (Yuan et al., 2022).

3.6 Deep learning and Artificial Intelligent

Artificial intelligence's machine learning (ML) branch used a vast amount of data to identify physical laws, both known and unknown, and then made decisions based on autonomous analysis. This made ML a promising field for designing, synthesizing, and characterizing materials as well as a good fit for solving complex problems involving numerous nonlinear processes. Lin et al. (2023) study aims to provide readers a new perspective on how machine learning (ML) has been changing the research and development paradigm of metal-organic frameworks (MOFs). The four main data sources for MOFs and how to select the suitable features are first presented to enable the reader to quickly acquire data and carry out machine learning. By mining the hidden knowledge in data, ML models can predict the physical and chemical properties of MOFs based on their structure, and AI algorithms can work backwards from desired properties to design new MOFs with specific functionalities. Furthermore, Lin et al. (2023) emphasizes the use of ML in the creation of MOFs from the standpoints of intelligent synthesis, rational design, and performance prediction. Lastly, suggestions are made regarding the potential and future difficulties of integrating ML with MOFs from the perspectives of data and algorithms.

Large datasets of current MOFs can be quickly screened by AI to find ones with the best qualities for certain uses. The intricate operating conditions and spatial heterogeneities within metal-organic frameworks (MOFs) pose significant challenges for the computational modelling of physical processes. Although density functional theory (DFT) is computationally prohibitive for systems with dimensions larger than nanometers and picoseconds, it may be able to explain interatomic interactions at the quantum mechanical level. The synthesis and testing of MOFs can be automated by robotics and artificial intelligence (AI), which will speed up experimental research and lower human error. To provide accurate and efficient machine learning parameters for MOFs, Vandenhoute et al. (2023) presented an additional learning method. Using parallelized improved sampling, on-the-fly training, and equivariant neural network potentials, the scheme iteratively explores and learns the phase space at the same time. Accurate and transferable potentials are obtained even for flexible frameworks with numerous structurally distinct phases, using a few hundred single-point DFT evaluations per material. The incremental learning approach can be applied anywhere and could lead to more accurate modelling of framework materials in bigger spatiotemporal windows.

IV. CONCLUSION AND RESPECT

This study aims to elucidate the use of metal organic framework conductivity in SERS detection. In addition to improving the sensitivity of SERS analysis, the use of MOFs in SERS substrate can effectively address the issue of substrate nanoparticle aggregation. The maximal permeability and inner surface area of MOFs are their most notable features. The development of novel materials for energy generation is significantly impacted by MOFs' and their composite materials' multipurpose nature. In conclusion, advances in our understanding of the stability, structure, and characteristics of these materials will promote their development for specialized applications, such as energy storage, industrial processes, medicinal delivery, electrical devices, and environmental cleanup. There are several advantages to using MOFs in the production of sensing materials. Several metals and organic linkers, conformationally flexible linkers, geometrically adjustable inorganic building blocks, and special and highly adjustable physicochemical and structural features like constant porosity and adjustable pore diameter are among the complex structures that fall under this category. Environmental pollutants have thus become a big worry since they possess the ability to irreversibly damage DNA, the nervous system, and the circulatory system. Numerous incurable conditions, such as malignancy, angiocardopathy, organ failure, and deformity, might result from these effects. Effective detection of environmental toxins is vital to preventing them from being a part of daily life. Because of this, MOFs have a bright future in a wide range of industries. Future product sales will be made safer and more ecologically friendly with the successful application of MOFs. This can be achieved by filling in the current knowledge gaps and finishing thorough toxicological evaluations.

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