Engineering the ZIF-8 Pore for Electrochemical Sensor Applications—A Mini Review

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ABSTRACT: Zinc imidazole framework-8, abbreviated as ZIF-8, is a member of the metal organic framework (MOF) family. The chemical architecture of ZIF-8 consists of zinc metal duly coordinated with an organic ligand/fragment, resulting in a cagelike three-dimensional network with unique porosity. Because of such a unique architecture and physicochemical property, ZIF-8 has recently been explored in various applications such as gas storage, catalysis, electrochemical sensing, drug delivery, etc. Electrochemical sensors are currently a hot topic in scientific advances, where small, portable, Internet of Things (IoT)-enabled devices powered by electrochemical output show a newer path toward chemo and biosensor applications. The unique electrochemical property of ZIF-8 is hence explored widely for possible electrochemical sensor applications. The application and synthesis of the bare ZIF-8 have been widely reported for more than a decade. However, new scientific advancements depict tailoring the bare ZIF-8 structure to achieve smart hybrid ZIF-8 materials that show more advanced properties compared to bare ZIF-8. The framework is formed by joining inorganic (metal-containing) units with organic linkers by reticular synthesis, which results in the formation of a cross-linked crystalline network with permanent porosity. This unique porosity of ZIF-8 has recently been utilized for the encapsulation of suitable guest species to enhance the native physicochemical activity of ZIF-8. These engineered ZIF-8 materials show excellent results, especially for electrochemical sensing application. This review is intended to describe the research, including the one done by our group, where the ZIF-8 pore size is used for encapsulating nanoparticles, enzymes, and organic compounds to avail suitable sensor applications.

1. INTRODUCTION

Metal organic frameworks (MOFs) have gained widespread interest for their applications in electrochemical sensing because of their specific design, unique pore size, amenable structure, and increased surface area for absorption. In general, MOFs are a crystalline hybrid material, made of organic and inorganic molecules via molecular self-assembly. MOFs have become a rapidly growing research field since their discovery in the late 1990s by Omar Yaghi at UC Berkeley. Since then, nearly 100,000 different synthetic MOF architectures have been reported so far and the number is increasing rapidly.1−3 MOFs are classified on the basis of their size and dimensions (one, two, and three). Three-dimensional MOFs are fascinating clusters, having unique sizes and shapes along with unique physicochemical properties. There are several 3D MOFs reported in the literature, and among them, zinc-imidazole framework 8 (ZIF-8), also recognized as zeolitic imidazolate frameworks (ZIFs), topologically isomorphic with zeolites, are extensively popular among the scientific community because of their exclusive structural and physicochemical properties.4,5 These chemical entities are topologically isomorphic with zeolites, with a metal-imidazole-metal angle of ~145°, relatively similar to the Si−O−Si angle in zeolite. One of the unique structural properties of ZIF-8 consists of a specific pore size to accommodate significant species including nanomaterial, receptor, and even biomolecules. ZIF-8 possesses inherent porous cavities, having a diameter of ~12 Å along with a narrow aperture of ~3.4 Å which influences the ZIF-8 to uptake guest molecules.6 These attributes allow the use of ZIF-8 for wide applications such as gas storage,7 chemical separation,8 catalysis,9 sensing,10 and drug delivery,11 as illustrated in Figure 1.

ZIF-8 can also be employed as a parent compound for the encapsulation of different hybrid materials such that the new composite compounds can offer advantages for gas storage or increased sensing (catalytic, optical, electrochemical, con-
ductive) properties as compared to the bare ZIF-8. There are various reports where nanoparticles/chemical species have been grafted over the ZIF-8 microstructure for advanced applications. These composites are basically hybrid in nature, showing dual properties of both ZIF-8 and its counterpart. On the other hand, nanoparticle-encapsulated ZIF-8 is a unique hybrid composite that not only shows this hybrid property but also has an enhanced inherent physicochemical property. These species can also be used to protect biomolecules from external stimuli. The unique pore sizes of ZIF-8 act as a safe pocket protected by the framework and hence the encapsulation of nanosized species can be stabilized by in situ encapsulation. One of the unique applications of such hybrid species is in electrochemical sensor applications.

Electrochemical sensors are currently believed to be a popular scientific topic because of their unique properties, low cost, and on-field accessibility compared to the conventional chemical analysis, which is not only expensive but most importantly prohibits the ability of rigorous testing and on-field analysis. Electrochemical sensors, which automatically provide signals that can readily be transformed to concentration terms, are therefore invaluable. A device designed for the detection of any event or changes in its environment and then providing a corresponding electrochemical output such as current or potential is called an electrochemical sensor. In electrochemical sensors, the response is derived from the interaction between the chemistry and electricity. An electrochemical sensor is primarily made of three significant components, analyte, transducer, and a signal processor. These devices basically operate on fundamental electroanalytical principles, for example, conductometry, amperometry, potentiometry, impedometry, etc. Such techniques utilize signal transduction to obtain a corresponding electrochemical output as a function of the potential/current at the electrode−electrolyte interface. There are plenty of electrochemical sensors reported so far, mostly used in biomedical, industrial, energy, Pharma, and environmental applications.

The implications of modern Internet of Things (IoT)-based sensor systems can be understood by the advancements made in the field of machine learning in sensor arrays. One of the unique components of an electrochemical sensor is its transducer. Electrochemical transducers are unique materials that are able to show a signal response upon interacting with the analyte, hence generating a dose-dependent sensory output. There are many materials with different shapes, sizes, and electrochemical properties that have been used as electrochemical transducers, and ZIF-8 is the newest edition.

ZIF-8 possesses a unique electrochemical property that makes it a suitable candidate for electrochemical sensor application, mostly as a transducer. These sensors are very popular but still face several challenges, as pristine ZIF-8 possesses limited physicochemical properties. To enhance the chemical as well as electrochemical activity of pristine ZIF-8, scientists have come up with unique solutions, such as the creation of hybrid nanoparticle@ZIF-8 species, nanoparticle@ZIF-8 composites, and the most advanced nanoparticle-encapsulated ZIF-8. Encapsulation features advanced structural alteration where the ZIF-8 pore size is utilized as a host to accommodate suitable nanoparticles. Reports with such a species are coming out in very large numbers because of its unique features, but there is no review paper reported yet that gathers such works. The aim of this review paper is to accommodate those reports that utilize encapsulating nanomaterials into the ZIF-8 microstructure, especially for sensor application. We have envisioned that the scope of this review paper lies in the intersection of materials science and electrochemical sensing, which we believe will help many readers pursuing advanced research in materials as well as electrochemical sensor studies.

2. STRUCTURAL MANIPULATION OF ZIF-8 MICROSTRUCTURE

Nanoparticle@ZIF-8 composites can be synthesized in two ways: presynthesis modification or postsynthesis modification. The presynthesis method utilizes the generation of tiny and bare nanoparticles or a cluster of nanoparticles that further entrench in the cavities of pristine MOFs. For example, Gu et al. synthesized a gold nanoparticle (AuNP) and ZIF-8 nanocomposite by a simple hydrothermal method and successfully utilized the synthesized hybrid material as an enzyme-free sensor probe for the detection of dopamine. The author utilized quite a few conventional analytical characterizations to investigate the structural properties of the as-synthesized AuNP@ZIF-8 nanocomposite. The synthesized nanocomposite exhibits a superior sensitivity and possesses a low limit of detection (LOD) along with greater selectivity, stability, and reproducibility for the determination of dopamine molecules. The author said the reason for such a unique sensing capability of the probe is the synergetic presence of AuNPs and ZIF-8 together with enhanced surface coverage. The author also examined the inherent pore size distribution of the synthesized Au@ZIF-8 nanocomposite and found that these species consist of homogeneous pores with a concise arrangement and that the existence of micropores due to the adsorption at very low relative pressure results in an increase in volume. The electrochemical characterization of AuNP@ZIF-8 nanocomposite was done in different dopamine concentrations in 0.1 M phosphate-buffered saline using a AuNP@ZIF-8/GCE-modified glassy carbon electrode. Apparently, the as-synthesized AuNP@ZIF-8/GCE showed superi-
or electrochemical catalytic response to dopamine molecule. The result shows a calibrated dose response of a wider concentration range of 0.1 to 50 μM of dopamine. The lower detection limit (LOD) was calculated to be 0.01 μM (S/N = 3) and the sensitivity was calculated to be 6.452 μA mM⁻¹ cm⁻², which makes this fabricated electrochemical sensor superior compared to other reported dopamine sensors. The author proposed that the fabricated sensor shows substantial stability and reproducibility because of the presence of Au nanoparticles and ZIF-8 together. All this reported data by the author directs feasible application of a AuNP@ZIF-8 hybrid composite for a nonenzymatic dopamine sensor. The work is illustrated in Figure 2 below.

In the latter case, the author employed presynthesized nanoparticles, duly stabilized using conventional agents such as, capping agents, surfactants, or even external ions, to develop a hybrid material. One more important aspect of such hybrid material is the packing ability of the pristine MOF, as the hydrodynamic radius of the guest nanoparticle is much larger than the cavity size of the pristine MOF. We will now discuss this in two different sections.

2.1. Tuning the Pore Size of the ZIF-8 Microstructure.

Tuning the pore size of the ZIF-8 microstructure is a leap in the scientific advancement of MOF chemistry, as scientists saw a huge potential for tuning the cavity of ZIF-8 for subsequent applications. ZIF-8 has relatively moderate porous cavities (∼12 Å) along with smaller spaces with a formal aperture of ∼3.4 Å, although it has been calculated that the effective aperture window of the ZIF-8 cavity is ∼7 Å, which elucidates the uptake of guest molecules. Looking into the cavity size and pore aperture, anybody can conclude how any encapsulation became possible. Here comes the interesting fact about the tunability of the intrinsic ZIF-8 pore. It has been observed that in situ encapsulation directs the host molecule to inflate the intrinsic pore so that guest species can be accommodated. Interestingly, it has also been found that such tuning does not impact the basic architecture of ZIF-8, implying that ZIF-8 architecture is indeed sophisticated and customizable compared to other 2D porous materials. Along with the in situ strategy, the encapsulation step is also very sensitive and closely dependent on the concentration of the precursor chemical, along with the solvent used. Li et al. demonstrated tuning of ZIF-8 pores using amorphization. The modified heterostructure, reported by the author displays superior adsorption of C₆H₆, which results in a ~7x higher thermodynamic adsorption selectivity of C₆H₆/C₃H₈ compared to its crystalline counterparts. The graphical representation of the work is depicted in Figure 3. Moggach et al. provided a brilliant study to comprehend the adsorption mechanism of the ZIF-8 microstructure using high-pressure crystallography (HPC) and computational modeling, which clearly helps with understanding the fundamentals of the tunability of the ZIF-8 microstructure at the molecular level. The author performed single-crystal X-ray diffraction studies at high resolution and high pressure, duly combined with GCMC simulations, followed by standard computational density function theory (DFT) calculations to comprehend the gas adsorption behavior of synthesized ZIF-8. The method utilized a cryogenic process, loaded with a specific diamond anvil cell (DAC). The experiment was carried out by imposing extreme pressures to power liquefied gases into the framework. This process enables an increase in the gas population inside the framework architecture. Gases such as oxygen, nitrogen, argon, and methane were successfully bundled into pristine ZIF-8 using pressure transmitting medium (PTM) high-pressure crystallography and the method was utilized to regulate the extent of adsorption sites inside the pristine ZIF-8, at room temperature. The work mainly illustrates the requirement of combining high-quality X-ray experimental data with computational methods. The result depicts the occurrence of a wide variety of behavior for ZIF-8 and suggests that PTMs play a dynamic role in studying the architectural consequences of ZIF-8 upon applying high pressure. They have also calculated the energies of these important crystallographically sites using Grand canonical Monte Carlo (GCMC) simulations. There simulation experiments also added new pages of innovation with the X-ray crystallographic facts of synthesized ZIF-8, combined with the ranking of adsorption sites. The author also observed that some of the sites have low occupancies and the guest molecules are found disordered. The simulations, performed by the author also provided valuable data to confirm the molecular orientation of the guest molecule in the pores. Their effort toward crystallographic experiments, combined with computational modeling, can enable screening of the structural variations of pristine ZIF-8 upon the acceptance of gas molecules using crystallographic tools and allow for thoroughly calculating the most favorable interactions using computational techniques. These studies provide a clear picture to understand the fundamentals of adsorption into flexible porous materials such as ZIF-8 and their use in practical applications.
highlight that ZIF-8 pore sizes are being tuned for subsequent application, especially for gas storage and catalysis. The method used to tune the inherent pore size of ZIF-8 includes applying pressure, amorphization, etc. In another context, there are possibilities not to change the inherent cavity size of pristine ZIF-8, but to utilize it for subsequent applications, especially electrochemical sensing. We will discuss this aspect in the next section.

2.2. Encapsulation of Materials onto the ZIF-8 Pore.

As discussed earlier, the unique pores of ZIF-8 can be utilized for encapsulating suitable species, which may be beneficial for different applications. When we discuss the encapsulation of nanomaterials into the ZIF-8 pore, there are some fundamental properties of the parent compound that need to be considered. First of all, in a few cases, it is observed that the nanoparticles do not actually occupy the inherent void space, rather than being enclosed by the wall of the ZIF-8 framework. There are many such reported heterostructures, but their widespread application is limited. Encapsulation is a unique strategy to fabricate a composite material having unique physicochemical properties. There are many ways one can synthesize composite material and one is using conventional mixing. This strategy to fabricate composite materials often ends up forming heterogeneous phases, which is not very suitable for specific applications such as electrochemical sensing. On the contrary, in situ encapsulation of nanoparticle into suitable material such as ZIF-8 possesses a homogeneous phase and property because of its sensitivity toward electrochemical sensor application. ZIF-8 is highly hydrophobic in nature, which has disadvantages and advantages. The advantage lies in the pristine composite not allowing encapsulated guest species to be soluble in aqueous media, and hence the fabricated sensor becomes highly reproducible and free from damage because of external stimuli. The encapsulated nanoparticles need to be controlled completely within the framework material for researchers to fully understand the well-defined pore structures of ZIF-8. At this moment, this requirement has proven to be challenging to satisfy. Second, it is important to tune the properties such as size, shape, and composition of the nanoparticles to be encapsulated inside ZIF-8 so as to allow uniform composition and controlled behavior of the as-synthesized compound. Third, it is vital that they remain separated so that agglomeration of the guest nanoparticle is substantially reduced to maintain the inherent optical and catalytic properties. Nevertheless, the of nanoparticles agglomeration is a common issue across all the utilized current approaches. Finally, the current synthesis procedure heavily lacks the effective control over the spatial distribution of various types of nanomaterials within the ZIF-8 matrix. The ability of metal nanoparticles has been found to be useful for twin purposes: it sufficiently elevates the active surface area so that the electron tunneling distance is adequately small and it simultaneously increases the surface conductivity, resulting in superior charge mediation at the electrode surface. In general, ZIF-8 has been synthesized by simply mixing together zinc nitrate and 2-methyl imidazole in methanol. Once the framework is formed, it is so rigid that its inner pore cannot be utilized for any such encapsulation.

Hence, only one potential synthetic route has been used to synthesize a foreign-species-encapsulated ZIF-8 hybrid composite and that is the in situ method. In such a method, the desired encapsulating probe is dissolved in either zinc nitrate or 2-methyl imidazole and then mixed together. In that way, one or even two encapsulating probes are able to be encapsulated by mixing two species in two different starting solutions. Figure 4 shows a graphical representation for synthesis of bare ZIF-8 compared to encapsulated ZIF-8. Figure 4 depicts two different synthesis schemes for the preparation of pristine ZIF-8 (left) and nanoparticle encapsulated ZIF-8 (right). The only extra step in the synthetic route is to mix the desired nanoparticle with one of the starting reagents: either 2-methyl imidazole or zinc nitrate. The hydrophobic nature of pristine ZIF-8 along with its small pore size of ∼1.2 nm and its small pore aperture of 0.34 nm inhibits encapsulation of any nanomaterials once it is formed, whereas ZIF-8 extends its pore size to a substantial limit to accommodate nanoparticles with the in situ strategy. It is found that the ZIF-8 utilizes only the number of encapsulating species that it is able to accommodate and the remaining are found at its outer surface, which can be easily removed by washing. The most interesting fact about such tuning of the inherent ZIF-8 pore is that the hybrid species maintains its original structure and physical property. This depicts the efficiency of in situ encapsulation utilizing the inherent ZIF-8 pore to accommodate nanoparticles. The precursor concentration and the solvent also play a major role in preparing such a nanocomposite. Generally, a molar ratio of 1:8 for Zn (II):2-methylimidazole (2-MIM) has been widely utilized, whereas methanol and water are widely used as solvent for ZIF-8 synthesis. Moreover, molar ratios ranging from 1:9 to 1:13 have been utilized to obtain encapsulated ZIF-8. The pictorial depiction of ZIF-8 is presented very
simply, to represent the basic architecture of ZIF-8. The pictorial depiction may not be 100% chemically accurate but our goal is to concentrate onto the intrinsic pore of the ZIF-8 and to visualize that aspect we have represented the ZIF-8 architecture with the simplest possible way. Dong et al. reported for the first-time a glucose oxidase (GOx)- and polyvinylpyrrolidone (PVP)-stabilized Ni–Pd nanostructure encapsulated onto ZIF-8, to be used for glucose sensing application. The author has claimed this is the first effort where both glucose oxidase and nanoparticles can be encapsulated together into the ZIF-8 matrix. An in situ encapsulation strategy has been utilized to encapsulate GOx- and PVP-stabilized Ni–Pd nanoparticles into the ZIF-8 matrix, and subsequent characterization has been shown to prove the hypothesis. The as-synthesized heterostructure is also depicted as a host pocket where biomolecules like GOx are claimed to be stabilized but remain active inside the ZIF-8 pore, showing an excellent enzymatic glucose sensing response. The as-synthesized GOx@ZIF-8(NiPd) showed nanoflower morphology, which suggests the enhanced active surface area shows a superior dual activity of the combined hetero species. The NiPd hollow nanoparticles exhibit peroxidase-like activity, whereas GOx maintained the biochemical enzymatic activity. The author also demonstrated a correlation study using the colorimetric detection of glucose that was fabricated using the GOx@ZIF-8(NiPd)-based multienzyme system followed by a cascade reaction for the visual detection of glucose. Furthermore, the as-synthesized GOx@ZIF-8(NiPd)-modified probe displayed selective biochemical activity because of the presence GOx and showed high electrocatalytic activity for the oxygen reduction reaction (ORR) in the presence of the Ni–Pd nanoparticle. This proposed approach for the construction of an artificial multienzyme system shapes a potential connection of assistance between a nanzyme and a natural enzyme.
enzyme, unifying their properties and functionalities for its utilization in multicatalysis and tandem reactions. The work is illustrated graphically in Figure 5.

Coronas et al. successfully encapsulated a caffeine molecule in one step into the ZIF-8 matrix. This work discusses two different approaches adopted for encapsulation of caffeine inside ZIF-8. Method 1 describes a one-step, in situ presynthesis route, where caffeine is encapsulated in a ZIF-8 precursor and the framework is found to be formed around the preoccupied caffeine molecule. Method 2 described by the author includes a postsynthetic ex situ route for encapsulation of caffeine by contact methods using previously synthesized or purchased ZIF-8. The resultant compounds obtained were analyzed with standard physicochemical characterization techniques such as powder X-ray diffraction (P-XRD), thermogravimetry analysis (TGA), UV–vis spectroscopy, gas chromatography–mass spectra (GC-MS), Fourier transformed IR spectroscopy (FTIR), $^{13}$C NMR spectroscopy, and N 1s X-ray photo electron spectroscopy (XPS) for the comparison of both encapsulation methods. The structural and chemical characterization report points out that that the favored adsorption site of caffeine molecules inside the ZIF-8 framework is near the methyl and CH groups of the 2-MIM ligand. It is also found that a substantial van der Waals interaction takes place between caffeine molecules with both the methyl and the −CH of 2-MIM via CH···O hydrogen bonds with C=O groups, respectively. Moreover, the author has also proposed that the current method yields a substantial guest loading of $\sim 28$ wt % in only 2 h at room temperature and found that the probe has an ability for controlled release of the guest species. The work is illustrated in Figure 6 below.

There are few other reports where in situ encapsulation has been attempted where nanoparticles, biomolecules, and organic/inorganic molecules have been successfully encapsulated into the ZIF-8 matrix. We will discuss those artifacts in light of their application in electrochemical sensing in the upcoming sections.

### 3. ZIF-8-BASED ELECTROCHEMICAL SENSOR

As discussed earlier, ZIF-8 possesses a unique electrochemical property that makes itself a suitable candidate for electrochemical sensor application, mostly as a transducer. The role of an electrochemical transducer is to transduce the chemical interaction at the electrode interface into a meaningful electrical signal. ZIF-8 is fundamentally designated as a semiconducting material with inherent specific capacitance due to the presence of both metal ions as well as organic fragments. Upon interaction with the target analyte, a substantial shift in capacitance has been observed that can be captured as a function of the diffusion current or the impedance output. Because of the porous nature of ZIF-8, it is able to adsorb a small molecule to its interface, resulting in the presence of diffusion kinetics at the electrode–electrolyte interface. Moreover, the encapsulation of electrochemically relevant guest species such as ferrocene and gold nanoparticles enhances the intrinsic diffusion characteristics of the pristine ZIF-8 to a greater extent. This enables the material a suitable transducer for an amperometric sensor, where the diffusion current is measured over time to build a sensor matrix. There are many amperometric sensors built utilizing the electrochemical property of ZIF-8, which includes our works, discussed in two sections.

#### 3.1. Choice of Transducing Materials for Electrochemical Chemo/Biosensing Applications

Electrochemical sensors are a subclass of the sensor family, fundamentally consisting of three distinct components: a transducer, an analyte, and a signal processor. Among these three, the most important piece is the transducer, which is mostly composed of chemicals/materials and transduces a chemical interaction into a meaningful electrochemical signal output. The choice of transducing materials is solely dependent on the nature of the electrochemical reaction, the physicochemical property of the target analyte, the desired output parameter, etc. Electrochemical sensing, and more specifically chemo sensing or biosensing application, requires material for the transducer that can provide an electrochemical response as a function of the
calibrated dose and that possesses selectivity, sensitivity, and many more. Because of these purposes, the choice of transducing material is a critical factor in fabricating a robust electrochemical sensor. The conductivity of pristine ZIF-8 is \( \sim 2 \) nS/cm, which is considered poor conductivity, close to an insulating property. Moreover, pristine ZIF-8 shows poor electrocatalytic activity, which prevents this species from being used for various electrochemical applications. Moreover, the unique porosity of ZIF-8 draws superior adsorption and hence can be utilized in suitable electrochemical applications but strictly by suitable modification. The only characteristic property of pristine ZIF-8 is it is able to transport charges because its metal center is able to hold charges. Literature reports suggest numerous modifications have been attempted to make the ZIF-8 applicable for electrochemical application. To make pristine ZIF-8 suitable for electrochemical application, one should think to obtain superior conductivity and electrochemical property by preparing suitable composites.\(^{21}\) Nanoparticle-encapsulated MOF, which enhances its electrical as well as electrochemical activity to a great extent compared to pristine ZIF-8, was introduced. From highly conducting to semiconducting material, from microstructure to nanomaterials, there are huge numbers of materials and composites used so far for electrochemical sensor applications. Common conducting materials used for electrochemical sensor applications include graphene oxide, carbon nanotubes, gold nanoparticles, boron nitride nanotubes, room temperature ionic liquids, and conducting polymers such as polyaniline. These materials leverage conductivity or diffusion characteristics as a function of sensor response. There are many semiconducting materials also in use for electrochemical sensor applications which include metal oxide/sulfide nanoparticles such as zinc oxide, titanium oxide, molybdenum sulfide, zinc imidazole framework, etc. These materials possess superior capacitance, which makes them suitable candidates to build an amperometric/impedometric sensor. A graphical representation of commonly used conducting and semiconducting materials also in use for electrochemical sensor applications is depicted in Figure 7.

ZIF-8 possesses unique electrochemical properties that makes it a prime candidate as a transducing for electrochemical sensor application. Bulk ZIF-8 crystals demonstrate a high specific surface area of 1200–2100 cm\(^2\)/g, and their pore volumes ranges from 0.1 to 0.8 cm\(^3\)/g, which is nearly 60% of its whole structure, which increases its intrinsic double-layer capacitance and adsorption kinetics too. Such properties of ZIF-8 are actually superior compared to other common MOFs such as ZIF-4, ZIF-7, ZIF-9, ZIF-20, ZIF-68, etc. Conductive materials such as carbon nanotubes, reduced graphene oxides, room temperature ionic liquids, gold nanoparticles, and conducting polymers have conductivity in the range of mS/cm\(^2\) to S/cm\(^2\), whereas ZIF-8 possesses conductivity in the range of \( \mu S/cm^2 \) to mS/cm\(^2\) but possesses a high specific capacitance range from 150 to 350 F/g, which makes this material exquisite for electrochemical application. Moreover, the unique pore size of ZIF-8 can accommodate conducting nanoparticles, which is relevant to electrochemical application and makes such material more valuable toward relevant applications, specifically in the field of electrochemical sensors.\(^{22}\)

Paul et al. utilized the cavity of pristine ZIF-8 to encapsulate gold nanoparticles (AuNPs) as well as glucose oxidase (GOx) to fabricate a mediator-free enzymatic glucose sensor based on DC-based amperometry. An in situ synthesis route is utilized to encapsulate both enzyme and nanoparticle and perform several physicochemical characterizations to investigate the structural characteristics. The material is also characterized electrochemically using cyclic voltammetry (CV) and chronoamperometry (CA) and found to be suitable for biosensing application. The principle of an electrochemical glucose sensor has been depicted below for better understanding with the light of this work. The as synthesized hybrid material was used to fabricate a glucose sensor, utilizing amperometry. The fabricated glucose sensor shows a detection limit as low as 50 nM glucose, endorsing monitoring of glucose using a noninvasive pathway: sweat/saliva. Moreover, the as synthesized material was found to be active as a reversible electrocatalyst, which makes it more fascinating. The as-synthesized hybrid material shows superior electrocatalytic activity toward the reduction of \( \text{H}_2\text{O}_2 \) along with the oxidation of glucose. The reduction of \( \text{H}_2\text{O}_2 \) is found to have occurred because of the material’s participation in a subsequent oxygen reduction reaction (ORR). The author confirmed the glucose oxidation by performing standard spectroscopy analysis by assaying gluconate with glucose oxidase-peroxidase. This reversible redox stability of the FAD/FADH\(_2\) redox couple features the sophisticated fabrication of a label-free glucose sensor reported in the literature.\(^{23}\) The work is illustrated in Figure 8.

**Figure 8.** Synthesis scheme of the in situ encapsulation of glucose oxidase and gold nanoparticles encapsulated into the ZIF-8 matrix, which was utilized as a selective probe in an electrochemical glucose sensor.
The probe shows an interesting reversible property, enables the successive redox of H$_2$O and glucose, and results a mediator-free tandem reaction. In addition to the normal glucose sensor mechanism depicted below, this procedure was a somewhat intriguing and novel method as compared to other conventional sensing mechanisms for the detection of glucose.

\begin{equation}
\beta\text{-d-glucose} + O_2 + H_2O \xrightarrow{GO} \text{gluconate} + H_2O_2
\end{equation}

\begin{equation}
\text{GO}_x\text{(FAD)} + 2H^+ + 2e^- \leftrightarrow \text{GO}_x\text{(FADH}_2\text{)}
\end{equation}

As reported in this work, the detection mechanism involves a decrease in the cathodic current due to the fractional oxidation of hydrogen peroxide and the release of O$_2$ as bubbles in the peroxide solution. The likely electrode reaction for this detection phenomenon is depicted as follows:

\begin{equation}
\text{GO}_x\text{(FAD)} + H_2O_2 \rightarrow \text{GO}_x\text{(FADH}_2\text{)} + O_2
\end{equation}

The reaction is found to be reversible after a certain period, as the dissolved O$_2$ plays the opposite role to regenerate H$_2$O$_2$ by a conventional oxygen reduction reaction, which governs the forward reaction to be sufficiently sluggish.

One of the recent trends in electrochemical biosensors is the development of an electrochemical breathomics platform, which can be built on the basis of the trace level detection of volatile organic compounds (VOCs) present in our breath, which act as biomarkers for specific human disease states. ZIF-8 possesses a unique cavity that makes it a great candidate for the adsorption of gas, VOCs, etc. Using this property, a new episode of ZIF-8-based electrochemical sensor has been reported, especially by our group, discussed in the last section.

3.2. Encapsulated ZIF-8 for Advanced Electrochemical Sensor Application. Zeolitic imidazole framework-8 (ZIF-8), an attractive class of MOFs, can easily be used for the detection of volatile organic compounds and inorganic gases because of its porous nature and increased chemical stability. However, to use them in electrochemical sensing applications, we need to amend for hybrid structure by encapsulation of different nanoparticles inside the ZIF-8 moiety. The resultant hybrid structure can be easily employed for electrochemical sensing, as it will be highly Electrically conductive as well as electrochemically active in nature. Such bifunctional probes have recently been explored for the detection of trace levels of inorganic gases and volatile organic compounds such that the resultant sensor platform can be used for noninvasive breath monitoring application. In a study carried by Banga et al., the researchers synthesized a novel faradaic bifunctional probe by encapsulating ferrocene inside the ZIF-8 cavity and employing the same for electrochemical detection of ammonia to diagnose chronic kidney disease. The pictorial illustration of this work is shown in Figure 9. The successful synthesis of the bifunctional probe was thoroughly characterized using various physicochemical characterizations such as PXRD, FTIR, UV–vis spectroscopy, and dynamic light scattering (DLS) and the morphology was observed using field-emission scanning electron microscopy (FE-SEM). The major phase peaks for ZIF-8 and Fc@ZIF-8 were compared using PXRD spectra. It was observed that all the spectra for the bare compound, ZIF-8, match with that of Fc@ZIF-8, thereby suggesting that the hybrid compound holds the physical property of pristine ZIF-8, and it stays intact after encapsulation of nanoparticles. Also, the findings from FE-SEM suggest that the hybrid Fc@ZIF-8 material has a cubic polyhedral morphology. The author presented this work as a proof of concept for the encapsulation strategy of electrochemically important species (ferrocene) into ZIF-8 and its subsequent application for the detection of trace level ammonia, duly correlated with the early screening of kidney disease from human breath. The author used standard glassy carbon electrodes to evaluate the electrochemical nature of the as-synthesized material, whereas the actual ammonia sensing was performed using an in-house designed and prereported spiral electrochemical notification coupled electrode (SENCE) platform. The diffusion-limited response of the functionalized sensor was studied using chronoanperometry as the transduction mechanism. The sensor displayed a...
linear dose-dependent response in a concentration range of 20 μM to 1 mM ammonia. The cross reactivity was also established by exposing the sensor to various gases and VOCs such as nitrogen, carbon dioxide, nitric oxide, and heptane. The sensor demonstrated a highly selective and specific response for ammonia detection with high statistical significance.

The authors in another study also explored the non-faradaic properties of ZIF-8 by encapsulating a room temperature ionic liquid (RTIL) inside the ZIF-8 cavity. This hybrid synthesis process yields a composite compound that demonstrates dual functionality for gas sensing and is electrochemically active in nature such that it can be used for point-of-care diagnostics. The hybrid nanocomposite is made by encapsulation of [BMIM]BF4 inside the ZIF-8 moiety and is used for the detection of isopentane levels in the lower parts-per-billion range. The author utilized a DC-based chronoamperometry technique as the transduction tool to study the diffusion dynamics of isopentane levels ranging from 8 μM to 0.1 mM. Specifcity studies were performed to understand the selective sensing response of the hybrid nanocomposite. In this study, the authors demonstrated the utility and functionality of an advanced next-generation IoT-based microelectronic prototype, believed to be useful for on-field analysis. The developed prototype serves as a proof-of-concept device that is integrated with the RTIL-coated customized interdigitated electrode for the qualitative assessment of isopentane levels in a manner such that it can be utilized for noninvasive, point-of-care applications toward the prognosis of lung cancer. The hybrid sensing nature of ZIF-8 was investigated in another study, wherein the researchers synthesized a graphene oxide–ZIF-8 composite for sensing carene vapors with a limit of detection of 0.7 μM. This study exploits the properties of graphene oxide and ZIF-8 such that the hybrid compound has high electrochemical activity, and the ZIF-8 inhibits the self-restacking of the graphene oxide sheets such that the resultant compound is highly stable and can be employed for gas sensing. The morphology of the compound was studied using FE-SEM and AFM. After successful synthesis and characterization was complete, the hybrid compound was employed for carene vapor sensing ranging from 0.7 to 4.5 μM. This work performed with the benchtop potentiostat also paved the way for the development of a handheld, IoT-enabled, miniaturized prototype device. The author also showed the device response, integrated with a web app to obtain qualitative assessment in terms of positive or negative screening for carene. The results depicted that the presence and absence groups were significantly dissimilar, which strengthens the null hypothesis that the fabricated prototype can be utilized for the detection of clinically relevant VOCs such as carene. The synthesis of encapsulated ZIF-8 is very scant but has a significant impact in scientific advancement. We have summarized all the relevant work in this area in Table 1.

| sample | modified ZIF-8 | target analyte | transduction mechanism | limit of detection | ref |
|--------|---------------|----------------|------------------------|--------------------|-----|
| 1      | AuNP@ZIF-8    | dopamine       | electrochemical         | 0.01 μM            | 15  |
| 2      | amorphous ZIF-8 (a-ZIF-8) | propylene and propane | adsorption/desorption | 16  |
| 3      | GOx@ZIF-8(NiPd) nanoflower | glucose | colorimetric sensor | 9.2 μM | 18  |
| 4      | GOx@ZIF-8(AuNP) | glucose | amperometry | 50 nM | 23  |
| 5      | Fe@ZIF-8      | ammonia        | chronoamperometry       | 23 μM             | 21  |
| 6      | RTIL@ZIF-8    | isopentane     | chronoamperometry       | 8.3 μM            | 24  |
| 7      | GO/ZIF-8      | carene         | chronoamperometry       | 0.7 μM            | 25  |

4. CONCLUSION AND FUTURE PERSPECTIVES

In this review paper, we have systematically described the structural aspects of ZIF-8 and how it was exploited for relevant applications. Furthermore, we have described the tunability of the ZIF-8 pore size and how different attempts have been made to tune the ZIF-8 cavity. We have also introduced the concepts of encapsulation of materials into ZIF-8 pore and its significance in electrochemical sensing applications. We have cited various important literature regarding the ZIF-8/modified ZIF-8, especially for electrochemical sensor application. We believe this review paper will show new directions toward electrochemical sensor research, especially gas/VOC sensing. The unique physicochemical property of ZIF-8, upon being suitably modified by encapsulating relevant species, not only enhances the sensor performances but also shows promising future in biomedical industry. There is still a lot of scope of research in this field such as the optimization of the structural geometry of encapsulated ZIF-8, the reusability of sensor species by desorption, enhanced electronic stability, device fabrication, etc. We hope this review will lead to such a path of visibility.

ZIF-8 is an interesting material because of its unique physicochemical property. Along with its unique material property, it also possesses an exceptional electrochemical property, which makes it very useful for the fabrication of electrochemical sensor applications. The synthetic aspect of pristine ZIF-8 is now very common in the literature, whereas the synthesis of hybrid ZIF-8 is a new topic and needs to be explored extensively. There is enough scope to study hybrid MOF structures initiated with hybrid ZIF-8. One of the most interesting hybridizations includes utilizing the inherent pore of ZIF-8 to encapsulate foreign species including nanoparticles, enzymes, and organic molecules. The synthesis of such encapsulated MOFs is scant in the literature and hence there is a vast area of research in this field waiting for more scientific advancement. The unique pore of ZIF-8 gives an extreme degree of freedom to safely transport important molecules in biological matrix pointing toward the direction of advanced drug delivery, and for this reason there is a huge scope of research is present in the area of ZIF-8 and its biological application. Moreover, it has been found that the in situ encapsulation is very much dependent on precursor solution, which may be an interesting area of research for materials science personnel. Another important topic, which will be intriguing to investigate, is the native structure of ZIF-8 in terms of its substantial variation to accommodate guest entities. The unique fact emerged from these reports lies around the structural aspect of the modulation of ZIF-8 pore upon in situ encapsulation and strangely the structure remains...
intact upon expanding the pore. This is a unique topic for research, as it can unlock many mysteries regarding the tuning of inherent pore sizes of ZIF-8. ZIF-8 research can also be taken to a new level in electrochemical sensing application. One of the important properties of ZIF-8 is gas adsorption which can be leveraged to build sensitive electrochemical gas, VOC sensor. Along with gas and VOC, ZIF-8 can be employed to build new electrochemical sensors/biosensors because of its unique electrochemical property. Moreover, one of the prime advantages of using this material in biosensor applications is its unique pore, which is able to accommodate an enzyme for glucose sensor applications. Using the same fundamentals, other important biological probes such as antibody, DNA, and aptamer can be encapsulated to build selective impedometric sensor. Overall, there is a huge opportunity ahead in this field, which can be utilized to solve many scientific problems.

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Notes
The authors declare the following competing financial interest(s): S.P. and S.M. have a significant interest in EnLiSense LLC, a company that may have a commercial interest in the results of this research and technology. The potential individual conflict of interest has been reviewed and managed by The University of Texas at Dallas and played no role in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the report for publication.

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