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Abstract

Metal-organic frameworks (MOFs) are a new group of nanoporous materials developed by a typical metal-ligands coordination strategy. MOFs possess a range of unique characteristics, including high porosity, uniform pore structures, ultrahigh active surface area, robust structure, chemical functionality etc. Further, the physicochemical properties of MOFs are tunable based on our requirement, and, therefore, MOFs are afforded to apply in a wide range of applications. Particularly, MOFs have received considerable attention to use as a probe in electrochemical sensor applications. Because, the tunable porosity properties of MOFs offer to detect specific biomolecules as functions similar to enzyme-based sensors. However, the poor conductivity and less stability in aqueous media restrict their usage in many electrochemical applications. In recent years, several nanomaterials have been incorporated into MOFs to improve the conductivity and stability of the MOF-based catalysts. This chapter focus on the recent innovation, development, and improvement of MOFs-based catalysts used for different bioanalytical applications. Further, it described the fundamental electrocatalytic sensing mechanism of the MOF-based probes and summarized the electroanalytical parameters reported for different analytes.

Keywords (separated by '-')

Metal-organic framework - Electrocatalysis - Biosensor - Cancer biomarkers - Nucleic acids - Neurotransmitters

Metal-Organic Framework for Electrochemical Biosensing Applications

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Palraj Kalimuthu, Rasu Ramachandran, and Ganesan Anushya

Contents

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Keywords

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Abbreviations

5-hmC	5-hydroxymethylcytosine DNA
ADRB1	Adrenergic receptor gene
AED	Anodic electrodeposition
AgNPs	Silver nanoparticles
Apt	Aptamer
ATP	Adenosine triphosphate
AuNPs	Gold nanoparticles
BSA	Bovine serum albumin
BTC	1,3,5-benzenetricarboxylic acid
CC	Carbon cloth
CEA	Carcinoembryonic antigen
CPE	Convergent paired electrodeposition
Cu(tpa)	Copper terephthalate
CY	Cysteine
DMF	Dimethylformamide
DMSO	Dimethylsulfoxide
DNA	Deoxyribonucleic acid
DPE	Divergent paired electrodeposition
EIS	Electrochemical impedance spectroscopy
ELISA	Enzyme-linked immunosorbent assays
ERG	Electrochemically reduced graphene
GOD	Glucose oxidase
H_3NBB	$4',4''',4''''$- nitrilotris[1,1′-biphenyl]-4-carboxylic acid
HCV	Hepatitis C virus
HER2	Human epidermal growth factor receptor-2
HT	Hexanethiol
MACP	Ni-MOF/AuNPs/CNTs/PDMS
MB	Magnetic bead

miRNAs	microRNAs
MOFs	Metal-organic frameworks
MPF	Metalloporphyrin framework
mRNA	Messenger RNA
N-CNT	N-doped carbon nanotube
NS	Nanosheet (NS)
PANI	Poly(aniline)
PCPs	Porous coordination polymers
PCR	Polymerase chain reaction
PDMS	Poly(dimethylsiloxane)
PGA	Poly(glutamic acid)
PTK7	Tyrosine kinase-7
r-GO	Reduced graphene oxide
RNA	Ribonucleic acid
siRNAs	Small interfering RNAs
snRNAs	Small nuclear RNAs
SPCE	Screen-printed carbon electrode
ssDNA	Single-stranded oligonucleotide
TCPP	Tetra(4-carboxyphenyl)-porphyrin chloride
TDT	Terminal deoxynucleotidyl transferase
tRNA	Transfer RNA

1 Introduction

Biomolecules involve many essential functions in living organisms, including cell functions, energy production and transport, signal processing, building body mass, etc. However, any alteration in the biomolecules concentrations in body fluids can lead to diseases (Polshettiwar et al. 2021). Therefore, the accurate detection and quantification of biomolecules are very important to ensure the well-being of the cells and organs. Currently, several analytical methods have been used to detect biomolecules in vivo and in vitro, including enzyme-linked immunosorbent assays (ELISA), polymerase chain reaction (PCR), colorimetric electrochemical detection, chromatography-mass spectroscopy, vibrational spectroscopy, etc. (Lequin 2005; Laor et al. 1992; Ajay et al. 2017; Kalimuthu et al. 2012; Liu et al. 2001). Among them, electrochemical methods have received tremendous attention due to their facile fabrication strategy, fast response, cost-effectiveness, high sensitivity, easy operation, and portability (Kalimuthu et al. 2013, 2014). Further, a broad range of nanomaterials has been incorporated into the transducer to improve the performance of the electrochemical biosensor (Chen and Chatterjee 2013; Mahato et al. 2018).

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Metal-organic frameworks (MOFs), also called as porous coordination polymers (PCPs), have represented a new group of nanoporous materials. MOFs are prepared by a unique metal-ligands coordination strategy. The binding of metal ions to the arms of the linker molecules can produce a cage-like porous structure. The generated porous structure can have a massive internal surface area and active sites

(Dhakshinamoorthy et al. 2017; Jiang and Xu 2011). Interestingly, the physicochemical properties of MOFs can be tuned based on our requirement by controlling the metal-ligands coordination process (Czaja et al. 2009). This adaptable structural change of MOFs is more suitable and convenient for different types of functionalization for a wide range of analytes. Further, compared to conventional porous materials (porous oxides and zeolites), MOFs have uniform pore size, ultrahigh active surface area, and a well-connected pore structure. These unique characteristics allow MOFs to utilize numerous applications, including heterogeneous catalysis, biomedical imaging, drug delivery, gas storage, biochemical sensing, etc. (Gulbagca et al. 2019; Keskin and Kizilel 2011; Britt et al. 2008). Considerable works have been published regarding the utilization of MOFs as signal labels in electrochemical sensor applications (Kajal et al. 2022; Zhang et al. 2021). For instance, NiO and Ni nanoparticles embedded MOFs were developed by a facile calcination approach, and the resulting MOFs were successfully applied to quantify glucose concentrations in a human blood sample by an amperometric technique (Shu et al. 2017). Further, Wang et al. developed 2D MOFs nanosheet by a liquid-liquid interfacial reaction approach and the resulting materials were utilized as a probe to sense H_2O_2 in an alkaline medium (Wang et al. 2021). The durability of the fabricated sensor was examined by continuous measuring of H_2O_2 for a prolonged time and found that the catalytic response was almost unaltered up to 20,000 cycles.

However, most MOF-based catalysts lack conductivity and stability in electrolytes, limiting their applications in electrochemical sensors. The leading cause of the poor stability of MOFs in an aqueous medium is attributed to the easily breakable weak metal-ligand coordination bonds by water molecules (Sohail et al. 2018). In addition, ions present in the electrolytes can also be coordinated with the metal nodes, breaking the metal-ligand coordination bonds. Therefore, to improve the conductivity and stability of MOFs, various nanomaterials, including metal nanoparticles and carbon- and graphene-based materials, were integrated into the MOFs (Dhakshinamoorthy et al. 2017; Zhu and Xu 2014). This chapter summarizes the recent development of MOF-based electrocatalysts for biosensing applications. Particularly, the MOF-based biosensors developed for the detection of a range of small biochemical compounds (e.g., H_2O_2, glucose, dopamine, and cysteine), and biological macromolecules (proteins and nucleic acids) are discussed in detail. Further, the sensing mechanism, performance, and electroanalytical parameters of these analytes are outlined in Table 30.1.

2 Synthesis Methods of MOFs

Several approaches are routinely used to develop MOFs, including solvothermal/hydrothermal, slow evaporation, mechanochemical, sonochemical, microwave irradiation, electrochemical, etc. (Zhu and Xu 2014; Stock and Biswas 2012). Among them, the solvothermal/hydrothermal approaches have been extensively used to develop MOFs due to their simple protocol. However, the downside of these approaches is required prolonged time to form MOF crystals. More details of these