Springer Link

1.
2. Cellular and Molecular Bioengineering
3. Article
   Metal Organic Frameworks as Biosensing Materials for COVID-19

- Published: 06 July 2021

Metal Organic Frameworks as Biosensing Materials for COVID-19

- Godwin A. Udourioh,
- Moses M. Solomon &
- Emmanuel I. Epelle

Cellular and Molecular Bioengineering **volume 14**, pages535–553 (2021)Cite this article

Abstract

The novel coronavirus disease (COVID-19) pandemic outbreak is the most startling public health crises with attendant global socio-economic burden ever experienced in the twenty-first century. The level of devastation by this outbreak is such that highly impacted countries will take years to recover. Studies have shown that timely detection based on accelerated sample testing and accurate diagnosis are crucial steps to reducing or preventing the spread of any pandemic outbreak. In this opinionated review, the impacts of metal organic frameworks (MOFs) as a biosensor in a pandemic outbreak is investigated with reference to COVID-19. Biosensing technologies have been proven to be very effective in clinical analyses, especially in assessment of severe infectious diseases. Polymerase chain reactions (PCR, RT-PCR, CRISPR) - based test methods predominantly used for SARS-COV-2 diagnoses have serious limitations and the health scientists and researchers are urged to come up with a more robust and versatile system for solving diagnostic problem associated with the current and future pandemic outbreaks. MOFs, an

emerging crystalline material with unique characteristics will serve as promising biosensing materials in a pandemic outbreak such as the one we are in. We hereby highlight the characteristics of MOFs and their sensing applications, potentials as biosensors in a pandemic outbreak and draw the attention of researchers to a new vista of research that needs immediate action.

Introduction

As at 6.03 pm CEST, 10 March, 2021, there have been 118,684,343 COVID-19 cases, including 2,633,281 deaths confirmed globally by WHO, ECDC, NCDC and John Hopkins University.[120] Since the first case of COVID-19 was detected in China's Hubei province in late 2019, stringent measures such as lockdowns, travel bans, border closure *etc*. have been imposed in order to control or stop the spread of the outbreak, yet the global spread of the virus has continued to record significant increase with attendant global socio-economic burden.[31,88] In fact, reports from WHO and John Hopkins University reveals that the second wave of the outbreak is more devastating thus has left people in great fear.[93]

Sample testing is an essential first step to responding to any pandemic outbreak.[31,45] Diagnosis plays a decisive role in making prompt decisions on detection, contact tracing, isolation, management and treatment of infected persons.[45] However, in the ongoing COVID-19 outbreak, most countries are unable to meet up with the massive diagnostic testing order given by WHO.[79,83,86] This has resulted in a continuous spread due to community transmission.[79,86]

As suggested by WHO, the general benchmark for adequate testing for a positive rate is around 3–12% per 1000 persons.[23] South Korea, Uruguay, Germany and Australia recorded a positive rate of 1% hence being considered as countries with lowest COVID-19 related deaths in the world.[24,37] South Korea was able to achieve the feat through their intensive testing programs occasioned by "drive-through" and "phone booths" tests.[81] On the other hand, countries like Mexico and Nigeria have positive rates of 20–50% (a case is found for every few tests conducted), indicating the unlikelihood of testing widely enough to find all cases.[37] No wonder the number of new confirmed cases keep increasing daily.[120]

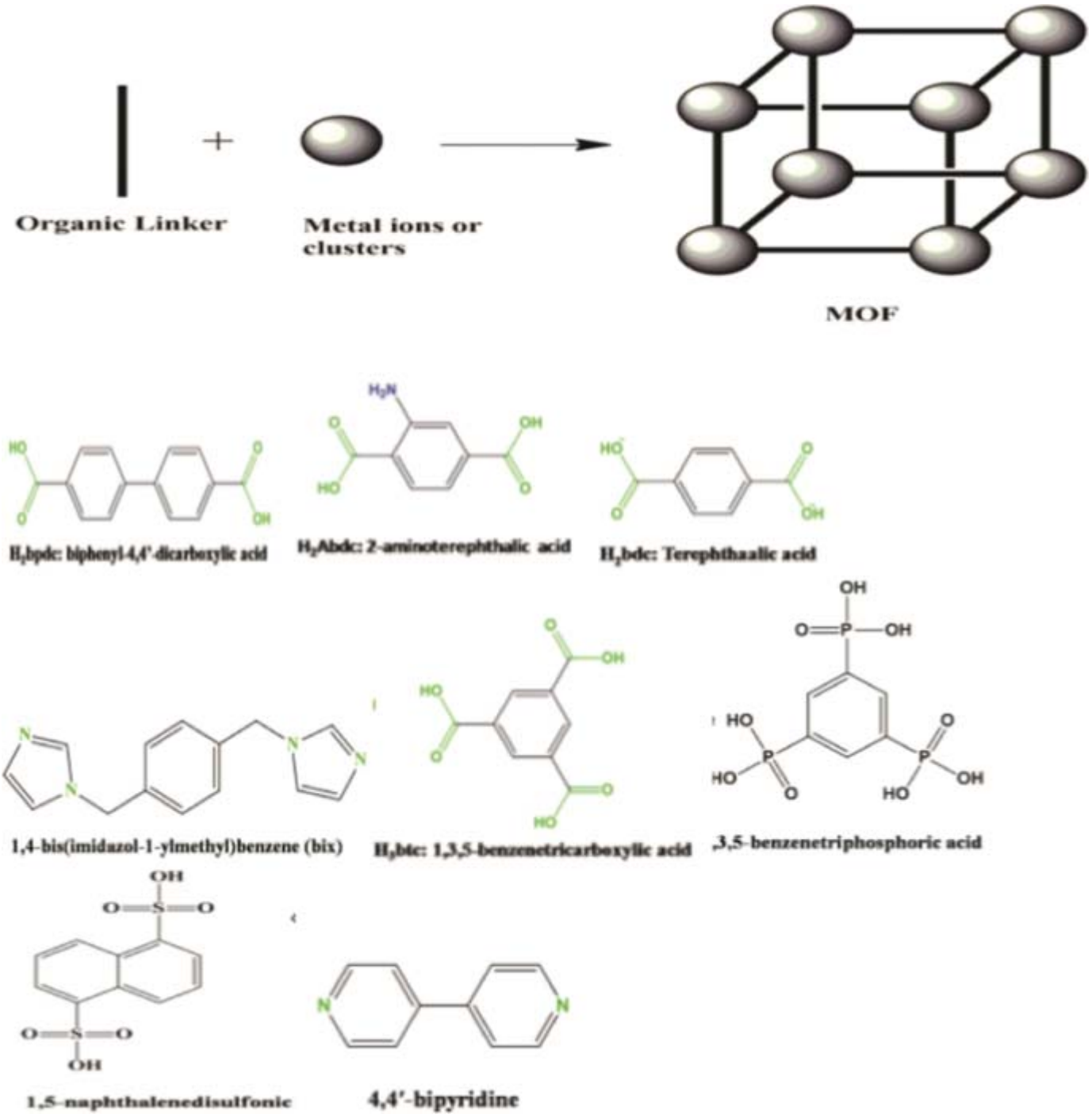
Apart from the disparity in country's political and policy frameworks which may hinder the control of the continuous spread of the pandemic, the biosensing technologies (technologies behind testing and diagnosis) are important factors to consider. A biosensor is a device used for the detection of biological and biochemical agents; employing a biologically derived or a biomimetic recognition element while either undergoing a biochemical reaction (for example, enzyme-based biosensors) or binding the target molecule in a highly specific way. Studies have shown that biosensing devices, materials or technologies for testing infectious diseases or at time of pandemic outbreak must rigorously satisfy requirements of accessibility and affordability, rapidity, high sensitivity and selectivity, robustness, flexibility and simplicity in usage, ability to be mass produced *etc*.[15,81]
The present trend in the daily reports on the confirmed cases of the COVID-19 globally may be a pointer to the fact that the biosensing technologies currently in used for SARS-COV-2 testing are not satisfactory. It is pertinent to review the type of assays, strength and limitations of the commonly used biosensing methods since the pandemic outbreak and explore the potentials of other versatile biosensing materials and technologies such as metal organic frameworks (MOFs) for possibility of development and utilization in solving diagnostic problem associated with the current and future pandemic outbreaks.

Metal Organic Frameworks (MOFs) and Their Characteristics

Metal Organic Frameworks (MOFs) are advanced structures that are highly ordered, porous and customizable. They grow in a crystal form and are extremely flexible, especially when combined with nanoparticles for additional functionality or attributes.[70,137] MOFs are made of metal clusters coordinated with organic linkers to generate a large Langmuir surface area and small-to-medium-sized pores.[54] MOFs are defined as porous structures constructed from the coordinative bonding between metal ions and organic ligands or bridging ligands.[138] The linkers or bridging ligands consist of carboxylates, or anions, such as phosphonate, sulfonate, and heterocyclic compounds while the inorganic units are the metal ions or clusters called secondary building units (SBUs).[138] The coordination number, geometry of the metal ions and

the nature of the functional groups determine the geometry of MOFs. Based on this we have octahedron with six points of extension, trigonal prism with five points, square paddle-wheel (four points), and triangle with three points. Some commonly used metals for synthesis of MOFs include La, Zn, Cr, Cu, In Co, Fe and Ag while some common organic linkers or ligands include 1,4-benzenedicarboxylate or terephthalate moiety (H_2bdc), Benzene-1,3,5-tricarboxylate moiety (H_3btc), 4,4′-biphenyldicarboxylate (H_2bpdc), 1,4-bis(imidazol-1-ylmethyl)benzene (Bix), 1,3,5-benzenetriphosphoric acid, 1,5-naphthalenedisulfonic acid, 4,4-bipyridine, 2,5-dihydroxybenzene-1,4-dicarboxylic acid (H_4dhbdc), 2,6-naphthalenedicarboxylic acid (H_2ndc), adamantane tetracarboxylic acid (H_4atc), 4,4′,4″-benzene-1,3,5-tryyl-benzoic acid (H_3btb).138 Figure 1 shows the typical skeletal structure of MOF and some examples of ligand structures.

Figure 1



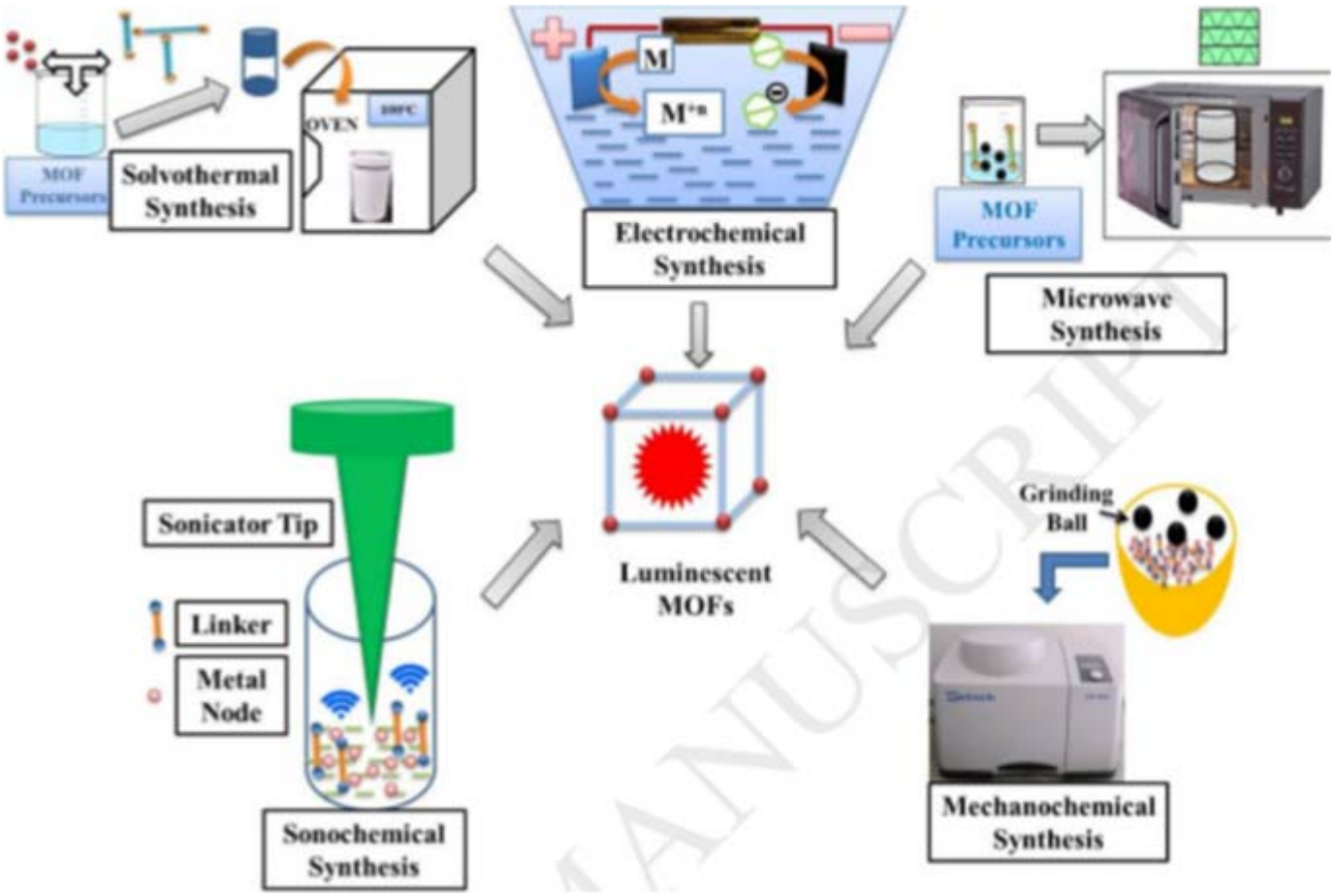
Typical Structure of MOF and Some examples of organic linkers of ligands. Adapted from Sharmin and Zafar.[137] © 2016 The Author(s).

Full size image

MOFs are often synthesized using solvothermal, ionothermal, diffusion, microwave, ultrasound-assisted and template-directed syntheses

methods.33,65,128,143 Figure 2 shows the different synthesis methods for MOFs. MOFs may be classified based on the type of metals and guest species into five categories, *viz*. transition metal MOFs, rare earth metal (REM) MOFs, composite structure MOFs, heterometallic MOFs, and S-block metal MOFs.103 Most MOFs are simply named after the institutions from where they were produced. Examples include MIL-101 [$Cr_3O(OH, F, H_2O)_3(1,4\text{-}bdc)_3$] and other MIL-series named after Materials Institute Lavoisier and commonly used for drug delivery,48 HKUST-1 [$Cu_2(H_2O)_2(CO_2)_4$] named after Hong Kong University of Science and used for adsorption and storage,67 UiO-66-NH_2 named after University of Oslo and used for biosensing 121 and an isoreticular MOF IRMOF-9 [$Zn_4O(bpdc)_3$] used for adsorption and storage.95 In comparison to other high-class materials such as graphenes, carbon nonatubes, gold nonatunes etc., MOFS are emerging class of porous inorganic-organic high profile hybrid compounds which have attracted much attention in recent time due to its stunning properties and wider applications.75 Figure 3 shows comparison of MOFs with other materials in terms of properties.

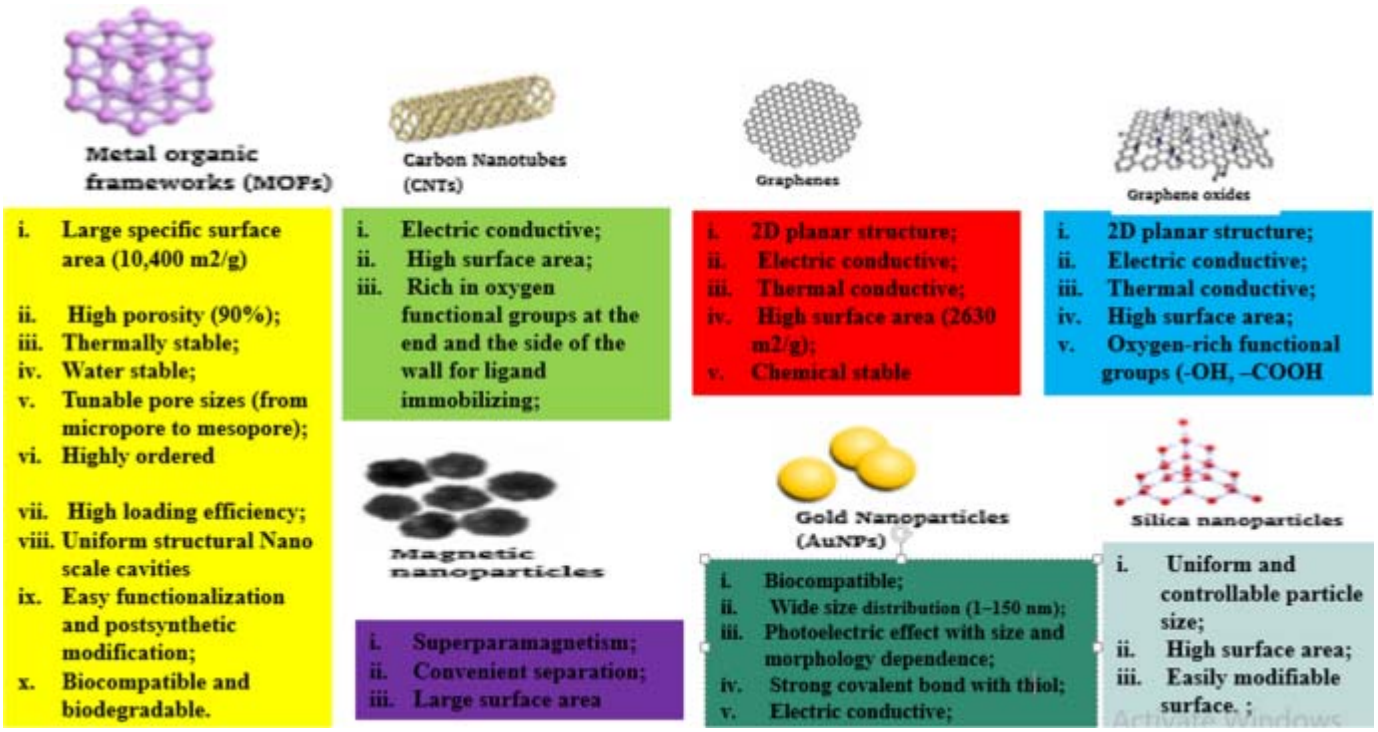
Figure 2



Schematic of commonly used approaches for high-throughput synthesis of MOFs. Reproduced with permission from Kukkar *et al.* 50. © 2018 Elsevier B.V.

Full size image

Figure 3



Stunning Properties of MOF Compared to other high class materials.

Full size image

MOFs as Biosensors

There are different sensing platforms, *viz*. luminescence, surface plasmon resonance, electrochemical, impedance, fluorescence imaging (magnetic resonance imaging MRI), interferometry and solvatochromism.[18,49,69,97,98,142] Recently, MOFs have been explored as Biological and biochemical sensors.[11,36] Hao and Yan[36] developed a lanthanide-functionalized MOF as a fluorescent probe for hippuric acid in urine which was considered as the biological indicators of toluene exposure. The fabricated sensor, according to the authors has several attractive features, including high sensitivity, excellent selectivity, fast response time (~ 1 min), broad linear range (0.05–8.0 mg/mL), and good reversibility and regeneration.[36] The sensor was successfully applied to determination of hippuric acid in human urines with recoveries in the range of 93.5–102.9%. The high porosity, tuneable chemical composition, large surface area, high crystallinity, and potential for post synthetic modification for molecular recognition have made MOFs promising candidates for biosensing

application.[80] Besides, the inherent luminescence of many MOFs have made it useful in sensing platforms.[97,98] Some MOFs and their biosensing applications are summarized in Table [1].

Table 1 Some MOFs and their biosensing applications/detection limits

Full size table

MOFs as Biosensing Materials in Pandemic Outbreaks

Viruses are often the culprit in epidermic and pandemic outbreaks. They are infectious agents, mostly in nanoscale capable of causing various diseases.[82] MOFs have been used as biosensors during epidermic and pandemic outbreaks.

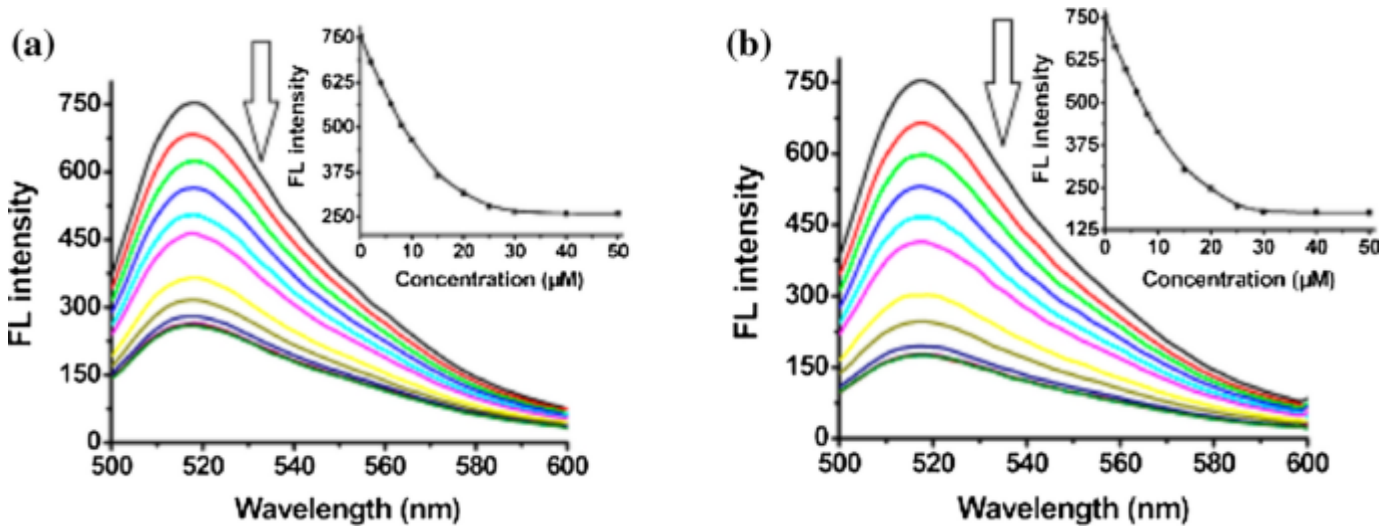
Sensing of Human Immunodeficiency Virus

The retrovirus is a RNA virus whereby its DNA is integrated into its host chromosomal DNA.[8,82] Detection at the early stage of infection may be difficult due to the rare proviral DNA expression in the infected host.[99] The Human Immunodeficiency Virus (HIV), which belongs to the genus Lentivirus within the family of Retroviridae and subfamily Orthoretrovirinae[99] is a human retrovirus. Based on the genetic characteristics and differences in the viral antigens, there are two types of HIV: HIV-1 and HIV-2.[99,100] The HIV-1 type is believed to have evolved from non-human primate immunodeficiency viruses from the Central African chimpanzees (SIVcpz)[30,32] while the HIV-2 type is linked to the West African sooty mangabeys (SIVsm) as the origin.[100] HIV infection results in acquired immunodeficiency syndrome (AIDS), a disease that is associated with the depletion of the CD_4^+T cell of the host.[8] According to the WHO, at the end of 2019, an estimated 38.0 million people are living with HIV and about 33 million deaths have resulted from AIDS-related sicknesses.[118] Because early diagnosis and treatment of HIV can improve survival and reduce morbidity, the Centers for Disease Control and Prevention have recommended routine testing.[4] Examples of such routine test are the western blot and enzyme-linked immunosorbent assay (ELISA) assay.[82] Nevertheless, because of reaction of samples with one or more of the antigens, these methods suffer from some false positive and negative outcomes.[82] Researchers have taken advantage of large specific surface area,

high porosity, fluorescence quenching, high loading efficiency, easy functionalization, and tunable pore properties of MOFs to deploy them in biosensing applications including the biosensing of HIV.

Yang *et al*.130 applied [$Cu_3(Cmdcp)_2(dps)_4.(H_2O)_4(SO_4)$]n for the detection of human immunodeficiency virus-1 double-stranded DNA (HIV-1 ds-DNA). The 3-dimentional structure of the MOF enhanced the distinction between the ds-DNA and ss-DNA molecules. The intrinsic quenching properties of the unsaturated Cu(II) metal ion coordination centre and the conjugated π-electron system of the aromatic groups on both linkers enabled electrostatic and hydrogen bonding *via* π-stacking interactions of the probe DNAs with the MOF, leading to photoinduced electron transfer (PET) fluorescence quenching. There was also a strong interaction between the probe DNA and the target DNA sequence. The non-target DNA sequences were between 50 and 86% less fluorescence than the target sequence in the dsDNA assay due to the diminished effect of its concentration. The probe recorded a high selectivity and 196pM detection limit for the viral dsDNA.130 Notably, the interaction of the MOF [$Cu_3(Cmdcp)_2(dps)_4{\cdot}(H_2O)_4(SO_4)$]n with the complimentary sequences of HIV ds-DNA: carboxyfluorescein FAM-labeled probe ss-DNA, 5′-FAM-TTCTTCTTTTTTCT-3′ (P-DNA-1) and SUDV RNA: 5-FAM-TTAAAAAGTTTGTCCTCATC-3 (P-DNA-2) showed that the fluorescence intensity of the complimentary sequences of both HIV ds-DNA and SUDV RNA decreased upon the addition of the MOF. The quenching efficiency (Q_E%) of both HIV ds-DNA and SUDV RNA sequences were 65 and 76% respectively, indicating that the MOF efficiently quenched the fluorescence of both P-DNA-1 and P-DNR-2 sequences. The fluorescence spectra of both HIV-1 ds-DNA and SUDV RNA complementary sequences are presented in Fig. 4.

Figure 4



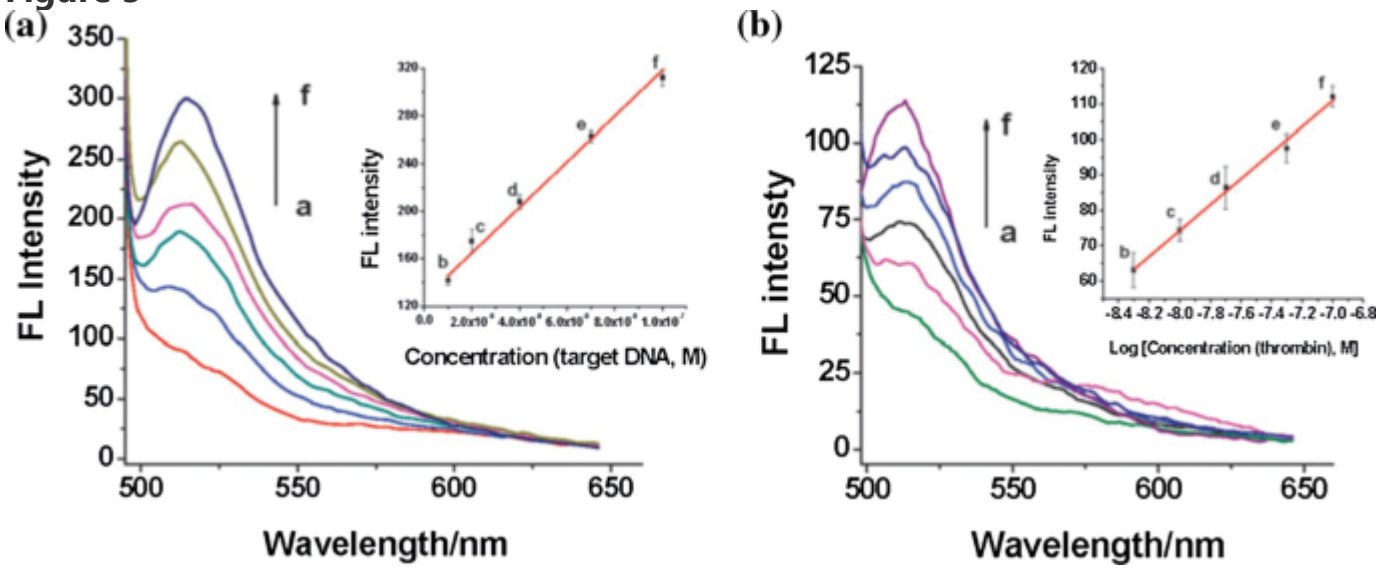
Fluorescence spectra of P-DNA-1 (a, 50 nM) and P-DNA-2 (b, 50 nM) incubated with MOF $[Cu_3(Cmdcp)_2(dps)_4.(H_2O)_4(SO_4)]n$ of varying concentrations at room temperature. Insets: plots of fluorescence intensity at 518 nm versus the concentrations of MOF $[Cu_3(Cmdcp)_2(dps)_4.(H_2O)_4(SO_4)]n$. Reproduced with permission from Yang et al.129. © 2015 American Chemical Society.

Full size image

Zhu *et al.*144 reported the successful application of a 2-D transition metal MOF Cu(H_2dtoa) [i.e. N,N′-bis(2-hydroxyethyl)dithiooxamidatocopper(ii)] for detection of HIV-1 U5 long terminal repeat DNA sequence with detection limits of 3nM, high sensitivity and selectivity. The mechanism of action was enhanced by the intrinsic quenching properties of the metal ion Cu^{2+}, coordination centre and conjugated π-electron system of the dithiooxamide linkers. These properties led to the non-covalent binding of the 6-carboxyfluorescein or FAM single stranded DNA (ssDNA) probe *via* π-stacking interactions with the MOF, which quenched its fluorescence in a process called photo induced electron transfer (PET).80,144 There occurred a turn-on sensing of the viral gene when the target DNA was added due to the release of the probe from the MOF and the fluorescence restoration.80 The probe-MOF exhibits a linear increase in the range of 10–100 nM and the sensor system was believed to be highly sensitive and selective. The Fluorescence spectra of the FAM-labeled DNA–Cu(H_2dtoa) in the presence of different concentrations of target DNA is shown in Fig. 5a. Similarly, Fig. 5b depicts the fluorescence

spectra of the FAM labeled probe DNA 2–Cu(H_2dtoa) in the presence of different concentrations of thrombin.

Figure 5



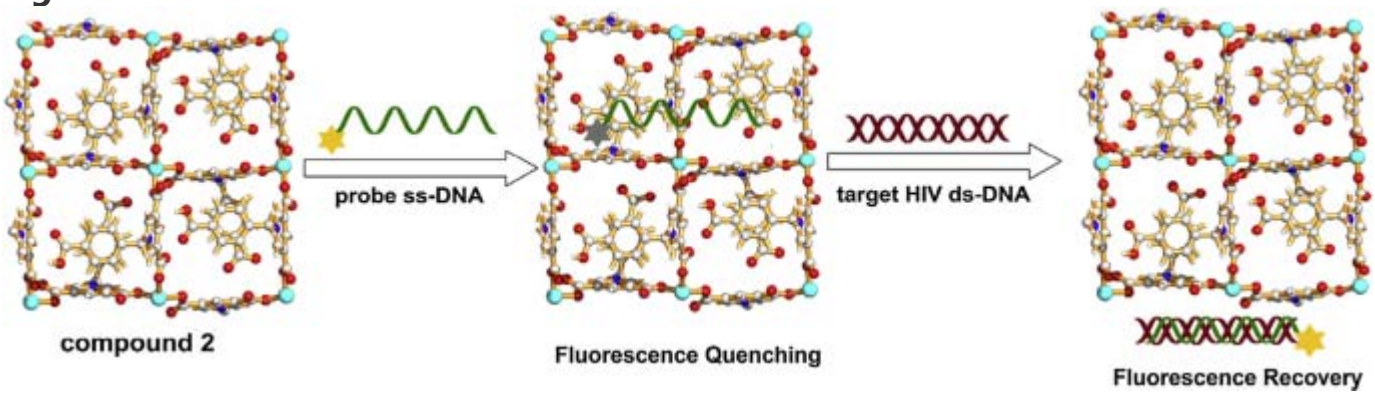
(a) Fluorescence spectra of the FAM-labeled DNA–Cu(H_2dtoa) in the presence of different concentrations of target DNA. Inset: plot of fluorescence intensity vs. concentrations of target DNA. (b) Fluorescence spectra of the FAM labeled probe DNA 2–Cu(H_2dtoa) in the presence of different concentrations of thrombin. Inset: plot of fluorescence intensity vs. logarithm of concentrations of thrombin. The concentration of dye-labeled probe DNA 1and DNA 2 is 50 nM. Reproduced with permission from Zhu *et al.*143 (© Royal Society of Chemistry 2013) and Miller *et al.*80 (© 2016 The Authors).

Full size image

Zhao *et al.*140 isolated six water-stable zinc(II) zwitterionic carboxylate compounds with 1D chain, 2D networks and 3D MOFs structures through the coordination reaction of $\{Na_3[Na_9(Cbdc\text{-}p)_6(H_2O)_{18}]\}_n$ with $Zn(NO_3)_2{\cdot}6H_2O$. Among the isolated compounds, the 2D sheet, $\{[Zn(Cbdcp)(bpe)_{1/2}]{\cdot}2H_2O\}n$ compound was found to efficiently quenched the fluorescence of P-DNA. The authors had selected a FAM-labeled P-DNA 50-FAM-TTCTTCTTTTTTCT-30 as complementary sequences for HIV ds-DNA and noticed that the fluorescence intensity of P-DNA decreased upon the addition of $\{[Zn(Cbdcp)(bpe)_{1/2}].2H_2O\}n$ compound. The quenching efficiency (QE%) was 73% with the saturation concentration calculated as 10mM. It was proposed that the compound formed a noncovalent complex P-DNA@2 system with its functional aromatic

rings, the carboxylic acid groups, the positively charged pyridinium and Zn^{2+} cation centers and 2D plane structure (Fig. 6).

Figure 6



Proposed mechanism for the detection of target HIV ds-DNA sequences based on a fluorescent biosensor formed from compound 2 and fluorophore-labeled probe ss-DNA. Reproduced with permission from Zhao *et al.*139. © 2016 Published by Elsevier B.V.

Full size image

Sensing of Ebola Virus (Sudan Virus) RNA Sequence

Ebola virus disease (EVD), formerly known as Ebola haemorrhagic fever is a viral hemorrhagic fever of humans and other primates that first appeared in 1976 in two simultaneous outbreaks.44 EVD is caused by Ebola viruses (EBOV), single-strand RNA viruses of the family Filoviridae.78 There are about five species of EBOV, namely Zaire, Bundibugyo, Sudan, Reston and Tai Forest. Although the fatality rate varies from specie to specie of EVD, it is in the range of 50–90%.44,104 The chronology of previous Ebola virus disease outbreaks and the actual fatality rate can be found in the WHO recent reports.119 EBOV infects its host cell by attaching to the receptors through the GP glycoprotein and getting endocytosed in host vesicles.44 The C-type lectins DCSIGN and DC-SIGNR is pivotal in the process as they bind to Ebola glycoproteins.44 The entry pathway of EBOV into host cell, the binding to cell-surface receptors, the slashing of the viral GP1 protein into N-terminal fragment Ebola within the endosome, and the digestion of cathepsin B into GP2 are illustrated in Fig. 7. The laboratory diagnosis of EBOV includes polymerase chain reaction, enzyme-linked immunosorbent assay (ELISA), antigen ELISA,

immunohistochemistry, fluorescence assay, electron microscopy, indirect immunofluorescence assay (IFA), immuno-blot (western blot), biosensors SPR, QCM, optical, and DNA-based fluorescence nanobarcodes methodology.[19,44,104]

Figure 7

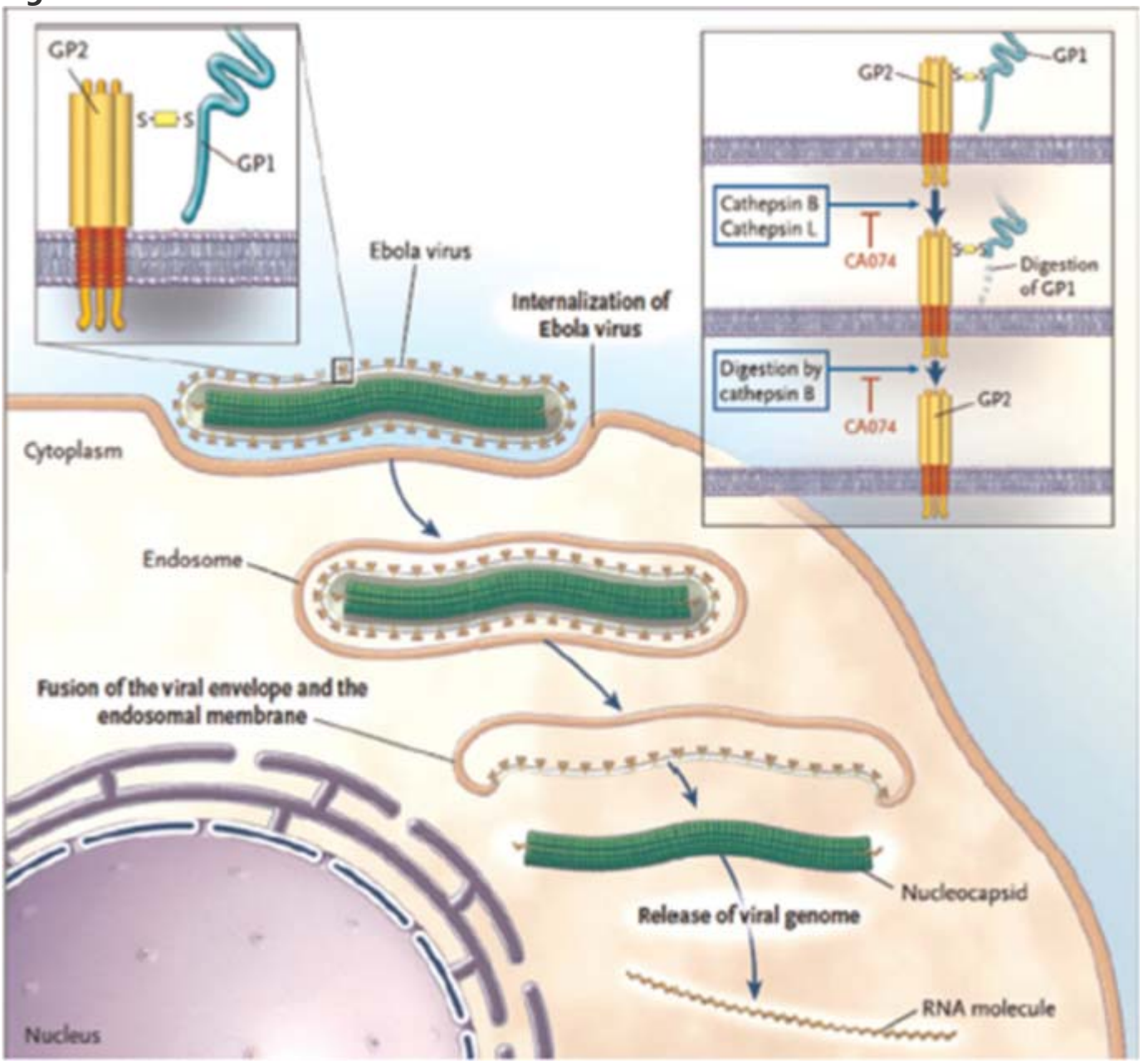


Illustration of the entry pathway of Ebola Virus into host cell [44]. The process begins with the EBOV getting attached to the cell surface receptors and internalizing in the endosome.[44,78,104,118] In the endosome, the endosomal proteases (cathepsin B and cathepsin L) fragment the viral GP1 protein into N-terminal 44,77,103. Cathepsin B thereafter digests it into GP2 that helps in the

fusion of the viral envelope and the endosomal membrane.[44,78,104] The viral genome is then release into the cytoplasm.[44,78,104] Upon release, the proteolysis of GP1 is inhibited by CA074[44,78,104] paving way for the progression of the infection. The figure was reproduced with permission from Kaushik *et al*.[44] © 2015 Elsevier B.V.

Full size image

References

1. (ECDC), E.C. for D.P. and C. Diagnostic testing and screening for SARS-CoV-2., 2020 [cited 2021 Mar 11]. https://www.ecdc.europa.eu/en/covid-19/latest-evidence/diagnostic-testing.
2. Ai, T., *et al*. Correlation of chest CT and RT-PCR testing for coronavirus disease 2019 (COVID-19) in China: A report of 1014 cases. *Radiology* 296:E32–E40, 2020. https://doi.org/10.1148/radiol.2020200642.

Article **Google Scholar**

3. AlHaydar, M., H. R. Abid, B. Sunderland, and S. Wang. Multimetal organic frameworks as drug carriers: Aceclofenac as a drug candidate. *Drug Des. Dev. Ther.* 13:23–35, 2019.

Article **Google Scholar**

4. American College of Obstetricians and Gynecologists. Routine human immunodeficiency virus screening. Committee opinion No. 596. *Obs. Gynecol.* 123:1137–1139, 2014.

Article **Google Scholar**

5. Bej, A. K., M. H. Mahbubani, R. M. Atlas, and R. K. Salkl. Amplification of nucleic acids by polymerase chain reaction (PCR) and other methods and their applications. *Crit. Rev. Biochem. Mol. Biol.* 26:301–334, 1991.

Article **Google Scholar**

6. Benzigar, M. R., R. Bhattacharjee, M. Baharfar, and G. Liu. Current methods for diagnosis of human coronaviruses: pros and cons. *Anal. Bioanal. Chem.* 2020. https://doi.org/10.1007/s00216-020-03046-0.

Article **Google Scholar**

7. Bhalla, N., P. Jolly, N. Formisano, and P. Estrela. Introduction to biosensors. *Essays Biochem.* 60:1–8, 2016.

Article **Google Scholar**

8. Boeke, J. D., and K. B. Chapman. Retrotransposition mechanisms. *Curr. Opin. Cell Biol.* 3:502–507, 1991.

Article **Google Scholar**

9. Broughton, J. P., *et al*. CRISPR–Cas12-based detection of SARS-CoV-2. *Nat. Biotechnol. Nature Research* 38:870–874, 2020. https://doi.org/10.1038/s41587-020-0513-4.

Article **Google Scholar**

10. Bruch, R., *et al*. CRISPR/Cas 13a-powered electrochemical microfluidic biosensor for nucleic acid amplification-free miRNA diagnostics. *Adv. Mater.* 31:1905311, 2019.

Article **Google Scholar**

11. Cai, H., Y. L. Huang, and D. Li. Biological metal–organic frameworks: Structures, host–guest chemistry and bio-applications. *Coord. Chem. Rev.* 15:207–221, 2019.

Article **Google Scholar**

12. Cai, S., J. Yan, H. Xiong, Y. Liu, D. Peng, and Z. Liu. Investigations on the interface of nucleic acid aptamers and binding targets. *Analyst.* 22:5317–5338, 2018.

Article **Google Scholar**

13. Cavka, J. H., *et al*. A new zirconium inorganic building brick forming metal organic frameworks with exceptional stability. *J. Am. Chem. Soc.* 130:13850–13851, 2008. https://doi.org/10.1021/ja8057953.

Article **Google Scholar**

14. Chen, G., *et al*. In vitro toxicity study of a porous iron(III) metal-organic framework. *Molecules* 24:1211, 2019.

Article **Google Scholar**

15. Chen, L., G. Zhang, L. Liu, and Z. Li. Emerging biosensing technologies for improved diagnostics of COVID-19 and future pandemics. *Talanta* 225:2021.

Article **Google Scholar**

16. Chen, M., N. Gan, T. Li, Y. Wang, Q. Xu, and Y. Chen. An electrochemical aptasensor for multiplex antibiotics detection using Y-shaped DNA-based metal ions encoded probes with NMOF substrate and CSRP target-triggered amplification strategy. *Anal. Chim. Acta* 968:30–39, 2017.

Article **Google Scholar**

17. Chen, Y.-A., *et al*. Fast and effective turn-on paper-based phosphorescence biosensor for detection of glucose in serum. *J. Chin. Chem. Soc.* 63:424–431, 2016.

Article **Google Scholar**

18. Cheng, Y. H., *et al*. Metal-organic framework-based microfluidic impedance sensor platform for ultrasensitive detection of perfluorooctanesulfonate. *ACS Appl. Mater. Interfaces* 12:10503–10514, 2020. https://doi.org/10.1021/acsami.9b22445.

Article **Google Scholar**

19. Coarsey, C. T., N. Esiobu, R. Narayanan, M. Pavlovic, H. Shafiee, and W. Asghar. Strategies in Ebola virus disease (EVD) diagnostics at the point of care. *Crit. Rev. Microbiol.* 14:779–798, 2017.

Article **Google Scholar**

20. Cui, F., and H. S. Zhou. Diagnostic methods and potential portable biosensors for coronavirus disease 2019. *Biosens. Bioelectron.* 165:112349, 2020.

Article **Google Scholar**

21. de Eguilaz, M. R., L. R. Cumba, and R. J. Forster. Electrochemical detection of viruses and antibodies: A mini review. *Electrochem. Commun.* 22:106762, 2020.

Article **Google Scholar**

22. Dincer, C., *et al*. Disposable sensors in diagnostics, food, and environmental monitoring. *Adv. Mater.* 31:1806739, 2019.

Article **Google Scholar**

23. Divya, S., R. Katz, E. Graeden, D.A. and T.T. Evidence Roundup: Why positive test rates need to fall below 3% - Harvard Global Health Institute. Pandemics. 2020. https://globalhealth.harvard.edu/evidence-roundup-why-positive-test-rates-need-to-fall-below-3/.

24. Dong, E., H. Du, and L. Gardner. An interactive web-based dashboard to track COVID-19 in real time. *Lancet Infect. Dis.* 157:533–534, 2020.

Article **Google Scholar**

25. Du, M., *et al*. Self-assembled fluorescent Ce(III) coordination polymer as ratiometric probe for HIV antigen detection. *Anal. Chim. Acta* 1084:116–122, 2019.

Article **Google Scholar**

26. Du, P., *et al*. Tumor microenvironment and NIR laser dual-responsive release of berberine 9-O-pyrazole alkyl derivative loaded in graphene oxide nanosheets

for chemo-photothermal synergetic cancer therapy. *J. Mater. Chem. B* 8:4046–4055, 2020.

Article **Google Scholar**

27. Dunne, M., B. Epp-Ducharme, A. M. Sofias, M. Regenold, D. N. Dubins, and C. Allen. Heat-activated drug delivery increases tumor accumulation of synergistic chemotherapies. *J. Control. Release* 308:197–208, 2019.

Article **Google Scholar**

28. Emery, S. L., *et al*. Real-time reverse transcription-polymerase chain reaction assay for SARS-associated coronavirus. *Emerg. Infect. Dis.* 10:311–316, 2004.

Article **Google Scholar**

29. Fang, Y., *et al*. Sensitivity of chest CT for COVID-19: Comparison to RT-PCR. *Radiology* 2020. https://doi.org/10.1148/radiol.2020200432.

Article **Google Scholar**

30. Faria, N. R., *et al*. The early spread and epidemic ignition of HIV-1 in human populations. *Science* 346:56–61, 2014.

Article **Google Scholar**

31. Fauci, A. S., H. C. Lane, and R. R. Redfield. Covid-19—Navigating the uncharted. *N. Engl. J. Med* 382:1268–1269, 2020.

Article **Google Scholar**

32. Gao, F., *et al*. Origin of HIV-1 in the chimpanzee Pan troglodytes troglodytes. *Nature* 397:436–441, 1999.

Article **Google Scholar**

33. Gao, J., C. Huang, Y. Lin, P. Tong, and L. Zhang. In situ solvothermal synthesis of metal-organic framework coated fiber for highly sensitive solid-phase

microextraction of polycyclic aromatic hydrocarbons. *J. Chromatogr. A* 1436:1–8, 2016.

Article **Google Scholar**

34. Habli, Z., S. Saleh, H. Zaraket, and M. L. Khraiche. COVID-19 in-vitro diagnostics: state-of-the-art and challenges for rapid, scalable, and high-accuracy screening. *Front. Bioeng. Biotechnol.* 8:605702, 2021.

Article **Google Scholar**

35. Hajian, R., *et al*. Detection of unamplified target genes via CRISPR–Cas9 immobilized on a graphene field-effect transistor. *Nat. Biomed. Eng.* 3:427–437, 2019.

Article **Google Scholar**

36. Hao, J.-N., and B. Yan. Recyclable lanthanide-functionalized MOF hybrids to determine hippuric acid in urine as biological indices of toluene exposure. *Chem. Commun.* 00:1–3, 2013.

Google Scholar

37. Hasell, J., *et al*. A cross-country database of COVID-19 testing. *Sci. Data* 7:1–7, 2020. https://doi.org/10.1038/s41597-020-00688-8.

Article **Google Scholar**

38. He, F., *et al*. Aptamer-based targeted drug delivery systems: Current potential and challenges. *Curr. Med. Chem.* 27:2189–2219, 2018.

Article **Google Scholar**

39. Ho, M. L., *et al*. The construction of glucose biosensor based on crystalline iridium(III)-containing coordination polymers with fiber-optic detection. *Sens. Actuators B Chem.* 190:479–485, 2014.

Article **Google Scholar**

40. Huang, Z., *et al*. Ultra-sensitive and high-throughput CRISPR-p owered COVID-19 diagnosis. *Biosens. Bioelectron.* 164:2020.

Article **Google Scholar**

41. Jia, Z., *et al*. $NiCo_2O_4$ spinel embedded with carbon nanotubes derived from bimetallic NiCo metal-organic framework for the ultrasensitive detection of human immune deficiency virus-1 gene. *Biosens. Bioelectron.* 133:55–63, 2019.

Article **Google Scholar**

42. Joshi, S. R., A. Sharma, G. H. Kim, and J. Jang. Low cost synthesis of reduced graphene oxide using biopolymer for influenza virus sensor. *Mater. Sci. Eng. C* 108:110465, 2020.

Article **Google Scholar**

43. Kailasa, S. K., *et al*. An overview of molecular biology and nanotechnology based analytical methods for the detection of SARS-CoV-2: promising biotools for the rapid diagnosis of COVID-19. *Analyst* 146:1489–1513, 2021.

Article **Google Scholar**

44. Kaushik, A., S. Tiwari, R. DevJayant, A. Marty, and M. Nair. Towards detection and diagnosis of Ebola virus disease at point-of-care. *Biosens. Bioelectron.* 18:254–272, 2016.

Article **Google Scholar**

45. Kelly-Cirino, C. D., *et al*. Importance of diagnostics in epidemic and pandemic preparedness. *BMJ Glob. Heal.* 4:1179, 2019.

Google Scholar

46. Kim, J., *et al*. Heteroassembled gold nanoparticles with sandwich-immunoassay LSPR chip format for rapid and sensitive detection of hepatitis B virus surface antigen (HBsAg). *Biosens. Bioelectron.* 107:118–122, 2018.

Article **Google Scholar**

47. Koczula, K. M., and A. Gallotta. Lateral flow assays. *Essays Biochem.* 60:111–120, 2016.

Article **Google Scholar**

48. Kotzabasaki, M., and G. E. Froudakis. Review of computer simulations on anti-cancer drug delivery in MOFs. *Inorg. Chem. Front.* 85:1255–1272, 2018.

Article **Google Scholar**

49. Kreno, L. E., J. T. Hupp, and R. P. Van Duyne. Metal-organic framework thin film for enhanced localized surface Plasmon resonance gas sensing. *Anal. Chem.* 82:8042–8046, 2010.

Article **Google Scholar**

50. Kukkar , D., Vellingiri, K., Kim, K.-H., A. Deep. Recent progress in biological and chemical sensing by luminescent metal-organic frameworks. Sens. Actuators B: Chem. 273:1346–1370, 2018. https://doi.org/10.1016/j.snb.2018.06.128

51. Kubo, S., *et al*. Development of an Automated Chemiluminescence Assay System for Quantitative Measurement of Multiple Anti-SARS-CoV-2 Antibodies. *Front. Microbiol.* 11:2021.

Article **Google Scholar**

52. Kumar, P., A. Deep, A. K. Paul, and L. M. Bharadwaj. Bioconjugation of MOF-5 for molecular sensing. *J. Porous Mater.* 21:99–104, 2014.

Article **Google Scholar**

53. Le Bonniec, B. F. Thrombin Handbook of Proteolytic Enzymes. Amsterdam: Elsevier, pp. 2915–2932, 2013.

Book **Google Scholar**

54. Lee, Y. J., Y. J. Chang, D. J. Lee, and J. P. Hsu. Water stable metal-organic framework as adsorbent from aqueous solution: A mini-review. *J. Taiwan Inst. Chem. Eng.* 19:176–183, 2018.

Google Scholar

55. Leeflang, M. M. G., A. W. S. Rutjes, J. B. Reitsma, L. Hooft, and P. M. M. Bossuyt. Variation of a test's sensitivity and specificity with disease prevalence. *CMAJ* 185:E537, 2013.

Article **Google Scholar**

56. Li, F. L., *et al*. Counterintuitive solid-state syntheses of indium-thiolate-phen cations as efficient and selective fluorescent biosensors for HIV-1 ds-DNA and sudan ebolavirus RNA sequences. *ChemistrySelect* 1:2979–2987, 2016.

Article **Google Scholar**

57. Li, J., K. Yang, Z. Wu, X. Li, and Q. Duan. Nitrogen-doped porous carbon-based fluorescence sensor for the detection of ZIKV RNA sequences: Fluorescence image analysis. *Talanta* 205:1, 2019.

Article **Google Scholar**

58. Li, J., K. Yang, Z. Wu, X. Li, and Q. Duan. Nitrogen-doped porous carbon-based fluorescence sensor for the detection of ZIKV RNA sequences: fluorescence image analysis. *Talanta* 2019. https://doi.org/10.1016/j.talanta.2019.06.091.

Article **Google Scholar**

59. Li, Y., *et al*. Aptamers-based sensing strategy for 17 β -estradiol through fluorescence resonance energy transfer between oppositely charged CdTe quantum dots and gold nanoparticles. *J. Nanosci. Nanotechnol.* 18:1517–1527, 2017.

Article **Google Scholar**

60. Li, Y., A. Guo, L. Chang, W.-J. Li, and W.-J. Ruan. Luminescent metal-organic-framework-based label-free assay of polyphenol oxidase with fluorescent scan. *Chem. - A Eur. J.* 23:6562–6569, 2017.

Article **Google Scholar**

61. Li, Z., Y. Yi, X. Luo, N. Xiong, Y. Liu, S. Li, R. Sun, Y. Wang, and B. Hu. Development and clinical application of A rapid IgM-IgG combined antibody test for SARS-CoV-2 infection diagnosis. *J. Med. Virol.* 11:1–7, 2020.

Google Scholar

62. Li, Z., *et al*. Development and clinical application of a rapid IgM-IgG combined antibody test for SARS-CoV-2 infection diagnosis. *J. Med. Virol.* 92:1518–1524, 2020.

Article Google Scholar

63. Lian, X., T. Miao, X. Xu, C. Zhang, and B. Yan. Eu3+ functionalized Sc-MOFs: Turn-on fluorescent switch for ppb-level biomarker of plastic pollutant polystyrene in serum and urine and on-site detection by smartphone. *Biosens. Bioelectron.* 97:299–304, 2017.

Article Google Scholar

64. Lin, S. X., *et al*. Effective loading of cisplatin into a nanoscale UiO-66 metal-organic framework with preformed defects. *Dalt. Trans.* 48:5308–5314, 2019.

Article Google Scholar

65. Liu, B., K. Vellingiri, S.-H. Jo, P. Kumar, Y. S. Ok, and K.-H. Kim. Recent advances in controlled modification of the size and morphology of metal-organic frameworks. *Nano Res.* 11:4441–4467, 2018. https://doi.org/10.1007/s12274-018-2039-3.

Article Google Scholar

66. Liu, C., *et al*. An electrochemical immunosensor based on an etched zeolitic imidazolate framework for detection of avian leukosis virus subgroup. *J. Microchim. Acta* 185:1–9, 2018. https://doi.org/10.1007/s00604-018-2930-3.

Article Google Scholar

67. Liu, J., Y. Wang, A. I. Benin, P. Jakubczak, R. R. Willis, and M. D. LeVan. CO_2/H_2O adsorption equilibrium and rates on metal-organic frameworks: HKUST-1 and Ni/DOBDC. *Langmuir* 26:14301–14307, 2010.

Article **Google Scholar**

68. Liu, J., Q. Yu, G. Zhao, and W. Dou. A novel immunochromatographic assay using ultramarine blue particles as visible label for quantitative detection of hepatitis B virus surface antigen. *Anal. Chim. Acta* 1098:140–147, 2020.

Article **Google Scholar**

69. Liu, L., Y. Zhou, S. Liu, and M. Xu. The applications of metal–organic frameworks in electrochemical sensors. *ChemElectroChem.* 14:6–19, 2018.

Article **Google Scholar**

70. Liu, X., L. Zhang, and J. Wang. Design strategies for MOF-derived porous functional materials: Preserving surfaces and nurturing pores. *J. Mater.* 15:440–459, 2021.

Google Scholar

71. Lu, R., J. Wang, M. Li, Y. Wang, J. Dong, and W. Cai. SARS-CoV-2 detection using digital PCR for COVID-19 diagnosis, treatment monitoring and criteria for discharge. *medRxiv* 2020. https://doi.org/10.1101/2020.03.24.20042689.

Article **Google Scholar**

72. Lu, X., *et al*. Response characteristics of bisphenols on a metal-organic framework-based tyrosinase nanosensor. *ACS Appl. Mater. Interfaces* 8:16533–16539, 2016. https://doi.org/10.1021/acsami.6b05008.

Article **Google Scholar**

73. Luo, L., F. Zhang, C. Chen, and C. Cai. Molecular imprinting resonance light scattering nanoprobes based on pH-responsive metal-organic framework for

determination of hepatitis A virus. *Microchim. Acta* 187:1–8, 2020. https://doi.org/10.1007/s00604-020-4122-1.

Article **Google Scholar**

74. Ma, H., *et al*. Electrochemiluminescent immunosensing of prostate-specific antigen based on silver nanoparticles-doped Pb(II) metal-organic framework. *Biosens. Bioelectron.* 79:379–385, 2016.

Article **Google Scholar**

75. Malfanti, A., *et al*. Oligo-guanidyl targeted bioconjugates forming rod shaped polyplexes as a new nanoplatform for oligonucleotide delivery. *J. Control. Release* 310:58–73, 2019.

Article **Google Scholar**

76. Marquez, S., and E. Morales-Narváez. Nanoplasmonics in paper-based analytical devices. *Front. Bioeng. Biotechnol.* 84:69, 2019.

Article **Google Scholar**

77. Mars, A., M. Hamami, L. Bechnak, D. Patra, and N. Raouafi. Curcumin-graphene quantum dots for dual mode sensing platform: Electrochemical and fluorescence detection of APOe4, responsible of Alzheimer's disease. *Anal. Chim. Acta* 1036:141–146, 2018.

Article **Google Scholar**

78. Marzi, A., and L. Banadyga. Ebola Virus (Filoviridae). In: Encyclopedia of Virology. Amsterdam: Elsevier, pp. 232–244, 2021.

Book **Google Scholar**

79. Massinga, M., A. Tshangela, S. J. Salyer, J. K. Varma, A. E. O. Ouma, and J. N. Nkengasong. COVID-19 in Africa: the spread and response. *Nat. Med.* 2020. https://doi.org/10.1038/s41591-020-0960-y.

Article **Google Scholar**

80. Miller, S. E., M. H. Teplensky, P. Z. Moghadam, and D. Fairen-Jimenez. Metal-organic frameworks as biosensors for luminescence-based detection and imaging. *Interface Focus* 6:20160027, 2016.

Article **Google Scholar**

81. Morales-Narváez, E., and C. Dincer. The impact of biosensing in a pandemic outbreak: COVID-19. *Biosens. Bioelectron.* 163:112274, 2020.

Article **Google Scholar**

82. Mozhgani, S. H., H. A. Kermani, M. Norouzi, M. Arabi, and S. Soltani. Nanotechnology based strategies for HIV-1 and HTLV-1 retroviruses gene detection. *Heliyon.* 15:e04048, 2020.

Article **Google Scholar**

83. Mugunga, J. C., *et al*. SARS-CoV-2 serosurveys in low-income and middle-income countries. *Lancet* 2021. https://doi.org/10.1101/2020.05.01.20087205.

Article **Google Scholar**

84. National Center for Immunization and Respiratory Diseases (NCIRD), D. of V.D. Interim Guidelines for Clinical Specimens for COVID-19 | CDC., 2021 [cited 2021 Mar 11]. https://www.cdc.gov/coronavirus/2019-ncov/lab/guidelines-clinical-specimens.html.

85. Nielsen, K., *et al*. Development of a lateral flow assay for rapid detection of bovine antibody to Anaplasma marginale. *J. Immunoass. Immunochem.* 29:10–18, 2008.

Article **Google Scholar**

86. Nkengasong, J. N., and W. Mankoula. Looming threat of COVID-19 infection in Africa: Act collectively, and fast. *Lancet* 15:841–842, 2020.

Article **Google Scholar**

87. Ozsahin, I., B. Sekeroglu, M. S. Musa, M. T. Mustapha, and D. UzunOzsahin. Review on diagnosis of COVID-19 from chest CT images using artificial intelligence. *Comput. Math. Methods Med.* 15:9756518, 2020.

Google Scholar

88. Paules, C. I., H. D. Marston, and A. S. Fauci. Coronavirus infections-more than just the common cold. *JAMA* 157:707–708, 2020.

Article **Google Scholar**

89. Qian, X., S. Tan, Z. Li, Q. Qu, L. Li, and L. Yang. A robust host-guest interaction controlled probe immobilization strategy for the ultrasensitive detection of HBV DNA using hollow HP5–Au/CoS nanobox as biosensing platform. *Biosens. Bioelectron.* 153:2020.

Article **Google Scholar**

90. Qin, L., *et al*. A water-stable metal-organic framework of a zwitterionic carboxylate with dysprosium: A sensing platform for Ebolavirus RNA sequences. *Chem. Commun.* 52:132–135, 2016.

Article **Google Scholar**

91. Qiu, G., Z. Gai, Y. Tao, J. Schmitt, G. A. Kullak-Ublick, and J. Wang. Dual-functional plasmonic photothermal biosensors for highly accurate severe acute respiratory syndrome coronavirus 2 detection. *ACS Nano* 2020. https://doi.org/10.1021/acsnano.0c02439.

Article **Google Scholar**

92. Qiu, G. H., *et al*. Synchronous detection of ebolavirus conserved RNA sequences and ebolavirus-encoded miRNA-like fragment based on a zwitterionic copper(II) metal–organic framework. *Talanta* 180:396–402, 2018.

Article **Google Scholar**

93. Rebucci, A. Johns Hopkins economist: "Reopening an infected economy is no shortcut" to financial recovery | Hub. [cited 2021 Mar

11]. https://hub.jhu.edu/2020/05/19/alessandro-rebucci-economic-impact-of-covid-19/.

94. Ribeiro, B. V., T. A. R. Cordeiro, G. R. OliveiraeFreitas, L. F. Ferreira, and D. L. Franco. Biosensors for the detection of respiratory viruses: A review. *Talanta* 2:100007, 2020.

Article **Google Scholar**

95. Rosi, O.M.Y.E.L.K. Isoreticular metal-organic frameworks, process for forming the same, and systematic design of pore size and functionality therein,with application for gas storage. World Intellectual Property Organization, 2002.

96. Roy, S., S.J. Malode, N.P. Shetti, and P. Chandra. Modernization of biosensing strategies for the development of lab-on-chip integrated systems. In: Bioelectrochemical Interface Engineering wiley, 2019, pp. 325–342.

97. Safaei, M., M. M. Foroughi, N. Ebrahimpoor, S. Jahani, A. Omidi, and M. Khatami. *A review on metal-organic frameworks: Synthesis and applications*. 2019. https://doi.org/10.1016/j.trac.2019.06.007.

Article **Google Scholar**

98. Samanta, P., S. Let, W. Mandal, S. Dutta, and S.K. Ghosh. Luminescent metal-organic frameworks (LMOFs) as potential probes for the recognition of cationic water pollutants. Inorg. Chem. Front. 2020.

99. Seitz, R. Human immunodeficiency virus (HIV). *Transfus. Med. Hemotherapy* 43:203–222, 2016.

Article **Google Scholar**

100. Sharp, P. M., and B. H. Hahn. Origins of HIV and the AIDS pandemic. *Cold Spring Harb. Perspect. Med.* 1:a006841, 2011.

Article **Google Scholar**

101. Shetti, N.P., S.D. Bukkitgar, K.R. Reddy, C.V. Reddy, and T.M. Aminabhavi. ZnO-based nanostructured electrodes for electrochemical sensors and biosensors in biomedical applications. Biosens. Bioelectron. p. 111417, 2019.

102. Stock, N., and S. Biswas. Synthesis of metal-organic frameworks (MOFs): Routes to various MOF topologies, morphologies, and composites. *Chem. Rev.* 2012. https://doi.org/10.1021/cr200304e.

Article Google Scholar

103. Tahir, R., K. Rizwan, and M. Bilal. Metal-organic framework-based engineered materials—Fundamentals and applications. *Molecules* 25:1598, 2020.

Article Google Scholar

104. Tan, D.-X., A. Korkmaz, R. J. Reiter, and L. C. Manchester. Ebola virus disease: potential use of melatonin as a treatment. *J. Pineal Res.* 57:381–384, 2014. https://doi.org/10.1111/jpi.12186.

Article Google Scholar

105. Tan, H., *et al*. A sensitive fluorescent assay for thiamine based on metal-organic frameworks with intrinsic peroxidase-like activity. *Anal. Chim. Acta* 856:90–95, 2015.

Article Google Scholar

106. Tang, Y.W., J.E. Schmitz, D.H. Persing, and C.W. Stratton. Laboratory diagnosis of COVID-19: Current issues and challenges. J. Clin. Microbiol.

107. Thompson, D., and Y. Lei. Mini review: Recent progress in RT-LAMP enabled COVID-19 detection. *Sens. Actuators Rep.* 2:2020.

Article Google Scholar

108. Vardhanabhuti, V. CT scan AI-aided triage for patients with COVID-19 in China. Lancet Digit. Heal. Elsevier Ltd, pp. e494–e495, 2020.

109. Velásquez-Hernández, M. D. J., *et al*. Degradation of ZIF-8 in phosphate buffered saline media. *CrystEngComm* 21:4538–4544, 2019.

Article Google Scholar

110. Vogelstein, B., and K. W. Kinzler. Digital PCR. *Proc. Natl. Acad. Sci. USA* 96:9236–9241, 1999.

Article **Google Scholar**

111. Wang, G. Y., C. Song, D. M. Kong, W. J. Ruan, Z. Chang, and Y. Li. Two luminescent metal-organic frameworks for the sensing of nitroaromatic explosives and DNA strands. *J. Mater. Chem. A* 2:2213–2220, 2014.

Article **Google Scholar**

112. Wang, H. S., *et al*. Insight into the unique fluorescence quenching property of metal-organic frameworks upon DNA binding. *Anal. Chem.* 89:11366–11371, 2017. https://doi.org/10.1021/acs.analchem.7b02256.

Article **Google Scholar**

113. Wang, Y., *et al*. Metal-organic frameworks for virus detection. *Biosens. Bioelectron.* 169:2020.

Article **Google Scholar**

114. Wei, X., *et al*. Fluorescence biosensor for the H5N1 antibody based on a metal–organic framework platform. *J. Mater. Chem. B* 1:1812–1817, 2013.

Article **Google Scholar**

115. Won, J., *et al*. Development of a laboratory-safe and low-cost detection protocol for SARS-CoV-2 of the Coronavirus Disease 2019 (COVID-19). *Exp. Neurobiol.* 29:107–119, 2020.

Article **Google Scholar**

116. World Health Organization. Zika virus., [cited 2021 Mar 15]. https://www.who.int/news-room/fact-sheets/detail/zika-virus.

117. World Health Organization. Dengue and severe dengue., [cited 2021 Mar 15]. https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue.

118. World Health Organization. HIV/AIDS., 2020 [cited 2021 Mar 12]. https://www.who.int/news-room/fact-sheets/detail/hiv-aids.
119. World Health Organization. Ebola virus disease., 2021 [cited 2021 Mar 14]. https://www.who.int/news-room/fact-sheets/detail/ebola-virus-disease.
120. Worldometer. Coronavirus Update (Live): 118,684,343 Cases and 2,633,281 Deaths from COVID-19 Virus Pandemic - Worldometer. [cited 2021 Mar 11]. https://www.worldometers.info/coronavirus/.
121. Wu, L.-L., *et al*. A metal-organic framework/DNA hybrid system as a novel fluorescent biosensor for mercury(II) ion detection. *Chem. - A Eur. J.* 22:477–480, 2016. https://doi.org/10.1002/chem.201503335.

Article Google Scholar

122. Xia, N., G. Wang, and W. Gong. Serological test is an efficient supplement for detecting RNA to confirm SARS-CoV-2 infection. *Preprint* Preprints, 2020 [cited 2021 Mar 11]. www.preprints.org.
123. Xiang, J., *et al*. Evaluation of enzyme-linked immunoassay and colloidal gold-immunochromatographic assay kit for detection of novel coronavirus (SARS-Cov-2) causing an outbreak of pneumonia (COVID-19). *medRxiv* 2020. https://doi.org/10.1101/2020.02.27.20028787.

Article Google Scholar

124. Xie, B. P., *et al*. Simultaneous detection of Dengue and Zika virus RNA sequences with a three-dimensional Cu-based zwitterionic metal–organic framework, comparison of single and synchronous fluorescence analysis. *Sens. Actuators B* 254:1133–1140, 2018.

Article Google Scholar

125. Xie, X., Z. Zhong, W. Zhao, C. Zheng, F. Wang, and J. Liu. Chest CT for typical coronavirus disease 2019 (COVID-19) pneumonia: Relationship to negative RT-PCR testing. *Radiology* 296:E41–E45, 2020.

Article Google Scholar

126. Xiong, C., W. Liang, Y. Zheng, Y. Zhuo, Y. Chai, and R. Yuan. Ultrasensitive assay for telomerase activity via self-enhanced electrochemiluminescent

ruthenium complex doped metal-organic frameworks with high emission efficiency. *Anal. Chem.* 89:3222–3227, 2017. https://doi.org/10.1021/acs.analchem.7b00259.

Article **Google Scholar**

127. Xu, T., *et al*. Development of droplet digital PCR for the detection of Tilletia laevis, which causes common bunt of wheat, based on the SCAR marker derived from ISSR and real-time PCR. *Sci. Rep.* 10:16106, 2020. https://doi.org/10.1038/s41598-020-72976-7.

Article **Google Scholar**

128. Yang, H. M., X. L. Song, T. L. Yang, Z. H. Liang, C. M. Fan, and X. G. Hao. Electrochemical synthesis of flower shaped morphology MOFs in an ionic liquid system and their electrocatalytic application to the hydrogen evolution reaction. *RSC Adv.* 4:15720–15726, 2014.

Article **Google Scholar**

129. Yang, J., W. Feng, K. Liang, C. Chen, and C. Cai. A novel fluorescence molecularly imprinted sensor for Japanese encephalitis virus detection based on metal organic frameworks and passivation-enhanced selectivity. *Talanta* 212:2020.

Article **Google Scholar**

130. Yang, S. P., *et al*. Platforms formed from a three-dimensional Cu-based zwitterionic metal-organic framework and probe ss-DNA: selective fluorescent biosensors for human immunodeficiency virus 1 ds-DNA and sudan virus rna sequences. *Anal. Chem.* 87:12206–12214, 2015. https://doi.org/10.1021/acs.analchem.5b03084.

Article **Google Scholar**

131. Yang, S. P., *et al*. Platforms formed from a three-dimensional Cu-based zwitterionic metal-organic framework and probe ss-DNA: selective fluorescent biosensors for human immunodeficiency virus 1 ds-DNA and sudan virus RNA

sequences. *Anal. Chem.* 87:12206–12214, 2015. https://doi.org/10.1021/acs.analchem.5b03084.

Article **Google Scholar**

132. Yang, S. P., *et al*. Lanthanum-based metal-organic frameworks for specific detection of sudan virus RNA conservative sequences down to single-base mismatch. *Inorg. Chem.* 56:14880–14887, 2017.

Article **Google Scholar**

133. Yang, Y., *et al*. Laboratory diagnosis and monitoring the viral shedding of SARS-CoV-2 infection. *Innov.* 1:2020.

Google Scholar

134. Ye, Z., Y. Zhang, Y. Wang, Z. Huang, and B. Song. Chest CT manifestations of new coronavirus disease 2019 (COVID-19): a pictorial review. *Eur. Radiol.* 30:4381–4389, 2020.

Article **Google Scholar**

135. Yin, Y., *et al*. Protein-metal organic framework hybrid composites with intrinsic peroxidase-like activity as a colorimetric biosensing platform. *ACS Appl. Mater. Interfaces* 8:29052–29061, 2016. https://doi.org/10.1021/acsami.6b09893.

Article **Google Scholar**

136. Yu, L., *et al*. Rapid detection of COVID-19 coronavirus using a reverse transcriptional loop-mediated isothermal amplification (RT-LAMP) diagnostic platform. *Clin. Chem.* 66:975–977, 2020.

Article **Google Scholar**

137. Yuan, S., *et al*. Stable metal-organic frameworks: design, synthesis, and applications. *Adv. Mater.* 30:1704303, 2018.

Article **Google Scholar**

138. Zafar, E.S. and F. Introductory Chapter: Metal Organic Frameworks (MOFs). In: Metal Organic Framework 2016, pp. 1–16.

139. Zeng, H. H., W. BinQiu, L. Zhang, R. P. Liang, and J. D. Qiu. Lanthanide coordination polymer nanoparticles as an excellent artificial peroxidase for hydrogen peroxide detection. *Anal. Chem.* 88:6342–6348, 2016. https://doi.org/10.1021/acs.analchem.6b00630.

Article Google Scholar

140. Zhao, H. Q., *et al*. A zinc(II)-based two-dimensional MOF for sensitive and selective sensing of HIV-1 ds-DNA sequences. *Anal. Chim. Acta* 922:55–63, 2016. https://doi.org/10.1016/j.aca.2016.03.054.

Article Google Scholar

141. Zhao, Y., Y. Yang, Y. Luo, X. Yang, M. Li, and Q. Song. Double detection of mycotoxins based on SERS labels embedded Ag@Au core-shell nanoparticles. *ACS Appl. Mater. Interfaces.* 7:21780–21786, 2015. https://doi.org/10.1021/acsami.5b07804.

Article Google Scholar

142. Zhou, J., G. Tian, L. Zeng, X. Song, and X. Bian. Nanoscaled metal-organic frameworks for biosensing, imaging, and cancer therapy. *Adv. Healthc. Mater.* 7:1800022, 2018. https://doi.org/10.1002/adhm.201800022.

Article Google Scholar

143. Zhu, W., P. Liu, S. Xiao, W. Wang, D. Zhang, and H. Li. Microwave-assisted synthesis of Ag-doped MOFs-like organotitanium polymer with high activity in visible-light driven photocatalytic NO oxidization. *Appl. Catal. B Environ.* 172–173:46–51, 2015.

Article Google Scholar

144. Zhu, X., *et al*. Metal-organic framework (MOF): A novel sensing platform for biomolecules. *Chem. Commun.* 49:1276–1278, 2013.

Article **Google Scholar**

145. Zhu, X. W., X. P. Zhou, and D. Li. Exceptionally water stable heterometallic gyroidal MOFs: Tuning the porosity and hydrophobicity by doping metal ions. *Chem. Commun.* 52:6513–6516, 2016.

Download references

Conflict of interest

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

Author information

Authors and Affiliations

1. **Analytical/Material Chemistry Laboratory, Department of Pure and Applied Chemistry, Faculty of Natural and Applied Sciences, Veritas University, Abuja, P.O.Box 6523, Garki, Abuja, Nigeria**
   Godwin A. Udourioh
2. **Department of Chemistry, College of Science and Technology, Covenant University, Canaanland, Km10, Idiroko Road, Ota, Ogun State, Nigeria**
   Moses M. Solomon
3. **Institute for Materials and Processes (IMP), School of Engineering, University of Edinburgh, The King's Buildings, Edinburgh, EH9 3FB, UK**
   Emmanuel I. Epelle

Corresponding author

Correspondence to Moses M. Solomon.

Additional information

Associate Editor Michael R. King oversaw the review of this article.

Publisher's Note

Rights and permissions

Reprints and Permissions

About this article

Cite this article

Udourioh, G.A., Solomon, M.M. & Epelle, E.I. Metal Organic Frameworks as Biosensing Materials for COVID-19. *Cel. Mol. Bioeng.* **14**, 535–553 (2021). https://doi.org/10.1007/s12195-021-00686-9

Download citation

- Received05 April 2021
- Accepted21 June 2021
- Published06 July 2021
- Issue DateDecember 2021
- DOIhttps://doi.org/10.1007/s12195-021-00686-9

Keywords

- **Covid-19**
- **Biosensors**
- **Metal organic frameworks**
- **Infectious diseases testing and detection**
- **Pandemic outbreak**