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MINI-REVIEW

Electrochemical biosensor detection on respiratory and flaviviruses

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Abstract
Viruses have spread throughout the world and cause acute illness or death among millions of people. There is a growing concern about methods to control and combat early-stage viral infections to prevent the significant public health problem. However, conventional detection methods like polymerase chain reaction (PCR) requires sample purification and are time-consuming for further clinical diagnosis. Hence, establishing a portable device for rapid detection with enhanced sensitivity and selectivity for the specific virus to prevent further spread becomes an urgent need. Many research groups are focusing on the potential of the electrochemical sensor to become a key for developing point-of-care (POC) technologies for clinical analysis because it can solve most of the limitations of conventional diagnostic methods. Herein, this review discusses the current development of electrochemical sensors for the detection of respiratory virus infections and flaviviruses over the past 10 years. Trends in future perspectives in rapid clinical detection sensors on viruses are also discussed.

Key points
- *Respiratory related viruses and Flavivirus are being concerned for past decades.*
- *Important to differentiate the cross-reactivity between the virus in same family.*
- *Electrochemical biosensor as a suitable device to detect viruses with high performance.*

Keywords Biosensors · Nanomaterials · *Flavivirus* · Dengue virus · Respiratory virus · Communicable disease

Introduction

Due to the cases of SARS-2-CoV (COVID-19) increasing exponentially since the end of 2019, the whole world was concerned and looking for detailed info about virus-based diseases (Ribeiro et al. 2020). Respiratory virus infections and flavivirus were among the most discussed viruses during the past few decades. Referring to the World Health Organization (WHO) reports, there have been several respiratory disease outbreaks since 2002, such as severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), H1N1 influenza (swine FLU), and COVID-19 (Ribeiro et al. 2020). Besides the respiratory viral diseases, flaviviruses including Zika virus (ZIKV), Japanese encephalitis virus (JEV), yellow fever (YFV), and dengue virus (DENV) also attracted the attention of people in the meantime (Kaya et al. 2020). Ebola virus (EBOVs), one of the flaviviruses that categorize in biosafety level 4, had also resulted in a high global mortality rate since the first outbreak in 1976 (Ibrahim et al. 2021). Hence, early detection to prepare proper medical care becomes the only way to block the spread by good prevention

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as well as reduce the fatality that is caused by the viruses above that without specific treatment (Shi 2021).

Examples of current conventional viral diagnosis techniques include reverse transcription PCR (RT-PCR), Western blotting–based tests, and enzyme-linked immunosorbent assay (ELISA) (Imran et al. 2021). The most common technique among those conventional methods is RT-PCR, which solves the problem of the utilization of immunological assays that require the production of antibodies (Ibrahim et al. 2021). However, RT-PCR has disadvantages of being time-consuming, requiring laboratory facilities, being costly, and even not indicating whether the patient was infected or subsequently recovered (Awan et al. 2020; Kafrashi et al. 2017; Kumar et al. 2022). In addition, it is difficult to keep the sample away from contamination since a high purification of the sample is needed during amplification (Kaya et al. 2020). The other available diagnostic tools have their different downsides. For example, (i) ELISA using IgM antibody of dengue virus still can give high rate of false positive result against other flaviviruses and low sensitivity in performing the POC rapid test, (ii) nucleic acid sequence-based amplification (NASBA) needs a sample preparation knowledge to handle the viral targets, which is inconvenience for public users (Kabir et al. 2021), (iii) loop-mediated isothermal amplification (LAMP) needs 65 °C incubation temperature, and (iv) clustered regularly interspaced short palindromic repeat (CRISPR) requires technically trained personnel to perform analysis (Abdul Ghani et al. 2022). Hence, it is crucial to have a simple, rapid, and cheap with highly sensitive and selective on-site diagnosis devices for humans to against the viral infectious diseases.

The development of economical biosensor is found to be the trend as it is ready for use by public users without any knowledge about laboratory sample preparation skills. Biosensors are analytical devices that consists of 3 parts, which are bioreceptor, transducer, and signal processor. Principally, biosensors capture and recognize the analyte through physical or chemical interactions and then convert into quantifiable electrical or optical signal (Saylan et al. 2019). Recent reviews on biosensors mostly emphasize the effects of different approaches such as electrode surface functionalization and the biological recognition component on the performance of sensors for detecting only SARS-2-CoV virus (Bukkitgar et al. 2021; Kumar et al. 2022; Suleman et al. 2021). However, several other viruses still dragged the attention among the community in the past decades and have become a challenge for doctors to recognize the infected virus due to similar symptoms. The late clinical treatment will cause further terrible consequences. Thus, a review on electrochemical sensors' development on respiratory virus and flavivirus detection may enable medical practitioners, biosensor experts, material scientists, and industrialists to easily access the recent updates and advancement in this field of research. Hence, in this manuscript, electrochemical sensors on virus (respiratory virus-based and flavivirus-based) diagnosis have been exclusively reviewed.

Electrochemical biosensor: a high performance analysis

The biosensor can be categorized as electrochemical sensors, optical sensors, and piezoelectric sensors due to the type of signal responses such as electric current, vibration frequency or photoelectricity (Misra et al. 2021; Perumal and Hashim 2014; Saylan et al. 2019). A sensor can be classified as an electrochemical sensor due to the transducer using electrochemical detection whereas a "bio" sensor due to the biorecognition elements, e.g. antibodies, aptamers, DNA, or RNA, used for the electrochemical reaction (Ong et al. 2018). The principle of electrochemical biosensors can be referred to Fig. 1. In short, electrochemical biosensors are sensors that combine the inherent bioelements and the sensitivity of the electroanalytical method to convert the chemical signals into a measurable and readable value (Ronkainen et al. 2010).

Among the type of biosensors, electrochemical biosensors are recommended to use in clinical applications because (i) it is cost-effective due to a simple connection to an electronic read-out, (ii) it has the capability of miniaturization to become POC devices, and (iii) it is robust and user-friendly (Imran et al. 2021; Kafrashi et al. 2017). Additionally, electrochemical sensors can be further divided into impedimetric (measurable impedance or component resistance and capacitance), potentiometric (measurable potential or charge accumulation), amperometric (measurable current), etc. based on the detection methods (Misra et al. 2021; Ronkainen et al. 2010). According to Monteil's team, voltammetry detection, i.e. linear sweep voltammetry (LSV), cyclic voltammetry (CV), differential pulse voltammetry (DPV), square-wave voltammetry (SWV), and stripping voltammetry (SV), was the primary detection method, followed by other electrochemical methods like impedance spectroscopy and field effect transistors (FET) (Monteil et al. 2021; Ronkainen et al. 2010).

Advanced nanotechnology during the past few decades introduced nanomaterials like nanoparticles or quantum dots, which enhanced the effectiveness of electrochemical sensors (Anthony et al. 2019; Tai et al. 2021). The sensors that further modify with nanomaterials are called nano-biosensors. Biosensors modified with nanomaterials over the electrode surface can improve the adsorption capacity, sensitivity, and structural compatibility and increase the loading of immobilized bioreceptors such as antibodies or nucleic acids (Castillo-Henriquez et al. 2020). Researchers can validate the quality of the fabricated biosensor as a commercial

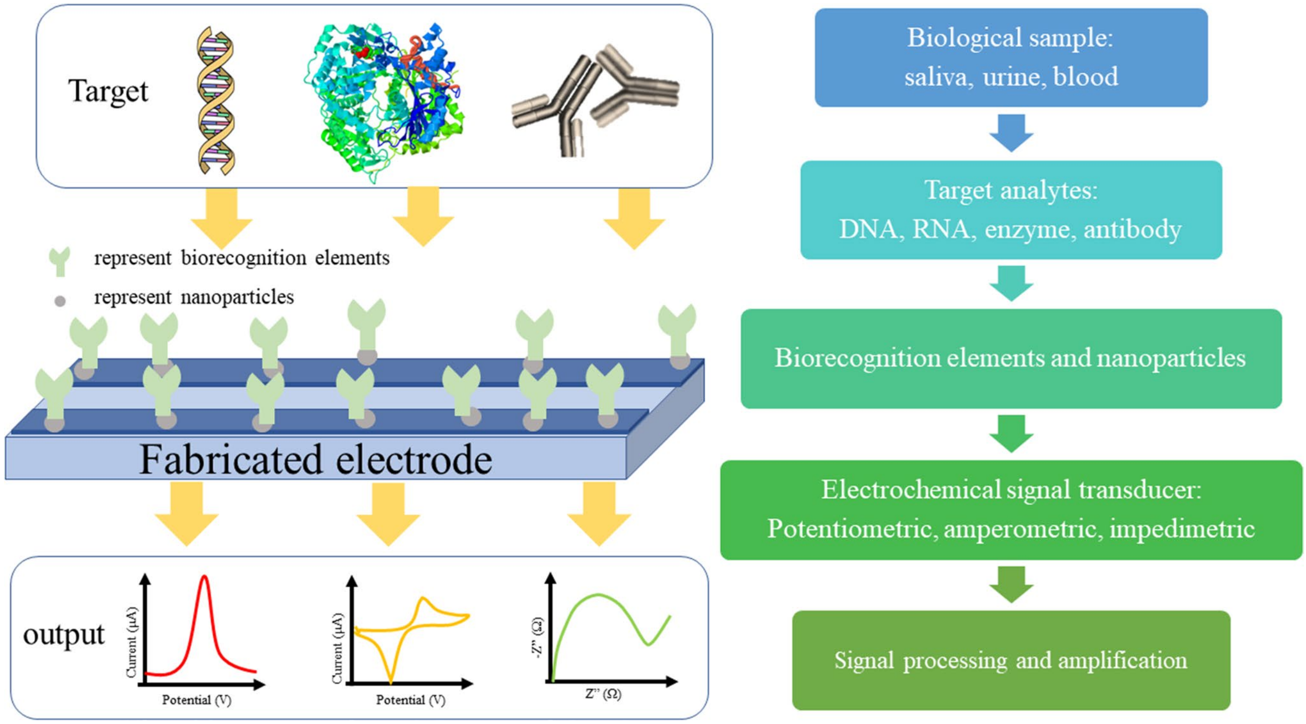

Fig. 1 The schematic diagram of an electrochemical nano-biosensor

clinical diagnostic device by considering sensitivity, detection limit (LOD), selectivity, reproducibility, and repeatability (Justino et al. 2016). At present, high-performance analysis is mandatory with the emerging and remerging of viral strains. Setting up a surveillance sensing system will aid to prevent these pandemics/epidemics with seasonal variations (Fig. 2).

Respiratory viral biosensing surveillance

Respiratory virus infections are being one of the most common causes of death in humans, from infants to the elderly people because these viruses are airborne viruses that can easily spread through the air and enter the nasopharynx area through the air and spread among people with or without symptoms (Nasrollahzadeh et al. 2020). There were over 95% of respiratory-related deaths caused by insufficiency of correct diagnosis and treatments such as the failure to predict the novel variants of pathogenic viruses (Misra et al. 2021). Hence, many researchers are trying to fabricate a new electrochemical sensor with greater efficacy. Zhou et al. studied about the combination of immunomagnetic separation, electrochemical detection, and multi-enzymatic amplification for a more sensitive H9N2 avian influenza virus diagnostics application (Zhou et al. 2013). First, they modified the gold electrode by concanavalin A (Con A) and horseradish peroxidase (HRP) layer by layer to enhance the catalytic properties. Magnetic beads (MBs) were conjugated with the enzymatic label of glucose oxidase-conjugated avidin D (GOD-A) to capture the targeted virus (H9N2). The modified m-AuE detected the virus that was captured by the GOD-MBs constructed on a sandwich-type immunoassay, and the current change was subsequently measured via differential pulse voltammetry (DPV). They reported that this method can reach a LOD of 1 ng/mL with a detection range of 50 to 2000 ng/mL with high specificity and reproducibility (Zhou et al. 2013). Singh et al. developed a label-free electrical immunosensor for H1N1 influenza virus detection by using the immobilized avidin and biotinylated antibodies on single-walled carbon nanotubes (SWCNTs), which deposited on polydiallyldimethylammonium chloride (PDDA) by dielectrophoresis (DEP) (Singh et al. 2014). This method preserved the perfect surface structure of SWCNTs after functionalization with antibodies as a platform of ultrasensitive virus detection (Singh et al. 2014). Instead of only detecting for one type of virus, Huang et al. introduced a silver nanoparticle (AgNPs)-coated graphene sandwich-type electrochemical sensor to detect the avian influenza virus (AIV) in the H7 series (Huang et al. 2016). They employed polyclonal antibodies (PAbs) on AgNPs as the label and monoclonal antibodies (MAbs) that immobilized on gold nanoparticles-graphene nanocomposites (AuNPs-G) to develop the electrochemical immunosensors. The

Table 1 Summary of performance characteristics of developed electrochemical biosensors for respiratory virus and flavivirus

Virus	Sample source	Designed sensor	Assay time	Detection technique	Linear range detection	LOD	Bioreceptor	Ref
H9N2 influenza virus	Chicken serum	GOD-MBs/Con-A/HRP/m-AuE	~30 min	DPV	50 to 2000 ng/mL	1 ng/mL	Antibody	Zhou et al. (2013)
H1N1 influenza virus	Bank of Pathogenic Viruses, South Korea	Biotinylated MAb-Avidin/PDDA-SWCNTs	~30 min	-	1 to 10^4 PFU/ml	1 PFU/mL	Antibody	Singh et al. (2014)
H1N1 influenza virus	-	Ab/rGO/CA/AuE	~120 min	EIS	1 to 10^4 PFU/ml	0.5 PFU/mL	Antibody	Singh et al. (2017)
H7 avian influenza virus	China Agricultural University	PAb-AgNPs/MAb-AuNPs-G	~70 min	LSV	1.6 to 16,000 pg/mL	1.6 pg/mL	Antibody	Huang et al. (2016)
H7 avian influenza virus	Abcam, UK	PAb-CNTs-MoSx/MAb-AuNPs-CNTs-MoSx-GCE	~70 min	LSV	1 to 25 ng/mL	0.43 ng/mL	Antibody	Tian (2017)
H5N1 avian influenza virus	Chicken serum	AIapt-Zyme-SH-DNA 3WJ/pAuNPs/AuE	~120 min	CV	-	1 pM	3WJ DNA	Lee et al. (2019)
SARS-Cov-2	Nasopharyngeal swab specimens	ncovNP/MIP-PmPD/Au-TFE	>30 min	DPV	2.22 to 111 fM	15 fM	Nucleoprotein	Raziq et al. (2021)
JEV	Human serum	Ab-HRP/Ab-APTES-GA-PrA/silanized electrode	~90 min	-	25 to 100 ng/mL	10 ng/mL	Antibody	Tran et al. (2012)
JEV	Institute of Health and Community Medicine, Universiti Malaysia Sarawak	Ab/AgNPs/SPCE	~20 min	EIS	0.1 to 20 ng/mL	2.6 ng/mL	Antibody	Chin et al. (2019)
JEV	Human serum	Ab/ CNPs/SPCE	~20 min	EIS	1 to 20 ng/mL	0.36 ng/mL	Antibody	Lai et al. (2017)
EBOV	Eurofins Genomics	Streptavidin–alkaline phosphatase/SH-DNA/SPGE	~155 min	DPV	10 to 75 nM	4.7 nM	DNA	Ilkhani and Farhad (2018)
ZIKV	-	SH-DNA/AuE	~90 min	EIS	25 to 340 nM	25 nM	DNA	Faria and Zucolotto (2019)
ZIKV	Invitrogen	Oligonucleotides/PTyr/rGO/GE	~50 min	DPV	1.72 to 1.72×10^{10} copies/mL	1.72 copies/mL	Oligonucleotide	Moço et al. (2019)
ZIKV	Fitzgerald	Anti ZIKV NS1/ZnO NRs/PCB	~60 min	CV	100 to 100,000 pg/mL	1 pg/mL	Antibody	Faria and Mazon (2019)
DENV	Human blood, serum	Anti DENV NS1/EDA/CNT-SPE	~62 min	CV	40 to 2000 ng/mL	12 ng/mL	Antibody	Dias et al. (2013)
DENV	First BASE Laboratories Sdn Bhd	ssDNA/AuNPs-SiNWs/SPGE	~120 min	DPV	10^{-11} to 10^{-7} M	1.63×10^{-12} M	DNA	Rashid et al. (2015)
DENV	Human serum	Anti DENV NS1/BSA/SPCE	~60 min	EIS	1 to 200 ng/mL	0.3 ng/mL	Antibody	Nawaz et al. (2018)
DENV	FASMAC, Japan	ssDNA/AuNP/N,S-GQDs	~20 min	DPV	10^{-14} to 10^{-6} M	9.4×10^{-15} M	DNA	Dutta Chowdhury et al. (2018)
DENV 2	Human serum	Ab-AuNPs/MWCNTs/AuE	~30 min	DPV	10^{-12} to 10^{-6} g/mL	3×10^{-13} g/mL	Antibody	Palomar et al. (2020)
DENV	Human serum	Ab-AgNPs/Ab-NS1/GE	~60 min	DPV	3 to 300 ng/mL	0.5 ng/mL	Antibody	Awan et al. (2020)
DENV 2	Fitzgerald	Ab-AuNPs/Anti DENV NS1/lateral flow cellulose paper-SPGE	~60 min	EIS	1 to 25 ng/mL	0.5 ng/mL	Antibody	Sinawang et al. (2016)
DENV 4	Abcam, UK	Apt/MCH/AuE	~30 min	EIS	0.01 to 1000 ng/mL	0.05 ng/mL	Aptamer	Bachour Junior et al. (2021)

GOD-MBs glucose oxidase-conjugated avidin D on magnetic beads, *Con A* concanavalin A, *HRP* horseradish peroxidase, *m-AuE* home-made gold electrode, *PDDA* polydiallyldimethylammonium chloride, *SWCNTs* single-walled carbon nanotubes, *MWCNTs* multi-walled carbon nanotubes, *rGO* reduced graphene oxide, *CA* cystamine, *AuNPs* gold nanoparticles, *AgNPs* silver nanoparticles, *CNPs* carbon nanoparticles, MoS_x nanostructured molybdenum sulphide, *PAb* polyclonal antibody, *MAb* monoclonal antibody, *MIP-PmPD* molecularly imprinted polymers poly-m-phenylenediamine film, *TFE* thin film electrode, *SPE* screen-printed electrode, *SPCE* screen-printed carbon electrode, *SPGE* screen-printed gold electrode, *EDA* ethylenediamine, *N,S-GQDs* nitrogen, sulphur-doped graphene quantum dots, *PTyr* polytyramine-conducting polymer, *GE* graphite electrode, *Apt* aptamer, *MCH* 6-mercapto-1-hexanol uses of AuNPs and graphene enhanced the electrochemical behaviour of detection due to high electrical conductivity. Linear sweep voltammetry (LSV) was used as a detection method for the detection performance of the modified electrode. This method indicated good specificity and reproducibility towards all H7 AIV (Huang et al. 2016). There was another group of researchers in China that focused on H7 AIV series detection with a different method. Tian et al. developed the electrochemical immunosensor from three-dimensional CNTs/MoS_x aerogel, which is a combination of nanostructured molybdenum sulphide (MoS_2) material and conductive networks of CNTs, with PAb-AuNPs bioconjugates (Tian 2017). The purpose of using 3D-CNTs/MoS_x nanocomposite increases the electroactive surface area for the enhancement of electrochemical properties. LSV was used for checking the performance of modified electrodes on detecting H7 AIV, via sandwich immunoreactions. This method showed a LOD of 0.43 ng/mL with good reproducibility (Tian 2017). Lee et al. fabricated a label-free electrochemical sensor by employing porous AuNPs that were immobilized with multifunctional DNA 3-way junction (AIapt/Zyme/SH-DNA 3WJ) to detect H5N1 AIV (Lee et al. 2019). Each fragment from the DNA 3WJ has specific functionality (Fig. 3). AIapt is used for HA protein detection, Zyme is used for electrochemical signal generation, and SH-DNA can immobilize the DNA 3WJ on electrodes without linkers. Hence, several steps can be eliminated to fabricate this biosensor such as the labelling process and choosing the linker. This method resulted in the LOD of 1 pM either in buffer solution or chicken serum by CV detection (Lee et al. 2019). The current outbreak of respiratory virus is SARS-Cov-2 (COVID-19). This pandemic is then rapidly spread by asymptomatic patients who are infected with the COVID-19 virus in the public quickly without any consciousness. To detect this virus, Raziq et al. fabricated a disposable electrochemical sensor using molecularly imprinted polymers (MIPs) with SARS-CoV-2 nucleoprotein (ncovNP) receptors as a rapid diagnostic tool (Raziq et al. 2021). They introduced MIP due to its chemical and thermal stability. MIPs are made by the combination of functional monomers and template by copolymerization (Yarman et al. 2022). Instead of testing in buffer, they also analysed the clinical samples from patients with the developed sensor. A LOD of 27 fM was successfully detected in the real samples with the linear range of 0.22 to 333 fM (Raziq et al. 2021).

Flavivirus biosensing surveillance

Flavivirus is a member belonging to *Flaviviridae* virus family, which can be widespread through arthropods such as mosquitoes. Examples of the virus include ZIKV, YFV, JEV, and the most common disease, DENV (CDC 2021, 2 September). There were numerous recent achievements in the electrochemical biosensing of flavivirus-related diseases by researchers in the past decades.

Japanese encephalitis virus (JEV)

JEV is a flavivirus that may cause a permanent neurological damage even the patient was recovered. Tran et al. had developed an electrochemical immunosensor for rapid detection of JEV. They emphasized the immobilization methods of JEV antibodies on the electrode and found that the covalent binding of glutaraldehyde combined with protein A (APTES-GA-PrA) had the best binding effect (Tran et al. 2012). In their investigation, APTES-GA-PrA became the best cross-linker to bind the JEV antibody without affecting the binding sites to antigen and could achieve a LOD of 10 ng/mL of JEV virus in the buffer (Tran et al. 2012). Another group of researchers focused on the implication of nanomaterials to minimize the costs for purchasing biorecognition elements. Chin et al. incorporated silver nanoparticles (AgNPs) onto electrode surfaces to increase the surface area for immobilization of recognition elements and enhance the sensitivity of electrodes (Chin et al. 2019). A lower LOD was exhibited with the use of AgNPs-modified SPCE in detecting the JEV virus indicating the possibility of nanomaterial in fabricating a highly sensitive biosensor.

Zika virus (ZIKV)

ZIKV was discovered as a new flavivirus that evolved from a geographically isolated virus to a global health problem in the mid-twentieth century (Khristunova et al. 2020; Nicolini et al. 2017). The similar symptoms and cross-reactivities of ZIKV with the other flavivirus complicate the diagnosis methods (Faria and Zucolotto 2019). However, in recent years, electrochemical sensors are suggested to replace serological or molecular analysis because it can be easily integrated with portable instrumentation with in situ detections of ZIKV (Lima et al. 2021). Faria et al. developed a label-free impedimetric electrochemical sensor using DNA as biorecognition element (Faria and Zucolotto 2019). They immobilized the thiol probe DNA on AuE. The detection of ZIKV was done when the hybridization occurred with targeted samples, and electrochemical impedance spectroscopy (EIS) was used as the detection technique. They found a decreasing in impedance when the concentration of ZIKV was increasing as more DNA double strands released from AuE after hybridization (Faria and Zucolotto 2019). Moço et al. (2019) immobilized oligonucleotides probe on a graphite electrode (GE), which was altered with the reduced graphene oxide (rGO) and polytyramine-conducting polymer (PTyr) to form a genosensor (Moço et al. 2019). PTyr and rGO were used to improve the conductive properties and reproducibility of the electrode. This electrochemical genosensor is able to detect a low concentration in femtomolar scale within 20 min in their report (Moço et al. 2019). Faria et al. developed an electrochemical immunosensor by using zinc oxide (ZnO NRs) nanorods on a printed circuit board (PCB) (Faria and Mazon 2019). The ZIKV-NS1 antibody was used as a probe to ensure the selectivity of biosensor, while the ZnO NRs provide a large and specific surface area for immobilization of the antibodies. This method can detect a LOD of 1 pg/mL in an incubation solution. They also reported that this method can detect ZIKV in urine samples without interference with other compounds (Faria and Mazon 2019).

Dengue virus (DENV)

Dengue viruses are mosquito-borne viruses that have 4 serotypes genetically and antigenically, DENV1, DENV2, DENV3, and DENV4 (Darwish et al. 2015; Kabir et al. 2021). It happens in most tropical and subtropical regions over the world and becomes the major health problem due to the high mortality rate (Eivazzadeh-Keihan et al. 2019). Dias et al. developed a carbon nanotube ink screen printing electrodes (CNT-SPE) with the biorecognition element of DEN protein NS1 to detect DENV (Dias et al. 2013). They produced SPE by incorporating the carboxylate CNTs into carbon ink, whereas NS1 protein was immobilized on the film by using ethylenediamine (EDA). CNT was introduced to increase the electroactive surface area and enhance the detection sensitivity (Dias et al. 2013). Rashid et al. used silicon nanowires and AuNPs (SiNWs/AuNPs) as sensing material on modified SPE to fabricate DNA biosensors (Rashid et al. 2015). The purpose of SiNWs/AuNPs was improving the conductivity and providing specific surface area for the DNA probes immobilization and hybridization. However, this method only can produce disposable sensor tips due to its low reproducibility (Rashid et al. 2015). Nawaz et al. had developed an electrochemical immunosensor that can circumvent the unknown disadvantage of using nanomaterials such as toxicity (Nawaz et al. 2018). They electrodeposited the bovine serum albumin (BSA) onto SPCE, where BSA was replacing the utilization of nanomaterials as a transducer and additionally provide non-random immobilization of DENV NS1 antibody. A challenge for the detection of DENV is the possibility of a false negative result due to different DENV serotypes (Darwish et al. 2015). Hence, fabrication of biosensors with high specificity, simplicity, and high speed to provide selected quantitative analytical data are crucial (Kabir et al. 2021). Then, Dutta et al. introduced a probe, which is nitrogen, sulphur-doped graphene quantum dots (N,S-GQDs) with AuNPs to apply in two-way DNA detection (Dutta Chowdhury et al. 2018). However, this probe only can determine the specific DENV

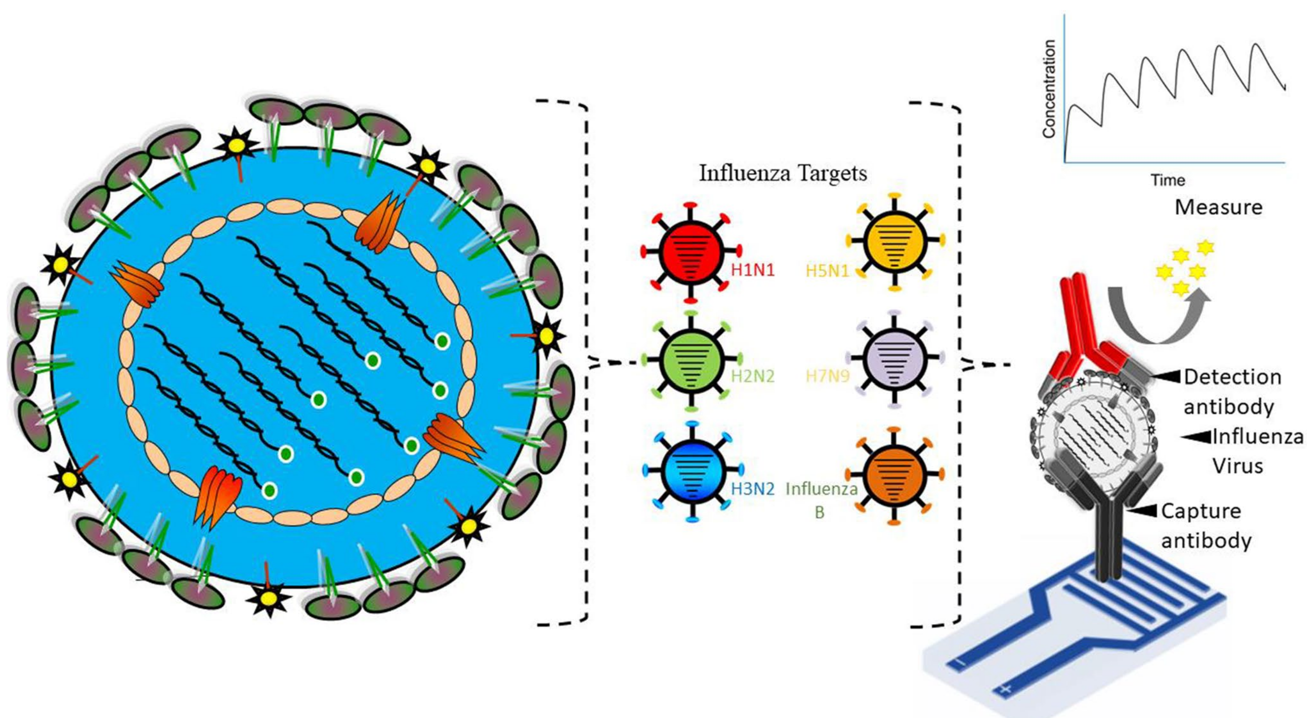

Fig. 2 Schematic representation of the general surveillance sensing system that is employed in detection of various influenza viruses. The early detection of different influenza virus enables patients to receive an accurate health surveillance and prevent pandemic/epidemic among public

serotype from fluorescence measurement and detect the sensitivity from electrochemical measurement separately (Dutta Chowdhury et al. 2018). Thus, this sensor needs tedious work and is unfriendly to users, although it has high specificity and sensitivity. Palomar et al. developed a specific electrochemical immunosensor towards DENV serotype 2. They modified homemade AuE with MWCNTs/AuNPs nanocomposite that immobilized with DENV 2 antibody (Palomar et al. 2020). The uses of nanocomposite enhance the surface area and electrochemical responses, whereas the specificity is due to the selection of the DENV 2 antibody as a biorecognition element. The result has proven the feasibility. However, the choice of DENV 2 antibody as a recognition probe was unsuitable to produce the biosensor commercially because of the high price. There are some recent research works about electrochemical biosensors to detect respiratory related viruses and flavivirus collected in Table 1.

Future perspective and challenges

A low LOD is one of the most important requirements for a highly sensitive electrochemical sensor, because it indicates the lowest concentration of target virus that can provide a detectable signal (Ahmad et al. 2018; Justino et al. 2016). The lower the LOD, the more sensitive the sensor is produced, which indicates that the virus could be detected in very early stage. Comparing the papers of Huang et al. (2016) and Tian (2017), which used very similar approaches, different LODs were reported. They both detected H7 influenza virus by LSV with antibody as bioreceptors, but Huang's team achieved a lower LOD (1.6 pg/mL) compared to LOD in Tian's report (430 pg/mL). The difference is mainly due to the nature of trace labels. Although Tian et al. pointed out that CNTs/MoS_x was an efficient catalytic support with a high specific surface area that can improve the electrical conductivity (Tian 2017), the LOD was still higher than using AgNPs as trace markers with their facile conditions that could enhance the electrocatalytic efficiency (Awan et al. 2020; Huang et al. 2016). To conclude, the choice of materials used in biosensor are crucial to get a high sensitivity application (Ahmad et al. 2018).

The other challenges are the low durability and reproducibility of the sensors due to the biofouling (Demeke Teklemariam et al. 2020). Most of the developed sensors are disposable, and unable to fully reversible that may cause a large amount of clinical waste. The importance of choosing proper eco-friendly biorecognition elements and nanomaterial probes can eliminate

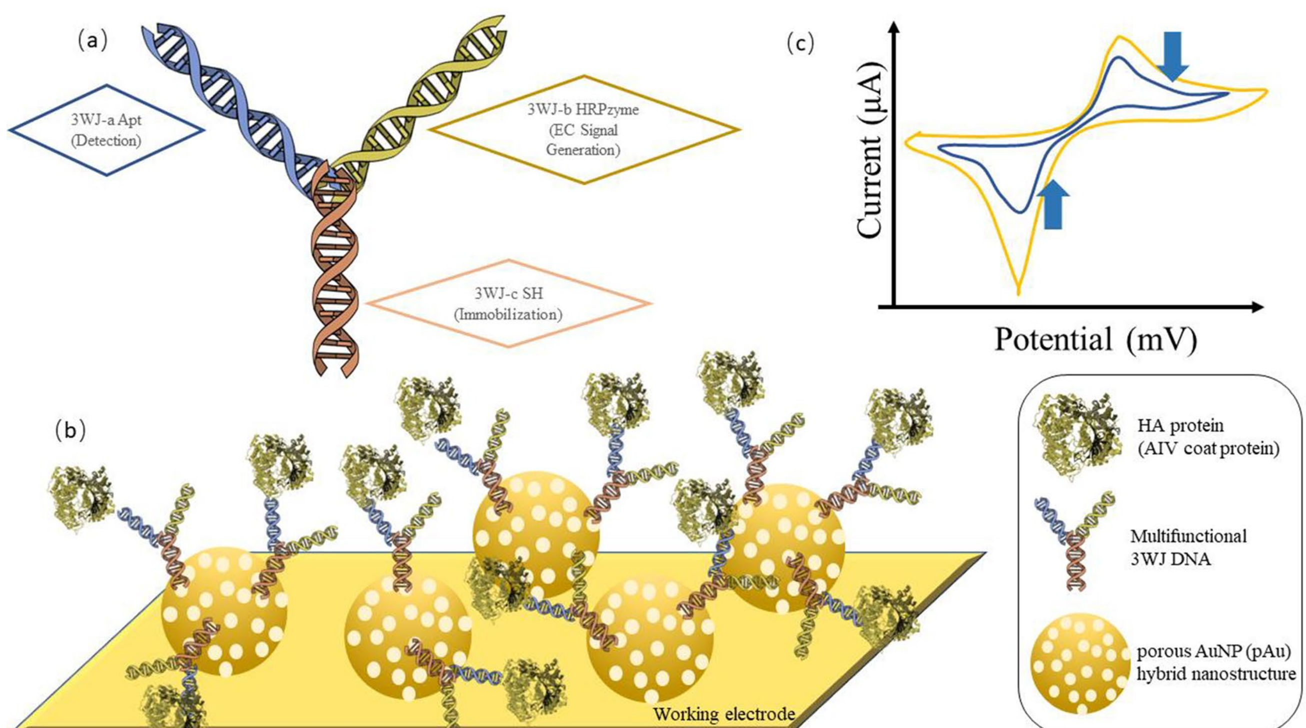

Fig. 3 **a** Functionality of every segment of three-way junction DNA (3WJ-DNA) (Lee et al. 2019). These biorecognition elements can be easily prepared to reduce the additional labelling process. 3WJ-a was introduced to virus detection part. 3WJ-b was introduced to avoid additional conjugation step for enzyme-related virus detection. 3WJ-c was introduced into thiol groups to immobilize the DNA 3WJ without additional linker material. **b** Schematic image of the fabricated AIV detection biosensor by using 3WJ DNA as bioreceptor on porous gold nanoparticles. **c** The expected decreasing of CV peak after detection of AIV

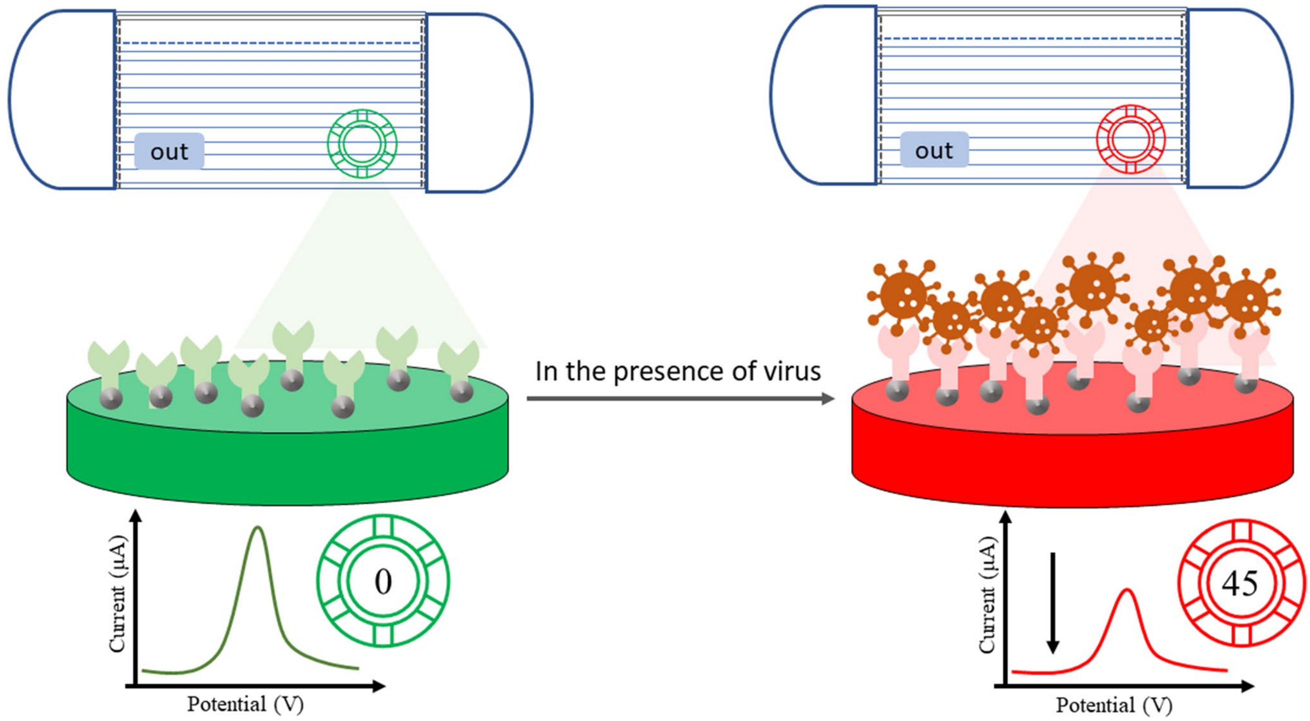

Fig. 4 Design of wearable face mask that applied with a sensor chip for real-time detection of virus spread through the air (Allawadhi et al. 2021). The nanosensor chip on the face mask shows the value on spot upon interaction with the targeted virus in the early stage. The sensor chip could connect with software application to check by phone, and it is detachable from washable face mask

the drawbacks (Khan et al. 2020). Modification and functionalization of nanomaterials, e.g. carbon nanotubes (CNTs), gold nanoparticles (AuNPs), quantum dots, and nanocomposites, on electrode surface can improve the sensor stability and amplify the corresponding electrochemical signal, due to high chemical durability, compatibility, large surface-to-volume ratio, and strong mechanical strength of nanomaterials (Curulli 2020). Among the nanomaterials, AgNPs have attracted great interest in clinical applications due to their antimicrobial, antiviral, high surface plasmon resonance (SPR), and low oxidation potential, which can enhance the signal in the detection and inhibition of viral diseases (Allawadhi et al. 2021; Niaz et al. 2018; Ravindran et al. 2013; Yu 2020). For instance, Huang et al. reported that the synthesized AgNP-G bioconjugates could be stored for at least 2 weeks under proper storage (Huang et al. 2016). In addition, they also reported that the prepared bioconjugates still showed 91.2% of their original response after 1 month of storage. However, there are also limitations associated in using nanomaterials, e.g. unstable morphology control, exhibit of toxicity, and low biocompatibility (Choi et al. 2021). Therefore, characterization of synthesized probe and optimization procedures with the respective analyte detection are vital to prepare a high-sensitivity, reproducibility, and portable sensor device (Dhal et al. 2020).

Moreover, the cross-reactivity between homologous viruses also may cause false results in differentiating the virus even affecting further treatment, control, or prevention (Zhang et al. 2021). Many electrode surface modifications with specific biorecognition elements, e.g. antibodies or DNA, can ensure the selectivity of a sensor, but most biorecognition elements are expensive because they are sensitive to degradation (Morales and Halpern 2018). Therefore, some synthetic analogue polymers that are imitating antibodies can be applied in the fabrication to maintain the native conformation (Khristunova et al. 2020). For example, Raziq et al. introduced MIPs to stabilize the sensor that was immobilized with 3WJ DNA (Raziq et al. 2021).

Despite the focus on the efficiency of electrochemical sensors, the form of the sensors can also be considered in designing the supportive viral detection devices in the future trend. For example, a wearable face mask that was applied with a biosensor chip was developed to help in tracking and identifying virus infections from the air by showing values upon detection in the early stage (Fig. 4) (Gowri et al. 2021). In addition, the form of the smart nano-biosensor chip can assist the public in self-checking with the only requirement of a smartphone as a data analytics platform on spot (Salimiyan rizi 2021). In fact, there is a huge potential for exploiting biosensors to detect viral infections as the global biosensor market is expected to grow by USD 19.79 billion from 2019 to 2027 (Lima et al. 2021). In conclusion, most of the sensing methods or devices still need further evaluation and verification before investing in the market to ensure the consistency and quality.

Conclusion

This review summarizes the studies on the applicability of electrochemical biosensors to detect respiratory-related viruses and flavivirus. Treatments and more accurate diagnoses of these viruses are still a huge challenge for the entire world even though scientists have worked out many facts about the virus, e.g., structure, origin, and infection mode (Eivazzadeh-Keihan et al. 2019; Nicolini et al. 2017). Moreover, even though there are many extensive investigations of different innovative systems that had been conducted to develop a new electrochemical sensor, there are still many other unknown parameters, e.g. supplied potential, environment temperature, and scan rate, that can affect the performance (Ahmad et al. 2018). Based on the literature, the developed sensors are efficient, but the requirements of laboratory and costly techniques are yet needed in handling the diagnosis process, surface immobilization condition, and sample preparation. Hence, priorities for the new measures are to be more commercialized, cost-effective, efficient, and user-friendly to improve the viral disease surveillance and management throughout the world.

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Author contribution Author PCA, VP, MNMI, SCBG, and PBR—planned the review and wrote up. Authors RA and DK—analysed the data. All authors read and approved the manuscript.

Data availability The sentence is a general statement about future trend of virus biosensing, which also mentioned by several researchers (Antiochia 2020; Kabay et al. 2022).

Declarations

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Consent for publication Not applicable.

Conflict of interest The authors declare no competing interests.

References

Abdul Ghani MA, Nordin AN, Zulhairee M, Che mohamad Nor A, Shihabuddin Ahmad Noorden M, Muhamad Atan MKF, Ab Rahim R, Mohd Zain Z (2022) Portable electrochemical biosensors based on microcontrollers for detection of viruses: a review. Biosensors (Basel) 12(8):666. https://doi.org/10.3390/bios12080666

Ahmad R, Wolfbeis OS, Hahn Y-B, Alshareef HN, Torsi L, Salama KN (2018) Deposition of nanomaterials: a crucial step in biosensor fabrication. Mater Today Commun 17:289–321. https://doi.org/10.1016/j.mtcomm.2018.09.024

Allawadhi P, Singh V, Khurana A, Khurana I, Allwadhi S, Kumar P, Banothu AK, Thalugula S, Barani PJ, Naik RR, Bharani KK (2021) Silver nanoparticle based multifunctional approach for combating COVID-19. Sens Int 2:100101. https://doi.org/10.1016/j.sintl.2021.100101

Anthony LS, Perumal V, Mohamed NM, Saheed MSM, Gopinath SCB (2019) An overview of unique metal oxide nanostructures for biosensor applications. In: Nanomaterials for Healthcare, Energy and Environment. Springer, Singapore. Vol. 118: pp. 51–69. https://doi.org/10.1007/978-981-13-9833-9_3

Antiochia R (2020) Developments in biosensors for CoV detection and future trends. Biosens Bioelectron 173:112777. https://doi.org/10.1016/j.bios.2020.112777

Awan M, Rauf S, Abbas A, Nawaz MH, Yang C, Shahid SA, Amin N, Hayat A (2020) A sandwich electrochemical immunosensor based on antibody functionalized-silver nanoparticles (Ab-Ag NPs) for the detection of dengue biomarker protein NS1. J Mol Liq 317. https://doi.org/10.1016/j.molliq.2020.114014

Bachour Junior B, Batistuti MR, Pereira AS, de Sousa Russo EM, Mulato M (2021) Electrochemical aptasensor for NS1 detection: Towards a fast dengue biosensor. Talanta 233:122527. https://doi.org/10.1016/j.talanta.2021.122527

Bukkitgar SD, Shetti NP, Aminabhavi TM (2021) Electrochemical investigations for COVID-19 detection-a comparison with other viral detection methods. Chem Eng J 420:127575. https://doi.org/10.1016/j.cej.2020.127575

Castillo-Henriquez L, Brenes-Acuna M, Castro-Rojas A, Cordero-Salmeron R, Lopretti-Correa M, Vega-Baudrit JR (2020) Biosensors for the detection of bacterial and viral clinical pathogens. Sensors (Basel) 20(23):6926. https://doi.org/10.3390/s20236926

CDC (2021) Flaviviruses. Retrieved from https://www.cdc.gov/vhf/virus-families/flaviviridae.html. Accessed 26 Jan 2022

Chin SF, Lim LS, Lai HC, Pang SC, Sum MSH, Perera D (2019) Electrochemical determination of Japanese Encephalitis Virus antigen using silver nanoparticles modified screen-printed carbon electrode. Nano Biomed Eng 11(4). https://doi.org/10.5101/nbe.v11i4.p333-339

Choi HK, Lee MJ, Lee SN, Kim TH, Oh BK (2021) Noble metal nanomaterial-based biosensors for electrochemical and optical detection of viruses causing respiratory illnesses. Front Chem 9:672739. https://doi.org/10.3389/fchem.2021.672739

Curulli A (2020) Nanomaterials in electrochemical sensing area: applications and challenges in food analysis. Molecules 25(23):5759. https://doi.org/10.3390/molecules25235759

Darwish NT, Alias YB, Khor SM (2015) An introduction to dengue-disease diagnostics. TrAC, Trends Anal Chem 67:45–55. https://doi.org/10.1016/j.trac.2015.01.005

Demeke Teklemariam A, Samaddar M, Alharbi MG, Al-Hindi RR, Bhunia AK (2020) Biosensor and molecular-based methods for the detection of human coronaviruses: a review. Mol Cell Probes 54:101662. https://doi.org/10.1016/j.mcp.2020.101662

Dhal A, Kalyani T, Ghorai S, Sahu NK, Jana SK (2020) Recent development of electrochemical immunosensor for the diagnosis of dengue virus NSI protein: a review. Sensors Int 1:100030. https://doi.org/10.1016/j.sintl.2020.100030

Dias AC, Gomes-Filho SL, Silva MM, Dutra RF (2013) A sensor tip based on carbon nanotube-ink printed electrode for the dengue virus NS1 protein. Biosens Bioelectron 44:216–221. https://doi.org/10.1016/j.bios.2012.12.033

Dutta Chowdhury A, Ganganboina AB, Nasrin F, Takemura K, Doong RA, Utomo DIS, Lee J, Khoris IM, Park EY (2018) Femtomolar detection of dengue virus DNA with serotype identification ability. Anal Chem 90(21):12464–12474. https://doi.org/10.1021/acs.analchem.8b01802

Eivazzadeh-Keihan R, Pashazadeh-Panahi P, Mahmoudi T, Chenab KK, Baradaran B, Hashemzaei M, Radinekiyan F, Mokhtarzadeh A, Maleki A (2019) Dengue virus: a review on advances in detection and trends - from conventional methods to novel biosensors. Mikrochim Acta 186(6):329. https://doi.org/10.1007/s00604-019-3420-y

Faria AM, Mazon T (2019) Early diagnosis of Zika infection using a ZnO nanostructures-based rapid electrochemical biosensor. Talanta 203:153–160. https://doi.org/10.1016/j.talanta.2019.04.080

Faria HAM, Zucolotto V (2019) Label-free electrochemical DNA biosensor for Zika virus identification. Biosens Bioelectron 131:149–155. https://doi.org/10.1016/j.bios.2019.02.018

Gowri A, Ashwin Kumar N, Suresh Anand BS (2021) Recent advances in nanomaterials based biosensors for point of care (PoC) diagnosis of Covid-19 - a minireview. TrAC 137:116205. https://doi.org/10.1016/j.trac.2021.116205

Huang J, Xie Z, Xie Z, Luo S, Xie L, Huang L, Fan Q, Zhang Y, Wang S, Zeng T (2016) Silver nanoparticles coated graphene electrochemical sensor for the ultrasensitive analysis of avian influenza virus H7. Anal Chim Acta 913:121–127. https://doi.org/10.1016/j.aca.2016.01.050

Ibrahim N, Jamaluddin ND, Tan LL, Mohd Yusof NY (2021) A review on the development of gold and silver nanoparticles-based biosensor as a detection strategy of emerging and pathogenic RNA virus. Sensors (Basel) 21(15):5114. https://doi.org/10.3390/s21155114

Ilkhani H, Farhad S (2018) A novel electrochemical DNA biosensor for Ebola virus detection. Anal Biochem 557:151–155. https://doi.org/10.1016/j.ab.2018.06.010

Imran S, Ahmadi S, Kerman K (2021) Electrochemical biosensors for the detection of SARS-CoV-2 and other viruses. Micromachines (Basel) 12(2):174. https://doi.org/10.3390/mi12020174

Justino CIL, Duarte AC, Rocha-Santos TAP (2016) Critical overview on the application of sensors and biosensors for clinical analysis. TrAC 85:36–60. https://doi.org/10.1016/j.trac.2016.04.004

Kabay G, DeCastro J, Altay A, Smith K, Lu HW, Capossela AM, Moarefian M, Aran K, Dincer C (2022) Emerging biosensing technologies for the diagnostics of viral infectious diseases. Adv Mater 34(30): e2201085. https://doi.org/10.1002/adma.202201085

Kabir MA, Zilouchian H, Younas MA, Asghar W (2021) Dengue detection: advances in diagnostic tools from conventional technology to point of care. Biosensors (Basel) 11(7):206. https://doi.org/10.3390/bios11070206

Kafrashi F, Afkhami A, Nabiabad HS, Madrakian T, Piri K (2017) Designing of a new label-free electrochemical impedimetric nanosensor based on selective interaction sequence of l-lysine with activase kringle domains for sensitive detection of activase protein. J Mol Liq 248:60–65. https://doi.org/10.1016/j.molliq.2017.10.034

Kaya SI, Karadurmus L, Ozcelikay G, Bakirhan NK, Ozkan SA (2020) Electrochemical virus detections with nanobiosensors. In: Nanosensors for Smart Cities. Elsevier. pp 303–326. https://doi.org/10.1016/b978-0-12-819870-4.00017-7

Khan MZH, Hasan MR, Hossain SI, Ahommed MS, Daizy M (2020) Ultrasensitive detection of pathogenic viruses with electrochemical biosensor: state of the art. Biosens Bioelectron 166:112431. https://doi.org/10.1016/j.bios.2020.112431

Khristunova E, Dorozhko E, Korotkova E, Kratochvil B, Vyskocil V, Barek J (2020) Label-free electrochemical biosensors for the determination of flaviviruses: dengue, Zika, and Japanese encephalitis. Sensors (Basel) 20(16):4600. https://doi.org/10.3390/s20164600

Kumar N, Shetti NP, Jagannath S, Aminabhavi TM (2022) Electrochemical sensors for the detection of SARS-CoV-2 virus. Chem Eng J 430:132966. https://doi.org/10.1016/j.cej.2021.132966

Lai HC, Chin SF, Pang SC, Henry Sum MS, Perera D (2017) Carbon nanoparticles based electrochemical biosensor strip for detection of Japanese Encephalitis Virus. J Nanomater 2017:1–7. https://doi.org/10.1155/2017/3615707

Lee T, Park SY, Jang H, Kim GH, Lee Y, Park C, Mohammadniaei M, Lee MH, Min J (2019) Fabrication of electrochemical biosensor consisted of multi-functional DNA structure/porous Au nanoparticle for avian influenza virus (H5N1) in chicken serum. Mater Sci Eng C Mater Biol Appl 99:511–519. https://doi.org/10.1016/j.msec.2019.02.001

Lima D, Mendes Hacke AC, Ulmer B, Kuss S (2021) Electrochemical sensing of trypanosome- and flavivirus-related neglected tropical diseases. Curr Opin Electrochem 30. https://doi.org/10.1016/j.coelec.2021.100838

Misra R, Acharya S, Sushmitha N (2021) Nanobiosensor-based diagnostic tools in viral infections: Special emphasis on Covid-19. Rev Med Virol e2267. https://doi.org/10.1002/rmv.2267

Moço ACR, Guedes PH, Flauzino JMR, da Silva HS, Vieira JG, Castro ACH, Gomes ÉVR, Tolentino FM, Soares MMCN, Madurro JM, Brito-Madurro AG (2019) Electrochemical detection of Zika virus in biological samples: a step for diagnosis point-of-care. Electroanalysis 31(8):1580–1587. https://doi.org/10.1002/elan.201900068

Monteil S, Casson AJ, Jones ST (2021) Electronic and electrochemical viral detection for point-of-care use: a systematic review. PLoS One 16(9):e0258002. https://doi.org/10.1371/journal.pone.0258002

Morales MA, Halpern JM (2018) Guide to selecting a biorecognition element for biosensors. Bioconjug Chem 29(10):3231–3239. https://doi.org/10.1021/acs.bioconjchem.8b00592

Nasrollahzadeh M, Sajjadi M, Soufi GJ, Iravani S, Varma RS (2020) Nanomaterials and nanotechnology-associated innovations against viral infections with a focus on coronaviruses. Nanomaterials (Basel) 10(6):1072. https://doi.org/10.3390/nano10061072

Nawaz MH, Hayat A, Catanante G, Latif U, Marty JL (2018) Development of a portable and disposable NS1 based electrochemical immunosensor for early diagnosis of dengue virus. Anal Chim Acta 1026:1–7. https://doi.org/10.1016/j.aca.2018.04.032

Niaz A, Bibi A, Huma, Zaman MI, Khan M, Rahim A (2018) Highly selective and ecofriendly colorimetric method for the detection of iodide using green tea synthesized silver nanoparticles. J Mol Liq 249:1047–1051. https://doi.org/10.1016/j.molliq.2017.11.151

Nicolini AM, McCracken KE, Yoon JY (2017) Future developments in biosensors for field-ready Zika virus diagnostics. J Biol Eng 11:7. https://doi.org/10.1186/s13036-016-0046-z

Ong CC, Gopinath SCB, Rebecca LWX, Perumal V, Lakshmipriya T, Saheed MSM (2018) Diagnosing human blood clotting deficiency. Int J Biol Macromol 116:765–773. https://doi.org/10.1016/j.ijbiomac.2018.05.084

Palomar Q, Xu X, Gondran C, Holzinger M, Cosnier S, Zhang Z (2020) Voltammetric sensing of recombinant viral dengue virus 2 NS1 based on Au nanoparticle-decorated multiwalled carbon nanotube composites. Mikrochim Acta 187(6):363. https://doi.org/10.1007/s00604-020-04339-y

Perumal V, Hashim U (2014) Advances in biosensors: principle, architecture and applications. J Appl Biomed 12(1):1–15. https://doi.org/10.1016/j.jab.2013.02.001

Rashid JIA, Yusof NA, Abdullah J, Hashim U, Hajian R (2015) A novel disposable biosensor based on SiNWs/AuNPs modified-screen printed electrode for dengue virus DNA oligomer detection. IEEE Sens J 15(8):4420–4427. https://doi.org/10.1109/jsen.2015.2417911

Ravindran A, Chandran P, Khan SS (2013) Biofunctionalized silver nanoparticles: advances and prospects. Colloids Surf B Biointerfaces 105:342–352. https://doi.org/10.1016/j.colsurfb.2012.07.036

Raziq A, Kidakova A, Boroznjak R, Reut J, Opik A, Syritski V (2021) Development of a portable MIP-based electrochemical sensor for detection of SARS-CoV-2 antigen. Biosens Bioelectron 178:113029. https://doi.org/10.1016/j.bios.2021.113029

Ribeiro BV, Cordeiro TAR, Oliveira EFGR, Ferreira LF, Franco DL (2020) Biosensors for the detection of respiratory viruses: a review. Talanta 2:100007. https://doi.org/10.1016/j.talo.2020.100007

Ronkainen NJ, Halsall HB, Heineman WR (2010) Electrochemical biosensors. Chem Soc Rev 39(5):1747–1763. https://doi.org/10.1039/b714449k

Salimiyan rizi K (2021) The smartphone biosensors for point-of-care detection of human infectious diseases: overview & perspectives-a systematic review. Curr Opin Electrochem. https://doi.org/10.1016/j.coelec.2021.100925

Saylan Y, Erdem O, Unal S, Denizli A (2019) An alternative medical diagnosis method: biosensors for virus detection. Biosensors (Basel) 9(2):65. https://doi.org/10.3390/bios9020065

Shi J (2021) Application of nanomaterials-based optical sensors for virus detections. J Phys Conf Ser 1906(1):012028. https://doi.org/10.1088/1742-6596/1906/1/012028

Sinawang PD, Rai V, Ionescu RE, Marks RS (2016) Electrochemical lateral flow immunosensor for detection and quantification of dengue NS1 protein. Biosens Bioelectron 77:400–408. https://doi.org/10.1016/j.bios.2015.09.048

Singh R, Sharma A, Hong S, Jang J (2014) Electrical immunosensor based on dielectrophoretically-deposited carbon nanotubes for detection of influenza virus H1N1. Analyst 139(21):5415–5421. https://doi.org/10.1039/c4an01335b

Singh R, Hong S, Jang J (2017) Label-free detection of influenza viruses using a reduced graphene oxidebased electrochemical immunosensor integrated with a microfluidic platform. Sci Rep 7:42771. https://doi.org/10.1038/srep42771

Suleman S, Shukla SK, Malhotra N, Bukkitgar SD, Shetti NP, Pilloton R, Narang J, Nee Tan Y, Aminabhavi TM (2021) Point of care detection of COVID-19: advancement in biosensing and diagnostic methods. Chem Eng J 414:128759. https://doi.org/10.1016/j.cej.2021.128759

Tai MJY, Perumal V, Gopinath SCB, Raja PB, Ibrahim MNM, Jantan IN, Suhaimi NSH, Liu WW (2021) Laser-scribed graphene nanofiber decorated with oil palm lignin capped silver nanoparticles: a green biosensor. Sci Rep 11(1):5475. https://doi.org/10.1038/s41598-021-85039-2

Tian J (2017) A high sensitive electrochemical avian influenza virus H7 biosensor based on CNTs/MoSx aerogel. Int J Electrochem Sci 2658–2668. https://doi.org/10.20964/2017.04.30

Tran QH, Hanh Nguyen TH, Mai AT, Nguyen TT, Vu QK, Phan TN (2012) Development of electrochemical immunosensors based on different serum antibody immobilization methods for detection of Japanese encephalitis virus. Adv Nat Sci Nanosci Nanotechnol 3(1):015012. https://doi.org/10.1088/2043-6262/3/1/015012

Yarman A, Kurbanoglu S, Scheller FW (2022) Present state of MIP-based sensors for SARS-CoV-2. In Sensing Tools and Techniques for COVID-19. pp 3–25. https://doi.org/10.1016/b978-0-323-90280-9.00007-9

Yu C-X (2020) Electrochemical biosensors with silver nanoparticles as signal labels. Int J Electrochem Sci 3869–3890. https://doi.org/10.20964/2020.05.53

Zhang X, Li G, Chen G, Zhu N, Wu D, Wu Y, James TD (2021) Recent progresses and remaining challenges for the detection of Zika virus. Med Res Rev 41(4):2039–2108. https://doi.org/10.1002/med.21786

Zhou C-H, Long Y-M, Qi B-P, Pang D-W, Zhang Z-L (2013) A magnetic bead-based bienzymatic electrochemical immunosensor for determination of H9N2 avian influenza virus. Electrochem Commun 31:129–132. https://doi.org/10.1016/j.elecom.2013.03.024