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REVIEW

Biosensors as transformative tools for multiplex detection of respiratory viral pathogens

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Abstract

Respiratory viral infections remain a major global health challenge, highlighting the need for rapid, sensitive, and accessible diagnostic approaches. Conventional diagnostic techniques, including reverse transcription–polymerase chain reaction (RT-PCR), viral culture, and enzyme-linked immunosorbent assays (ELISA), provide high analytical performance but are often limited by infrastructure requirements, cost, and turnaround time, restricting their use in decentralized or resource-limited settings. This review critically examines recent advances in biosensor technologies for respiratory virus detection, with a particular focus on electrochemical biosensors, Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-based biosensors detection systems, and emerging point-of-care (POC) diagnostic platforms. The manuscript discusses biosensor design strategies, detection mechanisms, analytical performance, and clinical applicability across major respiratory viral pathogens. In addition, current challenges related to clinical validation, scalability, standardization, and cost-effectiveness are analyzed. Overall, current evidence indicates that biosensor-based diagnostic platforms have significant potential to complement existing laboratory-based methods, particularly in decentralized and rapid testing settings. However, further large-scale clinical validation, regulatory standardization, and integration into healthcare workflows are required before widespread clinical implementation can be achieved.

Keywords Biosensor · Respiratory viruses · Point-of-care diagnostics · Electrochemical detection · CRISPR-Cas · Viral pathogen detection

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Abbreviations

RT-PCR	Reverse transcription polymerase chain reaction
ELISA	Enzyme-linked immunosorbent assay
POC	Point-of-care
RSV	Respiratory syncytial virus
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
LOD	Limit of detection
TPB-DVA COF	Tetraphenylbenzene-divinylazine covalent organic framework (a type of nanomaterial)
MWCNT-Au-Pt	Multi-walled carbon nanotube–gold–platinum (nanocomposite)
SAW	Surface acoustic wave
NASBA	Nucleic acid sequence-based amplification
5 S-4WJ	Five-stranded four-way junction (nucleic acid structure)
VHH	Variable heavy chain of heavy-chain antibody (nanobody)
PFU	Plaque-forming unit
$TCID_{50}$	50% Tissue culture infectious dose
IAVs-mRT-MCDA-LFB	Influenza A virus subtypes–multiplex reverse transcription multiple cross displacement amplification lateral flow biosensor
EGOFET	Electrolyte-gated organic field-effect transistor
ddPCR	Droplet digital polymerase chain reaction
EIS	Electrochemical impedance spectroscopy
DPV	Differential pulse voltammetry
CV	Cyclic voltammetry
SPR	Surface plasmon resonance
LSPR	Localized surface plasmon resonance
NanoMIPs	Nano-sized molecularly imprinted polymers
hACE2	Human angiotensin-converting enzyme 2
STM-BJ	Scanning tunneling microscopy break-junction
GC-FP	Grating-coupled fluorescent plasmonics
RAPID 1.0	A specific biosensor platform name
CNT-FET	Carbon nanotube field -effect transistor
MXene	A class of two-dimensional inorganic compounds (e.g., $Ti_3C_2T_x$)
gFET	Graphene field-effect transistor
ePAD	Electrochemical paper-based analytical device
acpcPNA	Pyrrolidinyl peptide nucleic acid (a specific type of PNA)
CRISPR	Clustered regularly interspaced short palindromic repeats
Cas	CRISPR-associated protein (e.g., Cas9, Cas12a, Cas13a)
crRNA	CRISPR RNA
RDB	Reverse dot blot
MCDA	Multiple cross displacement amplification
HAdV	Human adenovirus
rGO-FET	Reduced graphene oxide field-effect transistor
eIPs	Epitope-imprinted polymers
Nano RHB	Nanoscale robotic hand biosensor
ERA	Enzymatic recombinase amplification
LFA/LFB	Lateral flow assay / lateral flow biosensor
ICA	Immunochromatographic assay
PDQB	Likely a specific nanobead type, e.g., Polydopamine-coated Quantum Beads
HCR	Hybridization chain reaction
MAD	Minimal amplification-free detection
RT-RPA	Reverse transcription recombinase polymerase amplification
3Cpro	3 C protease (of rhinovirus)
DMR	Dynamic mass redistribution
R-EGFET	Rapid extended-gate field-effect transistor
MOF	Metal-organic framework
UiO-66	University of Oslo-66 (a specific type of MOF)
HN	Hemagglutinin-neuraminidase (protein of parainfluenza virus)
ACEF	Alternating-current electrothermal flow
BALF	Bronchoalveolar lavage fluid
RT-LAMP	Reverse transcription loop-mediated isothermal amplification
EIA	Enzyme immunoassay
RIA	Radioimmunoassay
CLIA	Chemiluminescence immunoassay
TEM	Transmission electron microscopy
AI	Artificial intelligence

Introduction

Respiratory viral infections represent a major global public health burden, contributing to substantial morbidity and mortality worldwide. Seasonal influenza viruses infect millions of individuals annually and are responsible for hundreds of thousands of deaths globally each year. (Carter

et al. 2020). Similarly, respiratory syncytial virus (RSV) remains a leading cause of lower respiratory tract infections in infants and elderly populations, while emerging viral outbreaks such as SARS-CoV, MERS-CoV, and SARS-CoV-2 have demonstrated the pandemic potential of respiratory pathogens and their capacity to overwhelm healthcare system (Tabatabaei et al. 2025). These epidemiological trends highlight the urgent need for rapid, sensitive, and scalable diagnostic approaches for early detection and outbreak containment(Yimer et al. 2024). Currently, reverse transcription polymerase chain reaction (RT-PCR) is considered the gold standard for respiratory virus detection due to its high analytical sensitivity and specificity. However, conventional diagnostic approaches including viral culture, RT-PCR, and enzyme-linked immunosorbent assays (ELISA) often require sophisticated laboratory infrastructure, trained personnel, and relatively long turnaround times. These limitations can significantly restrict large-scale screening capacity, particularly during outbreaks or in resource-limited settings where rapid clinical decision-making is critical. (Kumar et al. 2022).

In this context, biosensor-based diagnostic platforms have emerged as promising alternatives due to their ability to convert biological interactions into measurable signals in real time. (Karunakaran et al. 2015). Biosensors typically integrate biorecognition elements such as antibodies, nucleic acids, or enzymes with transducers capable of generating electrochemical, optical, or piezoelectric outputs. Among these, electrochemical biosensors have gained particular attention due to their high sensitivity, low cost, portability, and compatibility with point-of-care (POC) testing formats. (Saylan et al. 2019).

Recent advances have enabled biosensors to target multiple viral components, including surface proteins such as SARS-CoV-2 spike protein and influenza hemagglutinin, as well as viral nucleic acids. These features position biosensor technologies as potential tools for decentralized testing in clinical settings, community screening, and outbreak surveillance.(Choi 2020; Abdolmaleki et al. 2025). Compared with conventional diagnostic approaches such as RT-PCR and ELISA, biosensor-based platforms are not intended to replace gold-standard assays in all clinical contexts, but rather to complement them by addressing critical gaps in diagnostic accessibility and turnaround time(Aziz et al. 2021). While RT-PCR remains the benchmark for analytical sensitivity and specificity, it is constrained by centralized infrastructure, trained personnel, and longer processing times(10. 2025). In contrast, biosensors offer rapid time-to-result, minimal sample preparation, and point-of-care deployability, albeit often with reduced analytical robustness across heterogeneous clinical matrices(Lino et al. 2022). Framing biosensor technologies within this complementary diagnostic paradigm is essential for evaluating their translational relevance and realistic clinical utility. Therefore, this review aims to critically evaluate recent advances in high-performance biosensor technologies for respiratory viral detection, with emphasis on analytical performance, translational potential, and their complementary role alongside established diagnostic standards within point-of-care testing frameworks.

Respiratory viral pathogen

Multiple respiratory virus epidemics, both emerging and re-emerging, have significantly impacted global public health over the past few decades. In addition to the influenza pandemic in 2009 and the COVID-19 pandemic in 2020, these viruses have caused substantial morbidity and mortality worldwide. Respiratory viruses originate from five major viral families (Adenoviridae, Orthomyxoviridae, Picornaviridae, Coronaviridae, and Pneumoviridae). Most of these pathogens are RNA viruses, and many have zoonotic origins (Fig. 1). Understanding the patterns and characteristics of past outbreaks is essential for improving future prevention and mitigation strategies (Gray et al. 2021).

2009 H1N1 Influenza A pandemic (H1N1pdm09) virus

The H1N1pdm09 virus originated in Mexico in 2009 and rapidly disseminated globally, resulting in approximately 60.8 million infections and a minimum of 12,469 fatalities in the United States from 2009 to 2010 (Shrestha et al. 2011; 14. 2009). Improved methods of monitoring the spread of the influenza A virus were prompted by this swine-like virus, which is still circulating in pigs and humans today. This RNA virus is a member of the Orthomyxoviridae species (Gray et al. 2021).

Influenza B

The influenza B virus can be described as an enclosed, negative-sense, single-stranded virus with eight segments of genomic RNA that encode eleven or more viral proteins (Koutsakos et al. 2016).The following proteins are part of the complex: the polymerase subunits (PA, PB1 and PB2), the nucleoprotein (NP), the surface glycoproteins (HA, NA and NB), the matrix protein (BM1), the ion channel (BM2), the non-structural protein (NS1), and the nuclear export protein (NEP) (Zaraket et al. 2021).

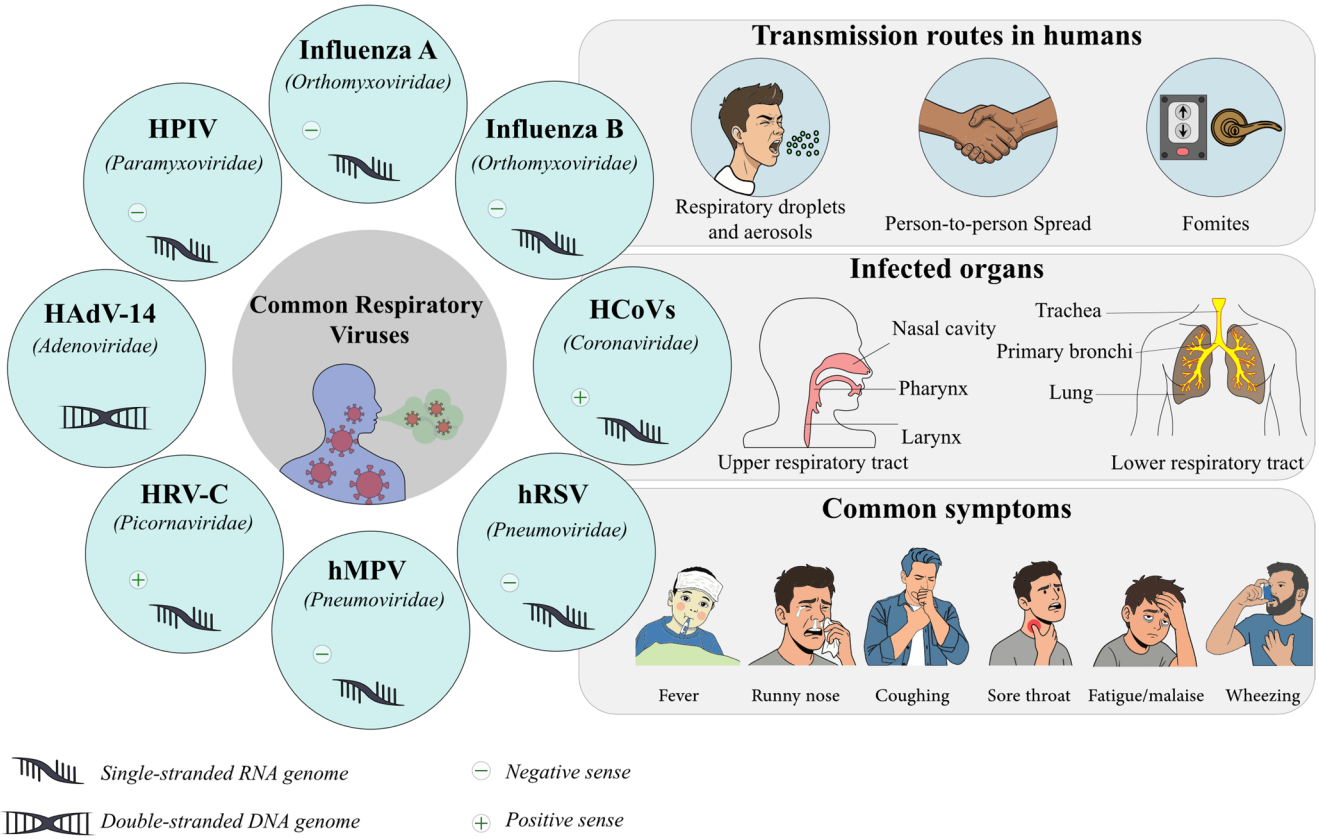

Fig. 1 Common respiratory viruses belong to diverse viral families with distinct genome structures. Transmission occurs through multiple routes, including inhalation of respiratory droplets and aerosols, as well as contact with contaminated surfaces. Viral entry primarily occurs via the nasal epithelium, oral cavity, and conjunctival mucosa. Following entry, infection may involve both the upper and lower respiratory tracts, resulting in a wide spectrum of clinical manifestations. (Figure created by the authors using graphical design software)

Human coronaviruses (HCoVs)

Coronaviruses causing severe acute respiratory syndrome (SARS-CoV), MERS-CoV, HCoV-OC43, HCoV-229E, HCoV-HKU1, and SARS-CoV-2 are the seven HCoVs identified thus far. Four of these viruses, namely HCoV-NL63, −229E, -HKU1, and -OC43, typically induce mild to moderate respiratory illnesses with a seasonal occurrence (Kesheh et al. 2022).Since 2000, three novel human coronaviruses have emerged, exhibiting a considerable death rate. While SARS-CoV and MERS-CoV resulted in epidemics in certain nations, SARS-CoV-2 intensified into a pandemic. All HCoVs can induce serious problems in elderly and immunocompromised patients (Kesheh et al. 2022).

Human respiratory syncytial virus (hRSV)

Newborns, immunocompromised individuals, and the elderly are most commonly infected with hRSVs, which are now recognized as human orthopneumoviruses. These viruses are members of the Pneumoviridae family and the Orthopenumovirus genus (Pacheco et al. 2021).Infection by hRSV may result in moderate symptoms, including fever, coughing, and wheezing, as well as severe manifestations such as bronchiolitis and pneumonia, which can necessitate hospitalization (Soto et al. 2020). hRSV infections are projected to result in 3.2 million hospitalizations annually, with 1.4 million admissions involving infants under six months of age (Shi et al. 2017).

Human adenovirus 14 strain (HAdV14)

HAdV14 reappeared in the United States in 2006, resulting in a minimum of 750 infections and 13 fatalities (Gautret et al. 2014).Similar to other viruses, monitoring for this "killer cold virus" is limited; nonetheless, existing data indicate its dissemination to at least Ireland, Canada, and China, where it continues to circulate. Although several

adenoviruses have crossed species barriers, this particular adenovirus is not considered zoonotic(Borkenhagen et al. 2019).HAdV14 is a member of the Adenoviridae family (Gray et al. 2021).

Rhinovirus group C (HRV-C)

HRV-C was discovered in 2004, subsequent to an outbreak of influenza-like disease in New York State (Lamson et al. 2006). In restricted surveillance investigations, HRV-C has been recognized as the predominant circulating strain of rhinovirus during the autumn and winter seasons across many nations (Lau et al. 2010). Research has linked HRV-C to a more serious range of respiratory symptoms, including asthma, wheezing, bronchitis, and pneumonia, compared to rhinoviruses A and B (Lau et al. 2010).The virus has transmitted from humans to nonhuman primates (Scully et al. 2018).This RNA virus is classified under the Picornaviridae family(Gray et al. 2021).

Human metapneumoviruses

hMPV was initially identified in 2001 in the Netherlands, however it is believed to have been circulating for at least 50 years prior (Van den Hoogen et al. 2001). Phylogenetic investigations suggest that divergence from an avian ancestor happened approximately 200 years ago (Schildgen et al. 2011).It accounts for 6–40% of acute respiratory infections in children under the age of five, and serological investigations reveal that almost all children have antibodies to it by the time they are five years old(Shafagati and Williams 2018). This RNA virus was previously classified as a subfamily of the Paramyxoviridae family, but as of 2016 it is now considered to be a member of the Pneumoviridae family (Gray et al. 2021).

Human parainfluenza virus (HPIV)

HPIV is a significant etiological agent of acute respiratory tract infections, including croup in pediatric populations and pneumonia in immunocompromised individuals (Russell et al. 2019). The four main serotypes of HPIV, which is a single-stranded, enveloped RNA virus belonging to the Paramyxoviridae family are distinguished by complement fixation and hemagglutinating antigens (Park et al. 2024; Hall 2001).HPIV-1 and HPIV-3 are classified under the genus Respirovirus, while HPIV-2 and HPIV-4 are categorized inside the genus Rubulavirus.Children typically experience croup when infected with HPIV-1 or HPIV-2, while serotype HPIV-3 is most commonly linked to pneumonia and bronchiolitis (Choi 2020).

Respiratory viral pathogen detection

Conventional methods for detecting infectious respiratory viral infections rely on virus-infected cell cultures, nucleic acids, or viral antigens and antibodies, necessitating skilled personnel, cumbersome equipment, and considerable time investment.Clinical laboratories also have limitations when it comes to procedures based on cytology, sequencing, or electron microscopy (Lu et al. 2021).

The most reliable method for identifying respiratory viruses in a lab setting is virus isolation and culture (Leland and Ginocchio 2007).Once viruses have been successfully isolated, other steps such as immunofluorescence labeling and electron microscopy are needed to confirm their existence (Goldsmith and Miller 2009). An additional technique for virus identification is hemadsorption, which relies on cell culture (Connor and Loeb 1983). The red blood cells clump together after adhering to the viral cell monolayer's plasma membrane; this makes them visible to the human eye. Cell culture is a precise standard method for virus detection; nevertheless, its four-week duration is excessively lengthy for application during a probable viral illness outbreak. The appearance of quick virus culture technologies, including centrifugal enhancement technology (shell vial method), has drastically reduced the test cycle from one week to one or two days, with the goal of expediting the virus isolation procedure (Gleaves et al. 1984).Virus isolation efficiency has been significantly improved by the shell vial approach for numerous viruses, including influenza, dengue, and a number of respiratory viruses (Lu et al. 2021).

Due to the diminutive size of most respiratory viruses, which precludes direct observation with a light microscope, transmission electron microscopy (TEM) is the exclusive approach for their direct detection (37. 2020; Hopfer et al. 2021; Nagayama and Danev 2008).Despite being supplanted by more sensitive techniques like PCR and immunofluorescence assays, TEM continues to hold significant relevance in certain facets of virology research, including the identification of novel viruses, virus characterisation, and titer assessment.A significant benefit of TEM is its independence from virus-specific detection reagents. This is of utmost importance in the event of a widespread epidemic of a virus that has not yet been identified, as there are currently no focused detection reagents or procedures available for this sort of virus. Negative staining transmission electron microscopy (TEM) has demonstrated its significance in the finding and detection of novel viruses, including Ebola and SARS viruses (Goldsmith and Miller 2009; Pattyn 1977; Drosten et al. 2003). Another instance is COVID-19, during which scientists obtained the electron micrograph of the virus in its initial phases and identified its morphological characteristics, thereby conserving crucial time for

prevention and management (Jennifer 2020). Nonetheless, owing to the substantial operational expenses of the device and the requirement for ample space and connectivity infrastructure, TEM analysis can be conducted exclusively at designated accredited centers.

Clinically, standard methods for identifying respiratory viruses are immunological in nature (e.g., enzyme-linked immunosorbent assay (EIA), radioimmunoassay (RIA)), relying on antigen-antibody interactions (Khanna et al. 2001). RIA uses radioisotope-labeled antibodies or antigens to detect them (Burke et al. 1982); however, an alternative technology called the enzyme immunoassay (EIA or ELISA) was developed because of the radiation risk that is involved with RIA. These two methods, along with chemiluminescence immunoassay (CLIA), which combines immunochemical reactions with a chemiluminescence approach, have been used routinely in clinical laboratories for protein identification due to their excellent sensitivity (Boonham et al. 2014). Specifically, ELISA, capable of detecting proteins at exceedingly low concentrations (10^{-12}~10^{-9} mol/L), has been employed in the identification of influenza viruses (Khanna et al. 2001). Clinical laboratories commonly use serological procedures based on chemiluminescence, which require large automated machinery. Subsequent to a respiratory viral infection, the immune system responds by generating antibodies against the virus. The levels of these antibodies can be used to track how well the immune system is responding to viral antigens. This includes both IgM responses, which indicate acute infections, and IgG produced either during the main infection or the acute phase of a secondary infection. However, while there is a window of opportunity between viral infection and antibody synthesis starting, immunoassays can produce misleading negative results (Lu et al. 2021).

When it comes to diagnosing respiratory viruses, nucleic acid identification technology has completely changed the game by doing away with the false negative window impact (Zhang et al. 2020). This method exhibits elevated sensitivity, commendable stability, and a reduced reaction time relative to conventional culture techniques. By expanding nucleic acids, it is possible to reverse-transcribe RNA into DNA and carry out PCR analysis; it is also possible to amplify a specific area of DNA sequence 106-fold in vitro. In addition, the sensitivity of the real-time RT-PCR test for influenza detection is on par with or higher than that of cell culture methods, which are regarded as reference methods for viral identification (Van Elden et al. 2001). It is also significantly quicker than the endpoint detection approach. A more modern nucleic acid detection-based technique for COVID-19 infection identification, the cobas®SARS-CoV-2 qualitative assay, was developed and even received emergency use authorization from the FDA (Lu et al. 2021). In order to qualitatively assess nasopharyngeal and oropharyngeal swab samples from patients who satisfy the clinical or epidemiological criteria for COVID-19 nucleic acids in SARS-CoV-2, the cobas® SARS-CoV-2 is a real-time RT-PCR assay for the cobas®6800/8800 system. Although the 8800 version of the system is capable of detecting 4128 samples every day, the 6800 version is capable of detecting 1440 samples per day.This nucleic acid amplification approach improves the time it takes to identify coronavirus by a factor of ten, freeing up valuable resources for illness prevention efforts, in comparison to other methods that are currently in use. Nucleic acid testing is a reliable way to detect respiratory viruses, although it does necessitate a well-equipped laboratory and operators with specialized training (Lu et al. 2021). Collectively, these conventional diagnostic techniques ranging from viral culture and TEM to immunoassays and nucleic acid amplification provide high analytical value but remain constrained by long turnaround times, dependence on centralized laboratory infrastructure, specialized personnel requirements, and limited suitability for decentralized or rapid testing scenarios. These limitations become particularly evident during outbreak surges, in resource-limited settings, or when timely clinical decision-making is essential. Such constraints underscore the need for alternative diagnostic platforms that can deliver rapid, sensitive, and accessible detection at or near the point of care. In this context, biosensor-based technologies have emerged as promising complementary tools capable of addressing several gaps inherent to traditional diagnostic workflows, as discussed in the following section.

Biosensor

The swift detection of infectious diseases and the prompt commencement of suitable treatment are essential factors that enhance optimal clinical outcomes and public health. Standard in vitro testing for infectious diseases is laborious, necessitating centralized labs, seasoned staff, and cumbersome machinery. Recent advancements in biosensor technology provide the potential to provide point-of-care diagnostics that meet or exceed traditional benchmarks in terms of timeliness, precision, and cost-effectiveness (Sin et al. 2014).

Chemical information derived from biomolecule concentrations can be converted into actionable analysis signals by use of a biosensor (Thévenot et al. 2001).Many other areas put it to good use, including environmental monitoring, process control, food safety, medical diagnostics, and many more (Kowalczyk 2020).Over the past four decades, advancements in biosensor research have significantly progressed, benefiting from developments in nanoscience,

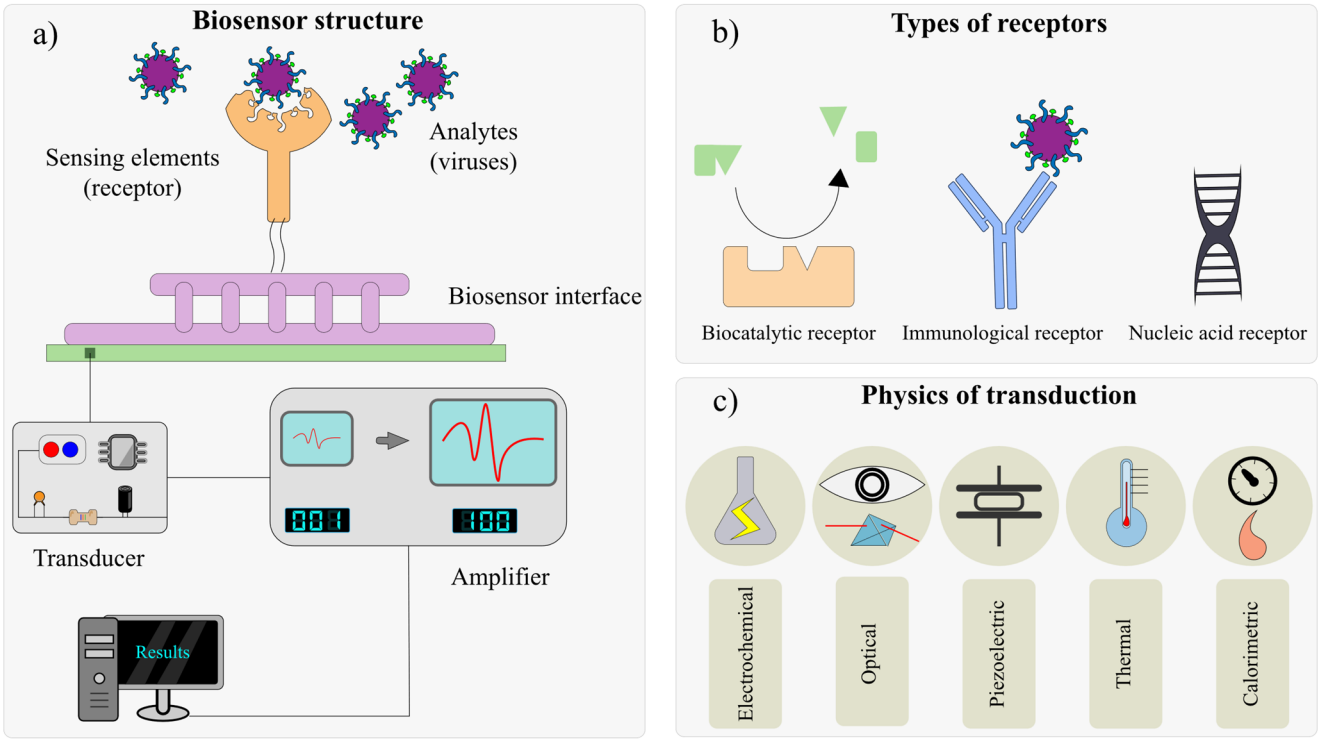

Fig. 2 General characteristics of biosensors. **a** The four fundamental components include sensing elements, interface, transducer, and electronic system; other components may be observed depending on biosensor structure or experimental design. **b** Biosensors are classified by receptor type into biocatalytic, immunological, and nucleic acid categories, each representing distinct mechanisms with vast diversity in specificity and function. **c** Based on transduction principles, biosensors are further divided into electrochemical, piezoelectric, optical, thermal, and calorimetric types. (Figure created by the authors using graphical design software)

electronics, biology, and silicon technology (Schuster 2018). Moreover, the advancement of artificial intelligence (AI) and large data has rendered intelligent biosensors a prominent area of research. Biosensors are becoming increasingly significant in everyday life and scientific inquiry (Song et al. 2021).

The four main components of a biosensor are as follows: first, the sensing elements, also called receptors, which bind to the analyte under test; second, the interface, which provides a working environment for the biosensor elements (Schmidt and Montemagno 2004); third, the transducer, which converts the physical or chemical information from the analyte's interaction with the sensing elements into electrical signals (Turner 2014); and finally, a suite of electronic equipment, including signal amplification, signal processing, and an interface circuit for data analysis and processing (Cavalcanti et al. 2008) (Fig. 2a).

Biosensors can generally be categorized according to three frameworks Biosensors can be categorized based on receptor types into biocatalytic biosensors (e.g., enzymes), immunological biosensors (e.g., antibodies), and nucleic acid biosensors (e.g., DNA) (Fig. 2b). The physics of transduction dictates that electrochemical, piezoelectric, optical, thermal, and calorimetric biosensors are all part of the process (2008) (Fig. 2c). It encompasses a wider range of biosensors in terms of their potential uses, including those in the medical and clinical domains, the environment, and wearable technology. Furthermore, commercial biosensors can be classified into two categories based on their design: laboratory-based or portable (2008).

Biosensor for respiratory viral pathogen detection

Biosensors offer a robust option for the real-time, sensitive, and on-site detection of viral antigens, nucleic acids, or complete virions via various biorecognition mechanisms. Progress in nanomaterials, microfluidics, and signal-transduction technologies has significantly improved the efficacy of these platforms, enabling customized detection methods for particular respiratory viruses, including influenza viruses, coronaviruses, RSV, adenoviruses, and rhinoviruses(Li et al. 2025). The subsequent subsections encapsulate current advancements in biosensor technology for each principal respiratory virus, emphasizing their analytical efficacy, recognition components, sample matrices, and applicability in clinical or point-of-care settings. In

recent years, increasing attention has been directed toward multiplexed and syndromic biosensor platforms capable of simultaneously detecting multiple respiratory viral pathogens from a single clinical sample. This approach is particularly relevant given the substantial overlap in clinical symptoms among respiratory infections caused by influenza viruses, SARS-CoV-2, RSV, adenoviruses, and rhinoviruses(Domnich et al. 2024). Multiplexed biosensors, including electrochemical sensor arrays, field-effect transistor–based platforms, CRISPR-assisted systems, and multiline lateral flow devices, enable parallel analysis of several viral targets, thereby reducing diagnostic time, cost, and sample volume requirements(Sadique et al. 2022). Despite their significant promise, multiplexed detection introduces additional technical challenges such as signal cross-reactivity, assay optimization, and data interpretation complexity, which must be carefully addressed to ensure analytical reliability and clinical applicability(Prabowo et al. 2021). The following subsections highlight both single-analyte and multiplexed biosensing strategies developed for major respiratory viruses, reflecting the evolving trend toward comprehensive, point-of-care respiratory diagnostics.

Influenza A virus

Electrochemical and optical biosensors have demonstrated remarkable capabilities for the sensitive and selective detection of Influenza A virus and its subtypes. An electrochemical DNA biosensor incorporating Tetraphenylbenzene-Divinylazine Covalent Organic Framework (TPB-DVA COF) nanomaterials with dual DNA probes achieves highly sensitive detection of Influenza A cDNA, covering a wide dynamic range (10 fM–10^3 nM) with an exceptionally low limit of detection (LOD) of 5.42 fM. Utilizing animal tissue samples as the detection matrix, this platform showed strong concordance with ddPCR results, confirming its analytical reliability. Its specificity and suitability for monitoring infection stages make it a promising tool for rapid clinical and field diagnostics (Yan et al. 2023).

Optical biosensors have also been employed for Influenza A detection. One such platform uses nanopillar structures as bioreceptors and sialic acid-mimicking peptides to detect hemagglutinin biomarkers. This label-free system, which operates through straightforward reflectance measurements over a range of 10^3–10^5 PFU, offers a practical approach for rapid immunodiagnosis of influenza viruses (Lee et al. 2021). Similarly, Electrolyte-Gated Organic Field-Effect Transistor (EGOFET) -based aptasensors employ influenza A-specific aptamers for fast and quantitative detection of intact viral particles, showing high selectivity even against control bioliquids and other viruses such as Newcastle disease virus and influenza B (Poimanova et al. 2023).

Electrochemical immunosensors provide additional options for detecting hemagglutinin proteins. For example, a platform using a Multi-Walled Carbon Nanotube–Gold–Platinum (MWCNT-Au-Pt) modified gold screen-printed electrode with anti-H1 monoclonal antibodies facilitates quantitative impedance-based detection of H1N1, with a linear range of 2.5–25 µg/mL and LOD of 3.54 µg/mL. Testing in synthetic saliva further supports its practical applicability (Büyüksünetçi and Anık 2023). Likewise, surface acoustic wave (SAW) biosensors employing phosphate-functionalized DNA probes allow highly sensitive, label-free detection of H1N1 DNA, with a linear range of 50 pM–10 nM and an LOD of 14.4 pM (Sun et al. 2024).

Other electrochemical approaches include systems based on square-wave voltammetry with a five-stranded four-way junction nucleic-acid recognition system, achieving excellent linearity, precision, and accuracy, with integration to Nucleic Acid Sequence-Based Amplification (NASBA) enabling isothermal amplification at 41 °C (Ojeda et al. 2024). Triple-mode DNA-RNA hybridization biosensors use multifunctional probes to generate electrochemical, fluorescent, and colorimetric signals, attaining an LOD as low as 0.3 aM and demonstrating effective detection in serum, saliva, and nasopharyngeal swabs (Dong et al. 2024).

Antibody-based electrochemical immunosensors target H1N1 hemagglutinin with high sensitivity, showing a linear range of 0.25–5 pg/mL, an LOD of 0.25 pg/mL, and a sensitivity of 92.1 µA $(pg/mL)^{-1}$ cm^2 (Bao et al. 2023). Potentiometric biosensors employing self-assembling monolayers detect whole virions (H1N1 and H3N2) in microliter volumes with LODs of 200 PFU/mL, enabling rapid point-of-care diagnosis with minimal sample preparation (Lee et al. 2022).

High-coverage molecular beacon probes, as developed in the FEVER pipeline, enable selective detection of Influenza A RNA with LODs of 50 nM (waveguide-based biosensors) and 1 nM (flow cytometry), further enhanced to 500 pM via exonuclease selection, providing rapid and accurate diagnostics (Courtney et al. 2021). Multiplexed molecular platforms such as Influenza A Virus subtypes–multiplex Reverse Transcription–Multiple Cross Displacement Amplification–Lateral Flow Biosensor (IAVs-mRT-MCDA-LFB) integrate isothermal amplification with dual-channel lateral flow biosensors, allowing highly sensitive detection of subtypes H1N1, H3N2, and H7N9 within one hour without cross-reactivity (Wang et al. 2025) (Fig. 3).

Electrochemical biosensors using carbon screen-printed electrodes enhanced with gold nanoparticles and monoclonal

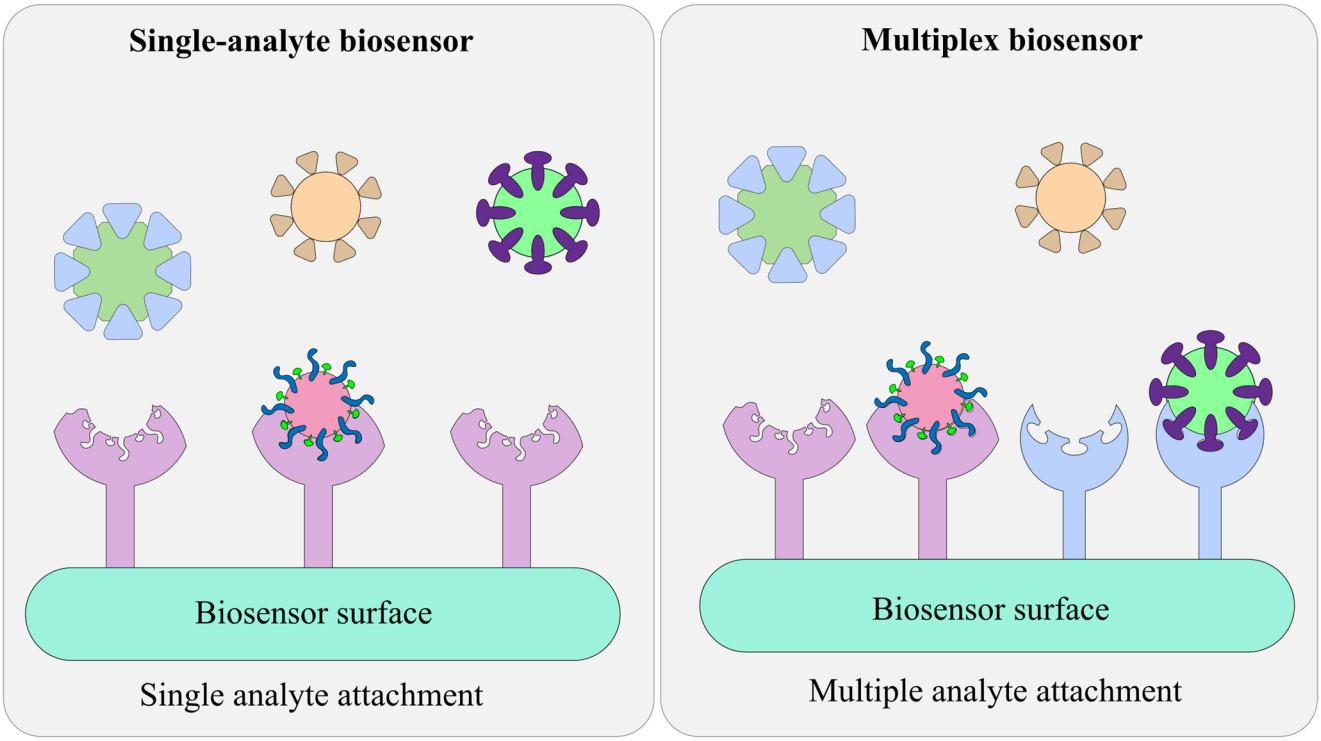

Fig. 3 Comparison of multiplex and single-analyte biosensors. Multiplex biosensors are designed to detect multiple targets simultaneously within a single assay, enabling comprehensive analysis and high-throughput diagnostics. In contrast, single-analyte biosensors focus on the selective detection of one specific target, providing high sensitivity and specificity but limited scope. (Figure created by the authors using graphical design software)

antibodies demonstrate stable and effective detection of the H1 hemagglutinin protein, supporting sensitive Influenza A diagnostics (Torres-Méndez et al. 2021). Whole-cell yeast biosensors with surface-displayed VHH antibody fragments enable quantitative detection of H1N1-HA and intact Virus particles across wide concentration ranges, providing rapid detection without analyte transfer (Seo et al. 2024). Reusable electrochemical biosensors employing enzyme-linked receptors on functionalized microbeads achieve femtomolar LODs for H1N1 nucleoprotein and maintain performance over multiple uses (Park et al. 2025).

Fluorescence-based approaches, such as multiplex fluorescence lateral flow immunoassays using quantum dot nanobeads, achieve low LODs (41 copies/mL) and fast detection in clinical samples within 20 min, offering a reliable point-of-care solution (Li et al. 2025). Affinity peptide-hydrogel microsphere sensors targeting H3N2 hemagglutinin provide quantitative detection with a LOD of 1.887 PFU/mL, demonstrating reproducibility, reusability, and adaptability for broader viral diagnostics (Kim et al. 2023).Overall, these diverse biosensor platforms electrochemical, optical, SAW, immune, and fluorescence-based offer high sensitivity, specificity, and practical applicability for rapid, point-of-care, and field-based detection of Influenza A Virus and its subtypes (Table1).

Influenza B virus

Electrochemical, optical, and fluorescence-based biosensors have demonstrated strong potential for the sensitive and selective detection of Influenza B Virus. A DNA biosensor employing DNA probes immobilized on gold nanoparticles can specifically identify the Influenza B nucleoprotein (NP) gene. Using nasopharyngeal swabs as the detection matrix, this platform accurately differentiates complementary viral sequences from mismatches, showing complete concordance with real-time PCR results. Although a specific LOD is not provided, the system represents a precise and sensitive methodology for rapid clinical diagnosis of Influenza B (Yahyavi et al. 2024).The FEVER pipeline has also been applied to Influenza B, generating high-coverage RNA probes assessed via waveguide-based optical biosensors and flow cytometry bead assays. This approach achieves RNA detection levels of 50 nM (optical) and 1 nM (flow cytometry), with further sensitivity enhanced to 500 pM through exonuclease selection. Such amplification-free detection provides a promising platform for rapid diagnostics and biosurveillance of Influenza B (Courtney et al. 2021).

This multiplexed colorimetric platform simultaneously detects Influenza A and Influenza B, enabling dual-target identification within a single assay. One optical/colorimetric

Table 1 Biosensors for Influenza A virus detection

Type of biosensor	Bioreceptor	LOD	Response time	Biomarker	Method	Matrix	References
Electrochemical DNA biosensor	Dual DNA probes	5.42 fM	Not Specified	Viral cDNA	Electrochemical (Dual-probe)	Animal tissue	(Yan et al. 2023)
Optical biosensor	Biomimetic peptide nanopillars	Not Specified (Range: 10^3–10^5 PFU)	Label-free, rapid	Hemagglutinin (HA)	Reflectance measurement	Not Specified	(Lee et al. 2021)
EGOFET-based aptasensor	Influenza A-specific aptamer	Not Specified	Rapid, quantitative	Intact viral particles	Field-effect transistor	Allantoic fluid	(Poimanova et al. 2023)
Electrochemical immunosensor	Anti-H1 monoclonal antibody	3.54 µg/mL	Not Specified	Hemagglutinin (H1)	Electrochemical Impedance Spectroscopy	Synthetic saliva	(Büyüksünetçi and Anık 2023)
Surface Acoustic Wave (SAW) biosensor	Phosphate-functionalized DNA probes	14.4 pM	Label-free, rapid	H1N1 target DNA	Frequency shift	Ambient conditions	(Sun et al. 2024)
Electrochemical biosensor	5 S-4WJ nucleic-acid system	Not Specified	Rapid (with NASBA)	Viral RNA	Square-wave voltammetry	Not Specified	(Ojeda et al. 2024)
Triple-mode biosensor	Multifunctional DNA probe	0.3 aM (in synthetic DNA)	Rapid, on-site	Viral Nucleic Acids	Electrochemical, Fluorescent, Colorimetric	Serum, Saliva, Swabs	(Dong et al. 2024)
Electrochemical immunosensor	H1N1-specific antibody	0.25 pg/mL	Rapid	Hemagglutinin	Amperometry	Not Specified	(Bao et al. 2023)
Potentiometric biosensor	Self-assembled monolayer	200 PFU/mL	Rapid (< 1 min)	Surface structures of virions	Potentiometry	Human saliva	(Lee et al. 2022)
Optical biosensor / Flow Cytometry	Molecular beacon probes	50 nM/1 nM	Rapid	Influenza A RNA	Waveguide optics / Flow Cytometry	Not Specified	(Courtney et al. 2021)
Lateral Flow Biosensor (LFB)	Specific primers	Higher than RT-PCR	< 1 h	H1, H3, H7 genes	RT-MCDA-LFB	Not Specified	(Wang et al. 2025)
Electrochemical biosensor	Monoclonal antibody	Not Specified	Not Specified	H1 hemagglutinin	EIS, DPV, CV	Not Specified	(Torres-Méndez et al. 2021)
Whole-cell biosensor	Yeast with VHH antibody (Q-body)	2.4×10^4 PFU/mL (virus)	Not Specified	H1N1-HA / Intact virus	Fluorescence	Not Specified	(Seo et al. 2024)
Reusable electrochemical biosensor	Enzyme-linked receptors on microbeads	Femtomolar	Reusable (50 tests)	Nucleoprotein	Electrochemical	Not Specified	(Park et al. 2025)
Multiplex Fluorescence LFA	Antibody-coated quantum dot nanobeads	41 copies/mL	< 20 min	Viral antigens	Fluorescence lateral flow	Clinical samples	(Li et al. 2025)
Fluorescence suspension sensor	Affinity peptide on hydrogel	1.887 PFU/mL	Reusable	H3N2 hemagglutinin	Fluorescence	Not Specified	(Kim et al. 2023)

biosensor utilizes gold nanoparticles functionalized with oligonucleotides as bioreceptors, producing a discernible color change within 20 min. This approach allows rapid, point-of-care detection, with minimal detectable doses around 10 nM, supporting clinical applicability for Influenza B (Zhang et al. 2024).Fluorescence-based lateral flow biosensors further expand diagnostic capabilities. Silica nanoparticles loaded with Cy5 and linked to monoclonal antibodies detect Influenza B nucleoprotein quantitatively, with a LOD of 0.55 µg per test within 30 min using only 100 µL of viral transport medium. The platform exhibits high specificity, with no cross-reactivity to related respiratory Viruses, making it suitable for rapid clinical diagnostics (Wiriyachaiporn et al. 2021). Another fluorescent lateral flow system incorporates Ag-doped $ZnIn_2S_4$ quantum dots within dendritic mesoporous silica nanoparticles, achieving a LOD of 1 ng/mL. The method demonstrates remarkable repeatability, with intra- and inter-assay variation below 9%, supporting early detection and epidemiological surveillance of Influenza B (Hu et al. 2024).

For highly selective detection of Influenza B virus particles, Raman-enhanced biosensors employ aptamers immobilized on PET membranes coated with silver nanoparticles, enabling detection through surface-enhanced Raman or fluorescence signals. This platform provides precise and accurate optical detection of Influenza B (Kukushkin et al. 2023). Similarly, multiplexed fluorescence lateral flow biosensors utilizing Virus-specific probes achieve LODs of

Table 2 Biosensors for Influenza B virus detection

Type of biosensor	Bioreceptor	LOD	Response time	Biomarker	Method	Matrix	References
Electrochemical DNA biosensor	DNA probe on AuNPs	Not Specified	Not Specified	Nucleoprotein (NP) gene	Electrochemical	Nasopharyngeal swabs	(Yahyavi et al. 2024)
Optical biosensor / Flow Cytometry	High-coverage RNA probes	50 nM/1 nM	Rapid, amplification-free	Influenza B RNA	Waveguide optics / Flow Cytometry	Not Specified	(Courtney et al. 2021)
Optical/Colorimetric biosensor	Oligonucleotide-functionalized AuNPs	~10 nM	~20 min	Viral Nucleic Acids	Colorimetric (naked eye)	Not Specified	(Zhang et al. 2024)
Fluorescence Lateral Flow Biosensor	mAb-coated silica nanoparticles (Cy5)	0.55 µg/test	<30 min	Nucleoprotein	Fluorescence lateral flow	Viral transport medium	(Wiriyachaiporn et al. 2021)
Fluorescent Lateral Flow Biosensor	Antibody-conjugated Ag: ZIS QDs	1 ng/mL	Rapid	Viral proteins	Fluorescence lateral flow	Not Specified	(Hu et al. 2024)
Raman-enhanced biosensor	Aptamer on AgNP-coated membrane	Not Specified	Not Specified	Intact virus	SERS / Fluorescence	Not Specified	(Kukushkin et al. 2023)
Fluorescence Lateral Flow Biosensor	Virus-specific probes	6.3×10^1 copies/µL	Rapid, on-site	Viral Nucleic Acids	Fluorescence lateral flow	Nose swab elution	(Lu et al. 2024)

6.3×10^1 copies/µL using nose swab eluates as the detection matrix, offering rapid, precise, and field-deployable point-of-care diagnostics for Influenza B alongside other respiratory Viruses (Lu et al. 2024).

Collectively, these diverse biosensor technologies—including electrochemical, optical, Raman-enhanced, and fluorescence-based lateral flow platforms—offer highly sensitive, selective, and rapid approaches for the detection and surveillance of Influenza B Virus in both clinical and field settings (Table 2).

Human coronaviruses

Biosensor technologies have demonstrated remarkable capabilities for the sensitive, rapid, and selective detection of SARS-CoV-2, targeting viral spike RBD, anti-spike antibodies, and viral RNA. Multilayer graphene-enhanced SPR biosensors (BK7/Au/$PtSe_2$/graphene) enable label-free detection with high refractive-index sensitivity, achieving spike RBD detection of 183.33°/RIU due to the improved plasmonic performance of $PtSe_2$ and graphene layers. Although experimental reaction times and LOD were not reported, this platform holds strong potential for next-generation point-of-care diagnostics and real-time coronaVirus monitoring (Akib et al. 2021).

NanoMIP-based LSPR biosensors, combining synthetic molecular binders with silver nanostructures, provide variant-independent detection by targeting conserved regions of spike RBD. The platform identifies Alpha, Beta, and Gamma variants with LODs of 9.71 fM, 7.32 fM, and 8.81 pM, respectively, delivering results from blood or nasal swab samples within 30 min without labels or biologics. Its rapid production cycle (≤8 weeks) ensures suitability for pandemic-responsive diagnostics and future variant monitoring (Bhalla et al. 2022).Capacitive biosensors using truncated human Angiotensin-Converting Enzyme 2 (hACE2) as the biorecognition element allow direct detection of intact SARS-CoV-2 in saliva. Enhanced with platinum nanoparticle-modified laser-induced graphene electrodes, these sensors provide impedance-based measurements with a LOD of 2,960 copies/mL in under 30 min. The technology demonstrates preferential binding to SARS-CoV-2 over other human coronaviruses, offering an affordable, non-invasive, and high-throughput screening solution for environments such as airports and schools (Moreira et al. 2022).

Single-molecule electrical biosensors utilizing STM-break-junction (STM-BJ) methodology achieve highly sensitive, label-free detection of SARS-CoV-2 RNA. By evaluating the electrical conductance fingerprints of individual nucleic acid molecules, the platform can distinguish SARS-CoV-2 sequences from other human coronaviruses and detect variant-specific alterations, highlighting its potential for miniaturized, rapid diagnostic devices (Arachchillage et al. 2023).Multiplexed grating-coupled fluorescent plasmonics (GC-FP) biosensors enable rapid, precise identification of SARS-CoV-2 antibodies (IgG, IgM, IgA) in serum and dried blood spots. They assess interactions with multiple antigens, including spike S1, spike S1S2, and nucleocapsid, achieving 100% selectivity and up to 100% sensitivity for serum samples (86.7% for dried blood spots). Quantitative responses up to a 1:1600 serum dilution correlate with commercial ELISA and Luminex assays, and integrated machine learning enhances assessment of previous COVID-19 infections, offering a robust platform for multiplexed serological testing (Cady et al. 2021).

Graphene-plasmonic photonic biosensors employ graphene layers alongside multilayered nanostructures (Al, Au, SiO_2, GZO) to enhance refractive-index sensitivity up to 664.8 nm/RIU, supporting integrated, label-free photonic detection of COVID-19 (Negahdari et al. 2023). Similarly,

RAPID 1.0 (A specific biosensor platform name) electrochemical biosensors functionalized with human ACE2 provide rapid detection in saliva, oropharyngeal, and nasopharyngeal swabs within 4 min, achieving sensitivities from 85.3% to 100% and specificities from 86.5% to 100%, serving as a rapid point-of-care alternative to RT-PCR (Torres et al. 2021).Electrochemical biosensors using screen-printed electrodes conjugated with antibody-peroxidase magnetic beads detect SARS-CoV-2 spike protein in saliva, urine, and serum, with LODs of 0.20, 0.31, and 0.54 ng/mL, respectively, over a 3.12–200 ng/mL range (Malla et al. 2022). Catalytic hairpin-based electrochemical systems coupled with DNA polymerization detect viral RNA in the 0.1–1000 pM range with a LOD of 26 fM, demonstrating single-base mismatch selectivity and efficacy in complex matrices (Peng et al. 2021).

Aptamer-based electrochemical biosensors employing gold nanoparticle-modified carbon electrodes detect SARS-CoV-2 spike protein at concentrations as low as 1.30 pM (66 pg/mL) after 40 min of incubation, highlighting rapid and sensitive diagnostics (Abrego-Martinez et al. 2022). Carbon Nanotube Field-Effect Transistor(CNT-FET) electrochemical biosensors using anti-SARS-CoV-2 S1 antibodies immobilized on carbon nanotube channels achieve detection ranges of 0.1 fg/mL to 5.0 pg/mL, with LOD of 4.12 fg/mL and strong selectivity against SARS-CoV-1 and MERS-CoV S1 antigens, providing a rapid (2–3 min), cost-effective primary care solution (Zamzami et al. 2022). MXene-AuNP electrode systems coupled with CRISPR/Cas13a enable direct RNA detection from clinical samples, including single-base L452R mutations in Omicron BA.2 and BA.5, allowing rapid, sensitive variant differentiation alongside RT-qPCR for early COVID-19 diagnosis (Chen et al. 2023). CRISPR-Cas13a-based fluorescence biosensors utilizing lateral cleavage and enzyme-free hybridization chain reaction achieve atomolar sensitivity for target RNAs from S, N, and Orf1ab genes, enabling rapid point-of-care detection in spiked oropharyngeal swabs (Yang et al. 2021). Additional multifunctional platforms combine DNA 3-way junction aptamers with graphene oxide-MoS_2 hybrids for MERS-CoV detection using electrochemical (EIS) and SERS methods, attaining extremely low detection thresholds in PBS and diluted saliva, demonstrating clinical relevance and sensitivity (Kim et al. 2022). Cotton fiber-based electrochemical immunosensors for MERS-CoV allow direct sample collection with detection limits as low as 0.07 pg/mL and high selectivity against other coronaviruses and influenza A, suitable for portable point-of-care use (Eissa et al. 2021).

Gold nanoparticle-based dual-mode biosensors detect SARS-CoV-2 spike antigen colorimetrically (LOD 48 ng/mL) and electrochemically (LOD 1 pg/mL), offering a fast and economical diagnostic option (Karakuş et al. 2021). Phase-shifted long-period fiber grating (PS-LPFG) optical biosensors allow label-free spike antibody detection, exhibiting selectivity for MERS-CoV, temperature insensitivity, reusability, and storage stability, providing a viable method for rapid COVID-19 diagnostics (Lee et al. 2021). Comprehensive reviews emphasize the utility of nano-biosensors including optical and electrochemical platforms using carbon nanofibers, graphene, In_2O_3 nanowires, quantum dots, and iron oxide nanoparticles for the selective detection of Coronaviridae Viruses such as SARS-CoV, SARS-CoV-2, and MERS-CoV. Integration with RT-LAMP and RT-PCR improves performance, although extensive validation in clinical samples is required for practical early diagnosis (Aquino et al. 2022) (Table3).

Human respiratory syncytial viruses

Biosensor technologies have demonstrated high sensitivity and specificity for the rapid detection of respiratory syncytial Virus (RSV), including both A and B subtypes. Plasmonic RSV biosensors utilizing modified plastic optical fibers functionalized with antibodies against the RSV fusion (F) protein achieve an exceptionally low limit of detection (LOD) of 0.88 PFU/mL in both standard solutions and nasopharyngeal swab samples. The point-of-care system provides results in approximately 10 min, demonstrating excellent selectivity against other Viruses and suitability for clinical and resource-limited settings (Passeggio et al. 2025).Electrochemical paper-based analytical devices (ePADs) employ immobilized pyrrolidinyl peptide nucleic acid probes to achieve label-free detection of RSV RNA, attaining a LOD of 0.36 pM without the need for amplification. Using RNA extracted from nasopharyngeal swabs, the platform demonstrated 100% clinical sensitivity and ≥97% specificity, providing a rapid, precise point-of-care diagnostic tool (Lomae et al. 2024).

CRISPR-Cas13a-graphene field-effect transistor (gFET) biosensors allow amplification-free detection of RSV RNA at concentrations as low as 1 aM, offering highly sensitive, fast, and specific detection without preamplification, highlighting their potential for point-of-care applications (Li et al. 2022). Impedimetric immunosensors based on pencil graphite electrodes coated with polymeric layers and immobilized anti-RSV antibodies attain a LOD of 22.54 PFU/mL with a linear range of 50–2000 PFU/mL and a reaction time of 30 min, delivering a rapid, economical, and sensitive diagnostic approach (e Silva et al. 2024).

Multiplexed point-of-care testing (POCT) systems enable simultaneous detection of RSV antigens and antibodies alongside other respiratory Viruses. Using only 30 µL of sample, the platform delivers results within 30 min

Table 3 Biosensors for human coronaviruses (SARS-CoV-2, MERS) detection

Type of biosensor	Bioreceptor	LOD	Response time	Biomarker	Method	Matrix	References
SPR Biosensor	Not Specified (Graphene-enhanced)	Not Specified	Real-time, fast	Spike RBD, RNA, Antibodies	Surface Plasmon Resonance	Not Specified	(Akib et al. 2021)
LSPR Biosensor	Synthetic nanoMIPs	9.71 fM (Alpha)	<30 min	Conserved Spike RBD	Localized SPR	Blood, Nasal swab	(Bhalla et al. 2022)
Capacitive Biosensor	Truncated hACE2	2,960 copies/mL	<30 min	Intact SARS-CoV-2	Impedance Spectroscopy	Saliva	(Moreira et al. 2022)
Single-Molecule Electrical Biosensor	Specific nucleic acid probes	Single-Molecule Sensitivity	Not Specified	Viral RNA	STM Break-Junction Conductance	Liquid samples	(Arachchillage et al. 2023)
Grating-Coupled Fluorescent Plasmonic (GC-FP)	Spike S1, S1S2, Nucleocapsid antigens	High Sensitivity (100% for serum)	Rapid	Anti-SARS-CoV-2 IgG, IgM, IgA	Fluorescent Plasmonics	Human serum, Dried blood	(Cady et al. 2021)
Graphene-Plasmonic Photonic Biosensor	Graphene biomolecular layer	Sensitivity: 664.8 nm/RIU	Label-free	Viral particles	Photonic crystal resonance	Not Specified	(Negahdari et al. 2023)
Electrochemical Biosensor (RAPID 1.0)	Human ACE2	High Sens./Spec.	4 min	Intact SARS-CoV-2	Impedance Spectroscopy	Saliva, Oropharyngeal, Nasopharyngeal	(Torres et al. 2021)
Electrochemical Biosensor	Antibody-peroxidase on magnetic beads	0.20 ng/mL (saliva)	Rapid, POC	Spike protein	Amperometry	Saliva, Urine, Serum	(Malla et al. 2022)
Electrochemical Biosensor	Catalytic hairpin assembly + TdT	26 fM	Rapid	SARS-CoV-2 RNA	Electrochemical (Ru complex)	Complex matrices, Clinical samples	(Peng et al. 2021)
Aptamer-based Electrochemical Biosensor	RBD-specific aptamer on AuNPs/SPCE	1.30 pM (66 pg/mL)	40 min incubation	Spike RBD	Electrochemical Impedance Spectroscopy	Pseudovirus samples	(Abrego-Martinez et al. 2022)
CNT-FET Electrochemical Biosensor	Anti-S1 antibody on CNT	4.12 fg/mL	2–3 min	S1 antigen	Field-Effect Transistor	Saliva	(Zamzami et al. 2022)
Electrochemical Biosensor	CRISPR/Cas13a system	Highly sensitive	Rapid, specific	Viral RNA (incl. variants)	Electrochemical	Clinical samples	(Chen et al. 2023)
CRISPR-based Optical Biosensor	CRISPR/Cas13a + HCR probes	Atomolar	<1 h	S, N, Orf1ab RNA	Evanescent wave fluorescence	Oropharyngeal swabs	(Yang et al. 2021)
Electrochemical/SERS Biosensor	DNA 3-way junction aptamer	0.405 pg/mL (EIS)	Not Specified	MERS Spike protein	EIS / SERS	PBS, 10% Saliva	(Kim et al. 2022)
Electrochemical Immunosensor	Specific antibody	0.07 pg/mL	Rapid, POC	MERS Spike protein	Electrochemical	Nasal sample, Saliva	(Eissa et al. 2021)

Table 3 (continued)

Type of biosensor	Bioreceptor	LOD	Response time	Biomarker	Method	Matrix	References
Colorimetric/ Electrochemical Biosensor	Antibody on AuNPs	1 pg/mL (EC)	Rapid	Spike antigen	Colorimetric / Electrochemical	Not Specified	(Karakuş et al. 2021)
Optical Fiber Biosensor	Spike protein	Not Specified	Label-free, rapid	Anti-Spike Antibodies	Phase-shifted long-period fiber grating	Virus transport medium	(Lee et al. 2021)

Table 4 Biosensors for human respiratory syncytial virus (hRSV) detection

Type of biosensor	Bioreceptor	LOD	Response time	Biomarker	Method	Matrix	References
Plasmonic Optical Fiber Biosensor	Anti-F protein antibody	0.88 PFU/mL	~10 min	Fusion (F) protein	Plasmonics	Nasopharyngeal swabs	(Passeggio et al. 2025)
Electrochemical Paper-Based Device (ePAD)	Pyrrolidinyl peptide nucleic acid (acpcPNA) probe	0.36 pM	Rapid, label-free	RSV RNA	Electrochemical	Nasopharyngeal swabs	(Lomae et al. 2024)
CRISPR Cas13a-graphene Field-Effect Transistor (gFET)	CRISPR RNA (crRNA)	1 aM	Amplification-free, fast	RSV RNA	Field-Effect Transistor	Not Specified	(Li et al. 2022)
Impedimetric Immunosensor	Anti-RSV antibody on polymer-coated electrode	22.54 PFU/mL	30 min	Viral antigens	Electrochemical Impedance	Not Specified	(e Silva et al. 2024)
Multiplexed POCT System	Not Specified	High Sens./Spec.	<30 min	RSV antigens/antibodies	Multiplexed Assay	Not Specified (30 µL sample)	(Teixeira et al. 2022)
3D DNA Walker-based Biosensor	AuNP-conjugated hairpin DNA	9.33 fM	45 min	RSV RNA	Fluorescence	Not Specified	(106. 2174)
CRISPR-RDB (Reverse Dot Blot)	Cas12a crRNA	Highly sensitive	Instrument-free, rapid	RSV RNA	Colorimetric (CRISPR/Cas12a)	Nylon membrane	(Hu et al. 2023)

with high sensitivity and specificity, providing a versatile and reliable tool for both clinical and field diagnostics (Teixeira et al. 2022).

Advanced nucleic acid-based platforms, such as 3D DNA walker biosensors, employ AuNP-conjugated hairpin structures and strand displacement amplification to achieve ultrasensitive detection of RSV with a LOD of 9.33 fM in 45 min, supporting early and highly sensitive diagnosis (106. 2174). CRISPR-RDB technology allows multiplexed, amplification-free identification of RSV in combination with influenza A/B and SARS-CoV-2. Utilizing Cas12a trans-cleavage and reverse dot blot readout, the system produces colorimetric signals on nylon membranes, enabling rapid, sensitive, instrument-free detection suitable for smartphone-based analysis (Hu et al. 2023).

Collectively, these biosensor platforms including plasmonic, electrochemical, CRISPR-based, and nucleic acid amplification-free technologies offer rapid, sensitive, and versatile approaches for point-of-care and field detection of RSV, supporting early diagnosis and improved disease management (Table 4).

Human adenoviruses

Biosensor platforms have demonstrated remarkable sensitivity, specificity, and versatility for the rapid detection of human adenovirus (HAdV), including serotypes 3, 5, 7, and 55. Nanoparticle-based lateral flow biosensors (LFBs) combined with isothermal multiple cross displacement amplification (MCDA) enable point-of-care detection of HAdV

hexon gene DNA at 10 fg, providing data within one hour without cross-reactivity, offering a fast and practical diagnostic tool for clinical and resource-limited settings (Wan et al. 2024).

Reduced graphene oxide field-effect transistor (rGO-FET) biosensors integrated with DNA aptamers allow selective and sensitive detection of HAdV-5, providing rapid and precise Virus identification suitable for clinical monitoring and applications in biotechnological processes such as gene therapy and viral vector production (Li et al. 2025). Portable piezoelectric biosensors utilizing computationally designed epitope-imprinted polymers (eIPs) target the capsid knob epitope, achieving a LOD of 10^2 PFU/mL, and offer a rapid, cost-effective, and highly selective method for point-of-care and field detection (Sehit et al. 2024). Aptamer-nanopore biosensors facilitate direct identification of infectious HAdV in diverse sample types including water, saliva, and serum. Using DNA aptamers as bioreceptors, these platforms enable ultrasensitive, label-free detection down to 1 PFU/mL, supporting rapid and versatile monitoring of adenoviral infections (111. 2021). Nanoplasmonic biosensors equipped with nanoscale robotic hands (Nano RHB) achieve real-time detection of HAdV particles, including vaccine vectors, with exceptional specificity and sensitivity as low as 100 copies/mL, providing effective tools for monitoring viral concentration and vector vitality (Li et al. 2022).

ERA-CRISPR/Cas12a-based nucleic acid detection enables rapid identification of HAdV55 by targeting the conserved hexon gene, attaining detection thresholds of 9 copies/reaction for plasmids and 2.5 copies/reaction for live strains within 30 min at 42 °C, without cross-reactivity, offering a precise and instrument-free method for on-site screening (Zhang et al. 2025).Nanobased immunosensors employing sandwich assays with visual colorimetric readouts provide rapid detection of HAdVs responsible for ocular infections, achieving a LOD of 10^2 PFU/mL in less than 2 min, and exhibit high specificity against Flu A/B, coronavirus, and MERS-CoV (Aloraij et al. 2022).

The HAdV-MCDA-CRISPR platform facilitates rapid and precise identification of HAdV types 3 and 7 by targeting the conserved hexon gene. This integrated workflow including DNA extraction, MCDA amplification, and CRISPR-based detection attains a detection limit of 5 fg plasmid DNA per reaction within one hour without cross-reactivity, demonstrating high diagnostic accuracy in clinical validation of 88 patient samples (Jia et al. 2025). Smartphone-based multiplex electrochemiluminescence platforms, combined with LAMP amplification, detect HAdV alongside H1N1, H7N9, and influenza B, achieving a detection limit of 10 copies/μL with 87.5% sensitivity and 91.7% specificity in clinical samples, offering a rapid, field-deployable diagnostic solution (116. 2025).

Modular microfluidic GFET biosensors integrated with CRISPR/Cas12a enable amplification-free nucleic acid detection at concentrations as low as 1 fM, providing high sensitivity, selectivity, stability, and streamlined fabrication suitable for point-of-care diagnostics (Zhang et al. 2024). Evalution™ microfluidic devices utilizing enzyme-free hybridization chain reaction (HCR) allow multiplexed detection of HAdV nucleic acids with LODs of 33–151 fM (309 ± 80 fM in clinical samples), supporting fast, sensitive, and high-throughput point-of-care application (Rutten et al. 2023).

CRISPR-Cas13a-based MAD (Minimal Amplification-free Detection) methods facilitate rapid, amplification-free detection of HAdV from nasopharyngeal swabs within 40 min, offering lateral flow readout and demonstrating 99.4% concordance with qPCR across 167 pediatric clinical samples, providing a straightforward and secure diagnostic strategy (Zhuang et al. 2025). Dual-mode colorimetric-fluorescent immunochromatographic assays (ICA) using PDQB nanobeads achieve LODs of 10^4 copies/mL in colorimetric mode and 500 copies/mL in fluorescence mode, offering rapid, sensitive, and precise detection for clinical diagnosis and epidemic surveillance (Yang et al. 2024).

HAdV-MCDA-CRISPR platforms combine CRISPR/Cas12a with multiple cross displacement amplification to detect HAdV serotypes 3 and 7. Fluorescence produced by CRISPR-mediated probe cleavage indicates the presence of target DNA, with bioreceptors comprising specific crRNA targeting the conserved hexon gene. The workflow including template preparation (15 min), MCDA amplification (40 min), and detection (5 min) completes within approximately one hour, achieving a detection limit of 1.92 copies/μL, high specificity without cross-reactivity, and clinical validation on 128 samples, offering a rapid, sensitive, and precise point-of-care HAdV detection method (121. 2025) (Table5).

Human rhinoviruses

Biosensor technologies have advanced rapid, sensitive, and specific detection of human rhinovirus (HRV), including HRV-A and HRV-C. CRISPR/Cas12a-based assays integrating RT-RPA amplification with fluorescence or lateral flow detection allow identification within approximately 50 min, achieving LODs of 0.1–0.5 copies/μL. Clinical validation in 80 samples demonstrated high accuracy, offering a rapid, portable, and reliable method for HRV detection (Qian et al. 2023).

Surface-enhanced Raman scattering (SERS)-based techniques combined with machine learning enable ultrasensitive detection and precise identification of HRV among other respiratory viruses. Virus particles immobilized on Au nanodimple electrodes produce robust SERS signals in 15

Table 5 Biosensors for human adenoviruses detection

Type of Biosensor	Bioreceptor	LOD	Response Time	Biomarker	Method	Matrix	References
Nanoparticle-based Lateral Flow Biosensor (LFB)	MCDA primers	10 fg	< 1 h	Hexon gene DNA	Colorimetric LFA	Not Specified	(Wan et al. 2024)
Reduced Graphene Oxide FET (rGO-FET)	Specific DNA aptamer	Highly sensitive & specific	Rapid	Virus particles	Field-Effect Transistor	Not Specified	(Li et al. 2025)
Portable Piezoelectric Biosensor	Computationally designed epitope-imprinted polymer (eIP)	10^2 pfu/mL	Rapid, cost-effective	Capsid knob epitope	Piezoelectric (Mass-sensitive)	Water, Human serum	(Sehit et al. 2024)
Aptamer-Nanopore Biosensor	DNA aptamer	1 pfu/mL	Rapid, direct	Intact infectious virus	Nanopore sensing	Water, Saliva, Serum	(111. 2021)
Nanoplasmonic Biosensor with Nano Robotic Hand	Not Specified	100 copies/mL	Real-time	Virus particles	Plasmonics	Not Specified	(Li et al. 2022)
ERA-CRISPR/Cas12a	CRISPR RNA (crRNA)	9 copies/rxn (plasmid)	30 min at 42 °C	Hexon gene	Fluorescence/Lateral Flow	Not Specified	(Zhang et al. 2025)
Nanobased Immunosensing Device	Specific antibody	10^2 pfu/mL	< 2 min	Viral antigens	Colorimetric (Sandwich assay)	Not Specified	(Aloraij et al. 2022)
HAdV-MCDA-CRISPR Assay	CRISPR RNA (crRNA)	5 fg/rxn	~1 h (total)	Hexon gene DNA	Fluorescence (CRISPR/Cas12a)	Clinical samples	(Jia et al. 2025)
Smartphone-based Electrochemiluminescence (ECL)	LAMP primers	10 copies/µL	Rapid, portable	Viral nucleic acids	Electrochemiluminescence	Clinical samples	(116. 2025)
Modular Microfluidic GFET Biosensor	CRISPR/Cas12a crRNA	1 fM	Amplification-free	Viral nucleic acids	Field-Effect Transistor	Not Specified	(Zhang et al. 2024)
Microfluidic HCR Biosensor	Complementary DNA probes	~309 fM (clinical)	Rapid, enzyme-free	Viral nucleic acids	Fluorescence (HCR)	Clinical samples	(Rutten et al. 2023)
CRISPR-Cas13a-based MAD Assay	CRISPR RNA (crRNA)	High sensitivity (99.4% vs. qPCR)	40 min, amplification-free	Viral DNA	Lateral Flow	Nasopharyngeal swabs	(Zhuang et al. 2025)
Dual-Mode Immunochromatographic Assay (ICA)	Specific antibody	500 copies/mL (Fluo.)	Rapid	Viral antigens	Colorimetric / Fluorescence	Not Specified	(Yang et al. 2024)
HAdV-MCDA-CRISPR	CRISPR RNA (crRNA)	1.92 copies/µL	~1 h (total)	Hexon gene DNA	Fluorescence (CRISPR/Cas12a)	Clinical samples	(121. 2025)

min, with species classification accuracies reaching 98.9% using PCA-SVM and 93.5% with CNN analysis, facilitating rapid, multiplexed, and on-site diagnostics (Ansah et al. 2023).

Thin film biosensors targeting the conserved 3 C protease (3Cpro) employ polyclonal antibodies for HRV detection, providing visual readouts in 28 min at room temperature with a detection limit of 12 pM (~1000 $TCID_{50}$). The assay identified 87% of HRV serotypes tested without cross-reactivity with other respiratory Viruses or bacteria. Clinical validation demonstrated detection in nasal secretions and pediatric nasal wash samples, supporting its use as a sensitive point-of-care diagnostic tool (Ostroff et al. 2001).

Multiplexed silicon-based thin film biosensors convert hybridization of HRV-specific nucleic acids into perceptible color changes, enabling rapid visual identification of viral sequences within 10 min. This approach allows straightforward differentiation of HRV RT-PCR products from infected cell lysates and simultaneous detection of multiple respiratory Viruses (Jenison et al. 2001).

Label-free optical platforms, such as the Epic®System, quantify dynamic mass redistribution (DMR) in host cells upon HRV infection, translating cellular alterations into measurable outputs. This high-throughput method facilitates sensitive, real-time monitoring of viral replication and screening of antiviral compounds, providing rapid and

Table 6 Biosensors for human rhinoviruses detection

Type of Biosensor	Bioreceptor	LOD	Response Time	Biomarker	Method	Matrix	References
CRISPR/Cas12a-based Assay	CRISPR RNA (crRNA)	0.1–0.5 copies/µL	~50 min	VP4 gene	Fluorescence / Lateral Flow	Clinical samples	(Qian et al. 2023)
SERS-based Platform with Machine Learning	Not Specified	Ultrasensitive	<15 min	Intact virus particles	Surface-Enhanced Raman Scattering (SERS)	Not Specified	(Ansah et al. 2023)
Fast Thin Film Biosensor	Polyclonal antibodies against 3Cpro	12 pM (~1000 $TCID_{50}$)	28 min (visual)	3 C protease (3Cpro)	Optical (color change)	Nasal secretions, Nasal wash	(Ostroff et al. 2001)
Thin Film Biosensor for Nucleic Acids	Rhinovirus-specific DNA probes	Not Specified	10 min	Viral RNA/DNA	Optical (color change)	Infected cell lysates	(Jenison et al. 2001)
Label-free Epic® System (Optical)	Living cells	Not Specified	Real-time	Viral replication (Cellular DMR)	Optical (Dynamic Mass Redistribution)	Cell culture	(Owens et al. 2009)
Electrochemically Enhanced Graphene FET (GFET)	Specific probe	5×10^{-16} g/mL (for proteins)	<60 s	Infectious pathogens / proteins	Field-Effect Transistor	Clinical samples ($n=402$)	(Dai et al. 2023)

precise characterization of HRV infection in cell-based assays (Owens et al. 2009).

Graphene field-effect transistor (GFET) biosensors enhanced with electrochemical preconcentration achieve tenfold signal amplification for the detection of trace HRV proteins, with LODs as low as 5×10^{-16} g/mL. Testing of 402 individuals demonstrated 97.3% sensitivity and 98.6% specificity, with results delivered in under 60 s, supporting fast, high-throughput, and accurate screening for HRV and other pathogens (Dai et al. 2023).

Collectively, these platforms including CRISPR-based, SERS, thin film, optical, and GFET biosensors provide rapid, sensitive, multiplexed, and point-of-care solutions for HRV detection and surveillance (Table 6).

Human metapneumoviruses

Biosensor and immunoassay technologies have enabled rapid, sensitive, and accessible detection of human metapneumovirus (hMPV). Fast immunoassays utilizing nanobodies and monoclonal antibodies targeting the conserved nucleoprotein (N) employ colloidal gold lateral flow test strips and double-antibody sandwich ELISA. These platforms allow detection of recombinant antigen, cell culture-derived hMPV, and nasopharyngeal swab samples, providing a rapid and practical tool for hMPV diagnosis, particularly during epidemic periods (Zhang et al. 2025).

Integration of reverse transcription recombinase polymerase amplification (RT-RPA) with CRISPR-Cas12a enables highly sensitive and rapid detection of hMPV. Using fluorescence or lateral flow readouts and four primer pairs targeting the nucleoprotein (N) gene, the assay concludes within 35–45 min, achieving a LOD of 6.97×10^2 copies/mL without cross-reactivity to other respiratory viruses. Evaluation of 28 clinical samples demonstrated strong concordance with qRT-PCR (96.4% for fluorescence, 92.9% for lateral flow), highlighting a rapid, sensitive, and equipment-free approach for clinical hMPV detection (Qian et al. 2021).

A one-tube RT-RPA/CRISPR-Cas12a assay targeting the nucleoprotein (N) gene facilitates visual detection of hMPV within 30 min, achieving a sensitivity of 1 copy/µL and showing no cross-reactivity with nine other respiratory pathogens. Clinical validation revealed 98.53%concordance with qRT-PCR, offering a straightforward, precise, and efficient method for rapid hMPV diagnostics (Du et al. 2024).

Collectively, these platforms including immunoassays, lateral flow devices, and CRISPR-based nucleic acid detection provide fast, sensitive, and accessible approaches for point-of-care and clinical hMPV detection.

Human parainfluenza virus

Human parainfluenza Virus (HPIV) remains an important contributor to respiratory morbidity, particularly in pediatric and immunocompromised populations, highlighting the need for a rapid and sensitive diagnostic tool. A recent biosensing strategy, an extended-gate field-effect transistor (R-EGFET) biosensor, has been developed for the specific detection of human parainfluenza Virus (HPIV). The platform employs UiO-66 metal-organic framework (MOF) nanoparticles to enhance electrical sensitivity, coupled with an aptamer targeting the viral hemagglutinin-neuraminidase (HN) protein as the bioreceptor. Detection is achieved by monitoring changes in electrical signals across the extended-gate membrane, with limits of detection of 22.254 fM in buffer, 36.202 fM in simulated saliva, 9.961 PFU/mL in bronchoalveolar lavage fluid (BALF), and 15.273 PFU/mL in human serum.

The incorporation of alternating-current electrothermal flow (ACEF) technology reduced target binding time to 10 min. This biosensor demonstrates excellent selectivity, compact design, and significant potential for rapid HPIV diagnosis in clinical specimens (Lee et al. 2025). Beyond electronic sensing, molecular diagnostic innovations have introduced CRISPR-Cas12a-powered microfluidics as a robust alternative. This approach integrates reverse transcription recombinase polymerase amplification (RPA) within a passive, capillary-driven chip to facilitate the simultaneous screening of HPIV alongside other respiratory pathogens. By delivering results in 45 min with a detection threshold of 10 copies/μL, this platform achieves a clinical sensitivity of 98.44%, offering a high-performance solution for point-of-care testing in settings where complex laboratory infrastructure is unavailable(132. 2025). The precision of such diagnostic tools is further reinforced by high-selectivity bioreceptors, as evidenced in studies utilizing Phase-Shift Surface Plasmon Resonance (PS-SPR). Research indicates that modern monoclonal antibodies effectively minimize cross-reactivity, such as SARS-CoV-2 and Influenza A/B. Even at elevated concentrations of 1.0×10^5copies/mL, HPIV consistently produces negligible background signals, ensuring that detection remains highly specific. This synergy between advanced nanomaterials and molecular specificity underscores the transition toward more reliable and rapid HPIV surveillance(133. 2023).

Emerging trends and future translation of biosensors for respiratory viral detection

Recent advances in biosensor technologies for respiratory viral detection reflect a clear transition from proof-of-concept analytical devices toward integrated, patient-centered diagnostic platforms. While many currently reported biosensors demonstrate excellent analytical performance under controlled laboratory conditions, emerging research trends increasingly emphasize clinical deployability, multiplexed detection, and real-world robustness(Laghrib et al. 2021). One of the most prominent trends is the integration of novel biorecognition strategies, including aptamers, synthetic peptides, and CRISPR-based recognition systems, which offer enhanced programmability, specificity, and adaptability compared to conventional antibody-based approaches. In particular, CRISPR-Cas–assisted biosensing platforms are evolving beyond amplification-dependent assays toward amplification-free or minimally amplified formats, enabling rapid detection with reduced complexity and improved suitability for point-of-care (POC) applications(Zhou et al. 2025).

Another significant research direction is the development of multiplexed and syndromic biosensors capable of simultaneously detecting multiple respiratory pathogens from a single sample(Teixeira et al. 2022). Given the substantial clinical overlap among respiratory viral infections such as influenza, SARS-CoV-2, RSV, adenoviruses, and rhinoviruses, multiplexed detection represents a critical advance for accurate diagnosis, patient stratification, and appropriate therapeutic decision-making(Vallières and Renaud 2013). Emerging electrochemical, field-effect transistor–based, and lateral-flow-integrated platforms increasingly support multi-analyte readouts, reflecting a shift toward comprehensive respiratory panels rather than single-pathogen tests(Hsieh et al. 2015; Soikkeli et al. 2023).

Despite these promising innovations, several critical research gaps continue to hinder large-scale clinical translation. A major limitation remains the insufficient validation of biosensor platforms using large, heterogeneous clinical cohorts. Many studies rely on spiked samples or limited clinical datasets, which may not fully capture the complexity of real-world specimens such as saliva, nasopharyngeal swabs, or bronchoalveolar lavage fluid(Prabowo et al. 2021). Matrix effects, sample variability, and interference from host-derived biomolecules often remain underexplored, limiting the predictive reliability of reported analytical metrics such as sensitivity and limit of detection. Additionally, reproducibility across laboratories and manufacturing batches remains a persistent challenge, particularly for nanomaterial-based biosensors, where subtle variations in synthesis and surface functionalization can significantly impact performance(Unser et al. 2015; 140. 2020).

From a translational perspective, future biosensor research must increasingly prioritize scalability, cost-effectiveness, and regulatory readiness. The integration of biosensors with portable electronics, smartphone-based readout systems, and user-friendly interfaces represents a key trend aimed at decentralizing diagnostics and reducing dependence on centralized laboratory infrastructure. Such approaches are particularly relevant for outbreak scenarios, resource-limited settings, and large-scale population screening, where rapid, accessible testing can directly influence disease transmission dynamics and patient outcomes(140. 2020; Hemdan et al. 2024).

Importantly, emerging biosensor platforms are beginning to align more closely with patient-centered healthcare models by enabling near-patient or at-home testing, shortening diagnostic turnaround times, and facilitating early intervention(142. 2025). When combined with digital health infrastructure and epidemiological surveillance systems, POC biosensors have the potential to reduce diagnostic delays, lower healthcare costs associated with advanced disease management, and improve overall outbreak preparedness.

However, realizing this potential will require coordinated efforts in standardization, clinical validation, and interdisciplinary collaboration among researchers, clinicians, and regulatory authorities(142. 2025). In addition to sensor performance, sample-specific preprocessing and handling considerations are increasingly recognized as critical determinants of real-world biosensor applicability. Different clinical matrices including saliva, nasopharyngeal swabs, serum/plasma, and bronchoalveolar lavage fluid present distinct biochemical and physical challenges that can influence detection accuracy(143. 2021). For example, saliva may require dilution or viscosity reduction to improve fluidic compatibility(Li et al. 2024), while nasopharyngeal swab samples often require viral lysis and nucleic acid preparation for nucleic acid–based sensing platforms. Similarly, serum and plasma samples may require centrifugation or dilution to minimize protein-related matrix interference, whereas bronchoalveolar lavage fluid often requires debris removal prior to analysis(Liu et al. 2023; He et al. 2022). Emerging biosensor platforms are increasingly incorporating microfluidic sample conditioning, automated extraction modules, and matrix-tolerant nanomaterial interfaces to enable direct or minimally processed sample analysis. Addressing these pre-analytical variables is essential for improving reproducibility, clinical reliability, and large-scale deployment of biosensor-based respiratory viral diagnostics.

Collectively, these emerging trends highlight a paradigm shift in respiratory viral diagnostics—from analytically optimized laboratory assays toward clinically integrated, scalable, and responsive biosensing ecosystems. Addressing existing research gaps while leveraging innovative biorecognition strategies, multiplexed detection, and POC deployment will be essential for translating biosensor technologies into reliable tools for future respiratory Virus surveillance, diagnosis, and patient care.

Conclusion

Respiratory viral infections remain a major and persistent global health burden, contributing to substantial morbidity, mortality, and healthcare system strain across seasonal outbreaks and pandemics. The COVID-19 pandemic further demonstrated the vulnerability of healthcare systems to diagnostic delays and dependence on centralized laboratory testing, particularly during periods of rapid transmission and resource saturation. In this context, the development of rapid, sensitive, and deployable diagnostic technologies represents not only a technological advancement but also a critical public health necessity.

This review systematically evaluated current biosensor technologies developed for the detection of major respiratory viral pathogens and examined their analytical performance, clinical applicability, and translational potential. Collectively, the reviewed studies demonstrate that next-generation biosensing platforms have achieved substantial improvements in sensitivity, specificity, and assay speed through the integration of nanotechnology, advanced biorecognition elements, and innovative transduction mechanisms. Across diverse viral families—including Influenza A and B, SARS-CoV-2, MERS-CoV, RSV, Adenoviruses, and Rhinoviruses—biosensors consistently demonstrate strong analytical performance, with several platforms reporting ultra-sensitive detection capabilities, rapid turnaround times often below 30 min, and reliable operation in clinically relevant biological matrices such as saliva, nasopharyngeal swabs, and blood samples.

Key technological advances include the evolution of biorecognition chemistry from conventional antibody-based recognition toward programmable systems such as aptamers, CRISPR-guided RNA platforms, and engineered peptide receptors, which enhance specificity, stability, and design flexibility. In addition, the integration of isothermal amplification strategies (e.g., RPA, MCDA, LAMP) with CRISPR-based detection has enabled highly sensitive detection while maintaining compatibility with point-of-care (POC) deployment. The emergence of multiplexed and multi-modal biosensing platforms further supports syndromic diagnostic approaches capable of simultaneously detecting multiple respiratory pathogens, which is particularly important given the overlapping clinical manifestations of respiratory viral infections.

Beyond analytical performance, decentralized POC biosensing technologies may have meaningful implications for patient outcomes and healthcare system efficiency. Earlier detection at or near the site of care can support faster clinical decision-making, timely patient isolation, and earlier initiation of targeted therapeutic strategies, which may collectively contribute to reducing disease transmission, hospitalization rates, and overall treatment burden. These advantages are particularly relevant in resource-limited settings and during outbreak surges, where access to centralized laboratory infrastructure may be limited.

Despite these promising advances, several critical barriers remain before widespread clinical implementation can be achieved. Future research must prioritize large-scale clinical validation across heterogeneous populations, standardized evaluation and reporting frameworks, improved automation of sample preparation workflows, and cost-effective scalable manufacturing strategies. Addressing these challenges will be essential to ensure regulatory acceptance, reproducibility across settings, and equitable global accessibility of biosensor-based diagnostics.

In conclusion, current evidence indicates that biosensor technologies are transitioning from proof-of-concept analytical tools toward clinically relevant diagnostic solutions for respiratory viral detection. Continued integration of advanced biorecognition strategies, multiplexed detection capability, and clinically validated POC deployment will be essential for enabling reliable real-world implementation. Ultimately, these technologies have the potential to improve diagnostic timeliness, support precision patient management, strengthen outbreak preparedness, and enhance healthcare system resilience against current and future respiratory viral threats.

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Declarations

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