Iran. J. Biotechnol. April 2024;22(2): e3722 DOI: 10.30498/ijb.2024.399314.3722

Review Article

Recent Advances in Development of Biosensors for Monitoring of Airborne Microorganisms

Zahra Mousavian[1], Ensieh Fahimi-Kashani[2], Vahidreza Nafisi [3*], Nafiseh Fahimi-Kashani [4]**

[1]Ph.D. Candidate, Department of Biotechnology, Iranian Research Organization for Science and Technology (IROST), Tehran, Iran
[2]Bachelor student, Faculty of Basic Sciences, Malayer International University, Hamedan
[3]Associate Professor, Department of Electrical Engineering and Information Technology, Iranian Research Organization for Science and Technology (IROST), Tehran, Iran
[4]Assistant Professor, Faculty of Chemistry, Isfahan University of Technology, Isfahan, Iran

[*]*Corresponding author*: Vahidreza Nafisi, Department of Electrical Engineering and Information Technology, Iranian Research Organization for Science and Technology (IROST), Tehran, Iran. Postal Code: 3313193685, Tel: 02157416303, Fax: 02156276620, Email: vr_nafisi@irost.org,

[**]*Co-Corresponding author*: Nafiseh Fahimi-Kashani, Faculty of Chemistry, Isfahan University of Technology, Isfahan, Iran, Zip code: 84156-83111, Tel: +3133913285, Fax: +3133912350, E-mail: nfahimi@iut.ac.ir,

Received: 2023/05/28 ; **Accepted:** 2023/09/12

Background: The early detection of infectious microorganisms is crucial for preventing and controlling the transmission of diseases. This article provides a comprehensive review of biosensors based on various diagnostic methods for measuring airborne pathogens.

Objective: This article aims to explore recent advancements in the field of biosensors tailored for the detection and monitoring of airborne microorganisms, offering insights into emerging technologies and their potential applications in environmental surveillance and public health management.

Materials and Methods: The study summarizes the research conducted on novel methods of detecting airborne microorganisms using different biological sensors, as well as the application of signal amplification technologies such as polymerase chain reaction (PCR), immunoassay reactions, molecular imprinted polymers (MIP) technique, lectin and cascade reactions, and nanomaterials.

Results: Antibody and PCR detection methods are effective for specific microbial strains, but they have limitations including limited stability, high cost, and the need for skilled operators with basic knowledge of the target structure. Biosensors based on MIP and lectin offer a low-cost, stable, sensitive, and selective alternative to antibodies and PCR. However, challenges remain, such as the detection of small gas molecules by MIP and the lower sensitivity of lectins compared to antibodies. Additionally, achieving high sensitivity in complex environments poses difficulties for both methods.

Conclusion: The development of sensitive, reliable, accessible, portable, and inexpensive biosensors holds great potential for clinical and environmental applications, including disease diagnosis, treatment monitoring, and point-of-care testing, offering a promising future in this field. This review presents an overview of biosensor detection principles, covering component identification, energy conversion principles, and signal amplification. Additionally, it summarizes the research and applications of biosensors in the detection of airborne microorganisms. The latest advancements and future trends in biosensor detection of airborne microorganisms are also analyzed.

Keywords: Airborne Pathogens, Antibody, Biosensor, Lectin, Nanoparticles, Point of Care (POC)

1. Background

Infectious diseases are indeed caused by a variety of microorganisms, including viruses, bacteria, fungi, and parasites. Pandemics of infectious diseases can have devastating consequences, with significant morbidity and mortality rates, as well as far-reaching socioeconomic, social, and political impacts across large geographic regions. Among these microorganisms, airborne microorganisms have garnered considerable attention as agents responsible for epidemic infectious diseases. This heightened interest is due to their capacity to spread through the air, making them highly transmissible through human exhalation and their ability to maintain viability in the airborne environment for extended periods (1–3). For instance, as of September 2022, the global impact of Coronavirus Disease 2019 (COVID-19), caused by the *severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)*, had tragically resulted in a staggering toll of 7 million lives lost worldwide (4).

Addressing the ongoing spread of infectious diseases is of paramount importance, demanding the implementation of robust public health policies and interventions to effectively mitigate their devastating impact. These crucial efforts should prioritize early identification through thorough monitoring and surveillance systems (5). The alarming mortality rates linked to pathogens like *SARS-CoV-2*, *Middle East respiratory syndrome (MERS)*, and *Influenza viruses* serve as somber indications of the seriousness of airborne infections. Notably, *MERS* recorded a mortality rate of 839 in the Middle East by September 2012. In another instance, in March 2013, an outbreak of the *influenza A virus* emerged in southeastern China, affecting more than 130 individuals. These instances underscore the potential lethality and widespread impact of airborne diseases, emphasizing the importance of effective prevention and control measures (6).

The ongoing propagation of these diseases is anticipated to persist and potentially escalate in the future. Hence, it is imperative to proactively identify and manage emerging outbreaks that have the potential to escalate into pandemics, with a heightened awareness of bioterrorism threats and concerns (7,8). Consequently, it is vital to identify strategies for prevention, diagnosis, and rapid treatment of pathogenic airborne microorganisms, which helps curb the pathogen's spread (7). In light of this perspective, the rapid and precise detection of airborne microorganisms has become a matter of paramount urgency. Specifically, there is a critical need for the development of a technical approach that can swiftly and accurately detect these microorganisms on-site. Consequently, there is a demand for a portable, fast, and high-throughput detection method to analyze and identify environmental microorganisms effectively. The advent of new technologies has opened up opportunities for real-time, on-site, and efficient analysis and detection of airborne microorganisms, offering promising solutions to this pressing public health challenge (11).

In recent years, the timely identification of pathogens in complex samples such as air has garnered significant attention. A range of conventional methods, including colony-forming units (CFU) calculation, spectrophotometer-based optical density (OD) measurement, and flow cytometry (FCM), have made significant contributions to the identification of airborne pathogens (12). Although these methods are widely considered the best techniques for pathogen detection, their use is often impeded by a variety of challenges. These challenges include the requirement of a lot of materials, the long time required to achieve results, the need for a skilled operator, the possibility of device errors, no colony formation in the culture environment, as well as variations in the reproduction speed of different bacterial species (13). Due to the limitations of conventional methods for identifying airborne pathogens, the development of new techniques is an active area of research and development. Immunoassay techniques (14) including enzyme-linked immunosorbent assay (ELISA), immunofluorescence staining, immunoblotting, and lateral flow immunoassay (LFIA) have emerged as promising tools for detecting airborne pathogens (14). These methods offer advantages such as rapid turnaround time, high specificity and sensitivity, and the ability to detect multiple pathogens simultaneously. Among the newer methods, genomic and proteomic molecular detection techniques such as polymerase chain reaction (PCR) and loop-mediated isothermal amplification (LAMP) have gained increasing attention (13). The continued development and refinement of such techniques are essential for improving our ability to detect airborne pathogens rapidly and accurately, thereby enabling effective public health interventions to mitigate their impact.

Over the long term, it would be more practical to develop direct and fast diagnostic methods for detecting infectious pathogens in exhaled air samples without the need for pre-enrichment. Point-of-care tests (POCT) are a promising diagnostic approach that could revolutionize infectious disease detection. The World Health Organization (WHO) has outlined the ASSURED criteria for an ideal POCT platform design, which include affordability, sensitivity, specificity, user friendliness, speed, equipment-free operation, and easy delivery (15). The development of POCT platforms that meet these criteria would allow for rapid diagnosis and treatment of infectious diseases in patients at the point of care, thereby improving patient outcomes and reducing the spread of disease. The continued research and development of innovative diagnostic approaches such as POCTs are essential to improving the ability to identify and combat infectious pathogens rapidly and efficiently (13,16). Although immunoassay techniques are commonly utilized in POCT, their utility is limited by the high cost and sensitivity requirements of monoclonal antibody preparation (17). While rapid diagnostic methods can provide highly accurate identification of a broad range of microorganisms, the complex and time-consuming sample preparation required for extracting different parts of the pathogen remains a significant challenge. Recently, various diagnostic biosensors have been developed for pathogen detection in various industries, including pharmaceuticals, food, and bioterrorism (18,19). Based on their attributes, biosensors can be applied in diverse fields, including medical diagnostics (such as monitoring blood glucose), detection of poisonous gases in chemical warfare, identification of plant diseases in agriculture, monitoring of environmental pollution, and the food industry (20). Recently, biosensors based on Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) technology have been developed for the detection of *SARSCOV-2*, which can be inserted within a mask (21).

2. Objective

This review highlights the growing importance of biosensors for monitoring airborne microorganisms in real-time. The article explores recent advancements in biosensor development, addressing a critical gap in clinical and public health practices by enabling rapid detection and surveillance of airborne pathogens. Various diagnostic techniques, such as antibody-antigen interactions, micro-PCR, MIPs, and lectin-based approaches, are covered. As technology progresses, new diagnostic methods are expected to emerge, enhancing our ability to detect and prevent the spread of airborne pathogens and contributing to global health and security efforts.

3. Biosensors for Monitoring Airborne Pathogens

Limited knowledge exists regarding the detection of airborne pathogens, particularly when using realistic sampling methods, despite significant progress in detecting pathogens in complex samples. Furthermore, there is a scarcity of commercially available biosensors for airborne infection detection. However, through appropriate design and diagnostic method selection, it is possible to develop field-deployable and stationary sensors capable of real-time identification of airborne diseases in hospitals, air vents, and public locations such as subway stations and airlines (22).

Several common diagnostic methods, such as plate culture, PCR, and immunoassay technology, are used to identify pathogens, including airborne pathogens. Pathogen detection methods by devices are a kind of detection method that biosensors are classified in this group. Today, the technology of portable, fast, and sensitive airborne biosensors for diagnostic purposes is being developed (20). The idea of biosensors was first presented by Leland C. Clark in 1962 and has grown significantly in all scientific fields, with specializations in biology, physics, and chemistry (23). A biosensor uses biological materials (e.g. tissue, microorganisms, organelles, cell receptors, enzymes, antibodies, nucleic acids, natural products), bioengineered materials (e.g., recombinant antibodies, engineered proteins, aptamers), or a biomimetic (synthetic catalysts, mixed ligands, MIP to mediate a biochemical reaction in the presence of an analyte to produce an optical, electrochemical, thermometric, piezoelectric, magnetic, or micrometric signal by a transducer (14,18). In general, biosensors consist of a biological recognition element, a transducer, and a final readout system (24) (**Fig. 1**).

3.1. Classification of Biosensors for Airborne Pathogens

Biosensors designed for the detection of airborne pathogens have been classified into distinct categories, primarily based on two critical factors: the transducer and the biological recognition element. These two elements play a pivotal role in determining the performance

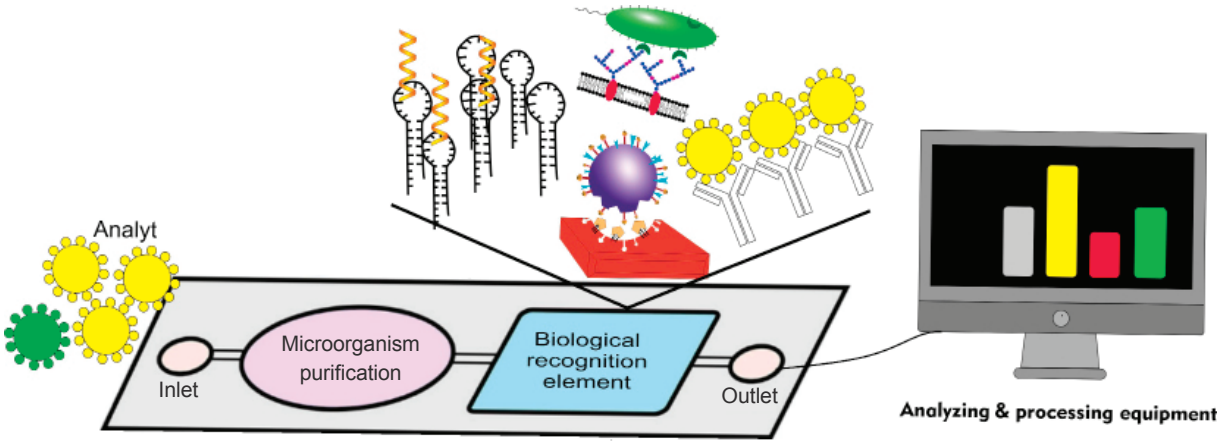

Figure 1. Process of analyte detection in a biosensor. Analyte enters the biosensor through an inlet. Within the biosensor, it undergoes purification to isolate genetic material or the desired cell component. Subsequently, it gets trapped by a specialized biological element. Finally, this trapped material is detected and analyzed for further examination (Original: Prepared by the authors).

and specificity of the biosensor in identifying and quantifying airborne pathogens. **Figure 2** provides a visual representation of the diverse range of functional and efficient biosensors used for the detection of airborne pathogens. These biosensors are categorized according to the specific transducers and recognition elements they employ, highlighting the versatility and adaptability of biosensing technologies in addressing the challenges of detecting airborne pathogens.

3.1.1. Category of Airborne Pathogens Biosensors Based on Transducer

Biosensors designed for the detection of airborne pathogens rely on transducers to convert various stimuli into measurable signals. The classification of biosensors based on the type of transducers they use is a well-established framework, with light-based, piezoelectric, and electrochemical biosensors being among the most prominent and widely recognized categories in this context.

3.1.1.1. Optical Biosensors

In the realm of airborne pathogen detection, optical biosensors operate based on the fundamental interaction between light and materials. Optical biosensors have ushered in a new era of possibilities and significant advancements in the domains of life sciences, medicine, and pharmaceuticals, particularly in the identification of biological analytes (25–27). They excel in measuring diverse properties of these analytes, offering simultaneous label-free and real-time detection, a cost-effective and straightforward approach for biosensors (28). Optical biosensors also deliver a substantial advantage by allowing direct visual observation of analytes. They harness an array of optical spectroscopy techniques, including absorption, fluorescence, phosphorescence, Raman spectroscopy, refraction, and surface plasmon resonance (SPR). Notably, SPR stands out as a real-time, online method capable of detecting changes at the dielectric-metal interface on nanostructured surfaces. This technology has demonstrated success in the detection and diagnosis of microorganisms such as *Bacillus anthracis*, *Mycobacterium tuberculosis*, *Staphylococcus aureus (S. aureus),* and *Streptococcus pneumoniae (S. pneumoniae)*. Given their versatility and wide-ranging applications, optical biosensors have evolved into indispensable tools in the field of biosensing for airborne pathogens (29,30).

SPR property of gold nanoparticles (AuNPs) is essential for detecting *S. aureus*. A biosensor called CS/AuNP/fusion-pVIII was created by combining cysteamine (CS), a specific fusion protein, and AuNPs to detect *S. aureus*. When *S. aureus* was present, it caused AuNP aggregation, changing the sensor's color from red to blue. This method is highly specific for *S. aureus*, with a detection limit of 19 CFU mL^{-1}. A recent development in sensor technology combines catalyzed hairpin

assembly (CHA) with a signal transducer to create a colorimetric sensor for detecting *S. pneumoniae*. This sensor works by binding target DNA (*S. pneumoniae*) to hairpin DNA through CHA, resulting in a new DNA sequence with a high G-rich content. When hemin is introduced, the G-rich DNA forms a complex with hemin, imitating the activity of horseradish peroxidase (HRP), leading to a noticeable change in color. This innovative colorimetric method allows for the detection of *S. pneumoniae* at a concentration as low as 156 CFU mL^{-1} (16).

3.1.1.2. Piezoelectric Biosensors

Piezoelectric biosensors employ piezoelectric crystals to convert stimuli int electrical potential. It uses specific biological recognition elements fixed to its surface. Interaction between the diagnostic elements and the target pathogen alters the sensor's frequency and generates current. Typically, a quartz crystal microbalance (QCM) is used as the mass-sensitive transducer in these biosensors, offering real-time monitoring, mass amplification, easy operation, and label-free detection (30).

Various rapid detection methods using a series piezoelectric quartz crystal (SPQC) sensor have been developed for *M. tuberculosis*. These methods include an immunosensor, a culture system based on detecting NH_3 and CO_2 from *M. tuberculosis* metabolism, and a culture system using phage amplification for rapid detection. While these methods have reduced detection time to 30 hours, they cannot distinguish between pathogenic and non-pathogenic bacteria. To detect *M. tuberculosis* at concentrations below 10^3 $CFU.mL^{-1}$, an extended incubation time of 96.3 hours is required (31). A quartz crystal microbalance (QCM) biosensor has been developed for the simple detection of *S. aureus*. It employs an *S. aureus-specific antibody* anchored on 10 MHz QCM sensors via protein A, with a stabilized layer containing iron nanoparticles. Importantly, this assay does not require labeling or sample preparation. It achieves a limit of detection of 7.41 $CFU.mL^{-1}$, making it highly sensitive for *S. aureus* detection (32).

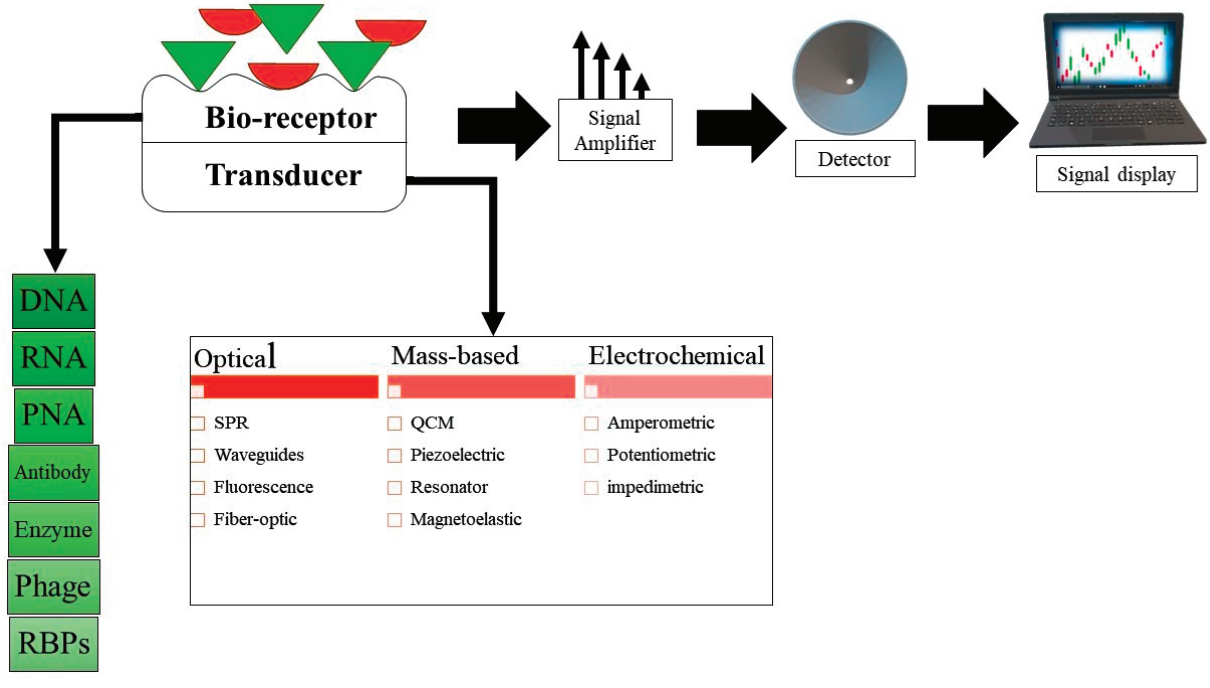

Figure 2. Classification of biosensors based on transducers and bio-probes for airborne pathogen surveillance. Classifying biosensors based on their transducers and the biological elements they utilize involves employing various components. Bio-Probes, which include DNA, RNA, antibodies, and enzymes, play a crucial role in monitoring airborne pathogens. Diverse tools and approaches, such as optical, electrochemical, and mass-based techniques, are used to identify particles and generate signals necessary for analysis (Original: Prepared by the authors).

3.1.1.3. Electrochemical Biosensors

Electrochemical biosensors involve a reaction on the transducer surface between biorecognition elements and the analyte, resulting in detectable electrochemical signals (voltage, current, impedance, capacitance). Some electrochemical biosensors measure current or voltage from oxidation and reduction reactions. They are categorized into impedimetric, potentiometric, amperometric, electro-chemiluminescent, voltametric, and conductometric methods based on the nature of electrochemical changes in the detection process (33). This biosensor, designed for detecting the *SARS-CoV-2* S1 spike protein, employs modified mammalian cells equipped with human chimeric spike S1 antibodies on their cell membranes. When the protein binds to these membrane-bound antibodies, it triggers notable and specific alterations in the cell's bioelectric characteristics, which can be identified through the Bioelectric Recognition Assay. Notably, this groundbreaking biosensor offers rapid results (within 3 minutes) and possesses an exceptional ability to detect extremely low concentrations, even as low as 1 $fg.mL^{-1}$ (34). In recent years, Primer Exchange Reaction (PER) has gained increasing interest as a method for the synthesis of single-stranded DNA (ssDNA). In this regard, a highly sensitive electrochemical biosensor was created for *avian influenza A (H7N9)* virus detection. This biosensor combines isothermal exponential amplification (EXPAR) with a hybridization chain reaction (HCR) using DNAzyme nanowires. Careful design ensures that neither primers nor DNAzymes with molecular beacons (MBs) interact with the fixed duplex probe on the electrode surface. This design enhances the production of target DNA, leading to increased cleavage of the duplex probes. Consequently, G-quadruplex-based nanowires self-assemble on the electrode surface, and in the presence of hemin, catalytic G-quadruplex-hemin DNAzymes are formed. These DNAzymes mimic HRP activity, generating electrochemical signals by increasing the reduction current of oxidized 3.3',5.5'-tetramethylbenzidine sulfate (TMB) in the presence of H_2O_2. The biosensor exhibits remarkable sensitivity, detecting the target DNA sequence with a limit as low as 9.4 fM (35).

3.1.2.Category of Airborne Pathogens Based on Bio-Recognition Elements

Bioreceptors encompass biomimetic components such as enzymes, antibody-antigen pairs, nucleic acids, Molecularly Imprinted Polymers (MIPs), whole cells or specific cellular components. These bioreceptors are designed to mimic biological processes and interact with precise bioanalytes, forming a crucial element in biosensor technology (30).

Each biological receptor comes with its own unique diagnostic mechanisms. These mechanisms are tailored to the specific receptor's properties and functions, enabling it to recognize, bind to, and often generate a measurable signal in response to a particular bioanalyte. This diversity in diagnostic mechanisms allows for the versatility and adaptability of biosensors in detecting a wide range of pathogens. Enzymatic biosensors employ catalytic reactions facilitated by enzymes that bind to the target pathogen (30).

Bifunctional magnetic nanobeads (bi-MBs) were designed to carry both target recognition molecules and signal molecules on their surface, serving as separation/enrichment and signal carriers. These bi-MBs were used to create an ultrasensitive electrochemical immunosensor for detecting *H7N9 avian influenza virus*. The method combined enzyme-induced metallization with bi-MBs and anodic stripping voltammetry, resulting in an exceptionally low detection limit of 6.8 $pg.mL^{-1}$ (36). Immunosensors detect the immunological response between antibodies and specific antigens. Stable immunological complexes have emerged as promising diagnostic tools for a range of conditions, including cancer, heart disease, and hepatitis A, as well as for industrial monitoring and environmental studies (37).

The conductive thread-based immunosensor (CT-IS) is designed with antibodies targeting the HA protein of the *pH1N1* virus integrated into conductive thread. When *pH1N1* virus is present, the interaction between the antibody and antigen causes increased strain on the conductive thread, leading to higher electrical resistance in the CT-IS. The sensor's effectiveness was tested using both HA protein and actual *pH1N1* virus samples, as well as patient samples infected with *pH1N1*. Significant resistance changes were observed in the pH1N1-infected patient samples (positive: n = 11), while minimal changes were seen in control samples from non-infected patients (negative: n = 9) (38). Nucleic acid-based biosensors utilize complementary strands of nucleic acids as diagnostic components, enabling the detection of analytes through ligation reactions between single-stranded DNA chains, resulting in the

formation of double-stranded DNA. Sequences that match the nucleic acid sequence of the target analyte can be synthesized, tracked, and immobilized onto the biosensor surface for precise detection (30).

Kim *et al.* have developed a swift and highly sensitive method for diagnosing COVID-19 by integrating an electrochemical biosensor with Recombinase Polymerase Amplification (RPA). The biosensor features a microelectrode array microchip with multiple working electrodes, coated with silver and gold nanoparticles for stability and reproducibility. Gold electrodes, known for their strong binding properties with thiol groups, were utilized. Specific primers modified with thiol groups enhanced the adsorption of target genes onto the electrodes, leading to a significant reduction in current density upon interaction with amplicons. This biosensor can rapidly detect target genes in around 20 minutes at room temperature, without the need for an expensive thermal-cycler, offering a quicker alternative to RT-PCR. Moreover, it boasts a lower limit of detection (LOD) for both the N gene (3.925 $fg.\mu L^{-1}$) and RdRp gene (0.972 $fg.\mu L^{-1}$) compared to conventional RPA techniques (39).

MIP is a type of synthetic receptor with specific recognition sites that is synthesized by the polymerization of functional monomers containing target analytes. After removing the target analytes from the polymer, cavities are formed according to the shape, size, and functional groups. The analyte binds to the MIP pores with ease, and they hold onto it until the signal is produced (40).

In the context of MIP biosensor, an innovative approach involved the creation of a red-emissive carbon nanostructure integrated with a molecularly imprinted Er-BTC MOF, serving as a fluorescence biosensor for the visual detection of DPA. This development is particularly significant given that DPA is a crucial biomarker associated with *Bacillus anthracis*, a subset of severe infectious diseases and bioweapons. The resulting fluorometric visual paper-based biosensor showcased remarkable capabilities, offering broad linear detection ranges for DPA spanning from 10 to 125 μM, and an impressive LOD as low as 1.28 μM (41).

For analytical purposes, various immobilized ligands, like antibodies, enzymes, cellular receptors, and oligonucleotide probes, are used to detect analytes. Increased analyte quantity requires meticulous monitoring, precise control, exceptional sensitivity, and speed. These days, lectins, carbohydrate-binding proteins, are being increasingly used in biosensor devices due to their high sensitivity to specific sugars in pathogens (42). Lectins can identify and bind to the specific glycan of the target analyte by specific and functional homo-oligomer glycans on their surface. Each pathogen attaches to a unique kind and chain of different carbohydrate branches of lectins in sensors based on lectins (43) .

For instance, in the field of lectin biosensors, researchers have developed plasmonic gold nanoparticles functionalized with Polyethylene Glycol (PEG) and either mannose or galactose. These biosensors have been employed to detect specific bacteria strains, such as *P. aeruginosa* and *E. coli*. Notably, they exhibit a remarkable LOD of 1.4×10^4 $CFU.mL^{-1}$, and the detection process is exceptionally rapid, taking only 30 minutes. The choice of carbohydrate ligand, whether it's galactose for *P. aeruginosa* or mannose for *E. coli,* depends on the target pathogen. Moreover, these lectin biosensors have demonstrated their capability to detect as few as 10^4 $CFU.mL^{-1}$, even in diluted meat samples, showcasing their potential in applications related to food safety and clinical diagnostics (44).

In **Table 1**, biosensors for detecting different airborne pathogens are specified based on the type of transducer (optical, piezoelectric, and electrochemical), biological elements, and detection time.

4. Detection Mechanisms of Biological Elements in Biosensors

As stated in the classification of biosensors, elements, and bio-receptors are the main parts of biosensors. Based on the different types of receptors, biosensors can be divided into enzymatic biosensors (the most common), immunoassay biosensors, nucleic acid or aptamer-based biosensors, MIP-based biosensors, and microbial or cellular component biosensors (such as lectin) (33).

4.1. Immunoassay-Based Biosensors

In immunoassay, polyclonal antibodies are attached to the biosensor as the biological receptor. The advantage of immunoassays is that they detect infections without breaking the cell wall, unlike other methods. Once the target antigen is detected, a suitable antibody is attached to the biosensor, allowing it to act as a "trap" for pathogens. The immobilized antibodies on the biosensor surface specifically bind to the pathogens, enabling their

Table 1. Biosensors based on transducers and different biological elements to detect airborne pathogens.

Transducer	Pathogen	Bioreceptor	Sample	LOD	Time	Ref.
SPR	*S. aureus*	CS[1]/AuNP/fusion-pVIII	Water	19 CFU.mL^{-1}	30 min	(16)
Colorimetric	*S. pneumoniae*	G-quadruplex/hemin	-	156 CFU.mL^{-1}	40 min	(16)
Electrochemical	*H7N9 AIV Virus*	Alkaline phosphatase	Buffer	6.8 pg[3].mL^{-1}	30 min	(36)
SPR	*SARS-CoV-2*	Oligonucleotide	Clinical	0.22 0.08 pM[4]	-	(1)
Colorimetric	*E. coli* *P. aeruginosa*	PEG Galactose Mannose	Homogenized meat	4×10^4 CFU.mL^{-1}	30 min	(44)
QCM	*Mycobacterium tuberculosis*	aptamer/DNA-AuNPs	Buffer	1 log CFU. mL^{-1}	1 day	(79) (31)
Electrochemical	*SARS-CoV-2*	Primer	Clinical	3.925 fg[5]/µl 0.972 fg/µl	20 min	(39)
Electrochemical	*SARS-CoV-2 S1*	antibodies	Buffer	1 fg/mL	3 min	(34)
QCM	*Staphylococcus aureus*	Polyclonal antibodies	Buffer	7.41 log CFU. mL^{-1}	1 day	(32) (80)
EIS[6]	H1N1Virus	Polyclonal antibodies	Throat swabs	80-100 virions/ µL	30 min	(81)
Fluorescence	*Bacillus anthracis*	MIP	Buffer	1.28 µM	-	(41)
EIS	*H7N9*	Primer	Synthetic	9.4 fM	60-90min	(35)

CS=Cysteamine, CFU=Colony Forming Units, pg=Picograms, pM= Particulate matter, fg= Femtogram, EIS = electrochemical impedance spectroscopy

Table 2. Applications of biosensors for detection of airborne pathogens by immunometric method.

Diagnostic method	Diagnostic elements	LOD	Time	Ref.
Antibody-Antigen immunoassay	Llama-derived nanobody	7-35 viral RNA copies/m^3 of air	5 min	(46)
Antibody-Antigen immunoassay Conductivity gene of nanowires	Anti-N2 and H3 antibody	10^4 viruses / µL air	2 min	(82)
Magnetic Fluorescence immunoassay	Attached antibodies to microspheres Fluorescence secondary antibodies against Mycobacterium tuberculosis	10^2-10^3 CFUs / mL liquid	50 min	(83)

detection and quantification. Pre-marked antibodies recognize pathogens when passed over immobilized antibodies on SPR, QCM, or cantilever sensors, generating a measurable signal. This quantifiable signal is valuable for POC devices, allowing comparisons between different assays. Immunoassay in biosensor technology shows promise for developing sensitive and accurate diagnostic tools across various detections. (24,45). Recently, a micro-immunoelectrode (MIE) biosensor was used for real-time detection of *SARS-CoV-2* in air. it is a type of electrochemical biosensor. The researcher implemented a high flow wet cyclone as a collection medium and a sample of this medium was transferred to the MIE biosensor. This device can detect the *SARS-CoV-2* virus within 5 min and LOD of 7-35 viral RNA copies/m^3 of air (46). **Table 2**

shows examples of tests performed to detect airborne pathogens by the immunoassay method.

Antibodies can be attached to sensors using physical and chemical techniques. Physical fixation is simple but may denature hydrophobic surface proteins and cause ligand migration during washing. One physical fixation approach involves electrostatically integrating antibody-antigen using microfluidics to attract pathogens. In polydimethylsiloxane, (PDMS) microfluidic channels, streptavidin beads self-assemble on positively charged (aminopropyl) trieth-oxysilane (APTES) strips. Antibodies are introduced and fixed to streptavidin, followed by antigen binding. A fluorescence-identifying solution is then introduced for antigen interaction and identification.

Chemical stabilization, on the other hand, maintains the structure of the ligand, preventing it from detaching after repeated washing. Chemically stabilizing antibodies on the surface is possible with organosilanes, self-assembled monolayers, dendrimers, and polyethylene glycol strands (24,47).

In magnetic fixation, antibodies are fixed using a magnetic medium on microfluidic sensors. Magnetic bead-based immunoassay techniques are integrated with digital microfluidic systems. Primary antibodies coupled with target analytes are mixed with tagged secondary antibodies. In the detection step, the magnetic bead is fixed by a magnet, separating the antibody-analyte mixture for detection. Secondary antibodies are tagged with enzymes or fluorescent markers, and chemiluminescence detection is conducted. This approach has disadvantages, like antibody stabilization and additional microfabrication steps. Antibodies can denature or dissociate from the surface over time, leading to a loss of capture efficiency and reduced assay sensitivity. Factors like pH and ionic strength can affect the stability of the magnetic bead-antibody complex. The reproducibility and validity of this method require further confirmation, and stabilization during sensor washing is necessary (48,49).

Antibody shelf life varies depending on intrinsic qualities and storage conditions. Commercial antibodies often contain additives like buffered phosphate salt solution, bovine serum albumin (BSA), sodium azide, and glycerol to enhance stability. Lyophilization, or freeze-drying, is the preferred method for the long-term preservation of monoclonal antibodies as it significantly extends shelf life. Freeze-dried antibodies are stable for 3-5 years when stored at -20 °C or below. This technique ensures molecular integrity, reduces temperature management requirements during transit, and preserves chemical and biological properties (50).

In general, the immunoassay method requires an expert and skilled person, and its long and expensive testing procedures are among its disadvantages (51).

4.2.PCR-Based Biosensors on a Small Scale

To achieve diagnostic POCs for rapid PCR, the miniaturization of the PCR device is a prerequisite to being able to place all the parts of the PCR process in a compact box. This tool mainly includes heating, optical, and electrical parts, a cooler, and a touch screen for adjusting and controlling parameters. To make the work easier, a rechargeable battery is built into the compact box as a power source (52). The first glass-based microfluidic PCR biosensor performed about 20 cycles of DNA replication in 1.5 to 18.7 minutes (53). An isothermal heater adjusts the temperature of the solution along the microfluidic channels during the PCR process to the ideal temperature for each PCR phase. The proportional-integral-derivative (PID) controller within an aluminum box beneath the sensor regulates this heat. For the PCR procedure, the isothermal heater generates temperatures of 50°C (creation of copy DNA (cDNA) from RNA), 95°C (annealing), and 63°C (ligation). The device was successful because it permitted quick temperature adjustments in PCR for small liquid quantities (54).

Despite great advances in PCR, such as improved nucleic acid extraction kits, primer kits, and portable PCR, very few studies have reported integrated, rapid, and portable PCR with aerosol sampling. However, several studies have attempted to partially correlate rapid PCR with air sampling (55).

The Onestart microfluidic sensors are portable, single-use PCR-based devices with a low manufacturing cost (<$10). They offer fast detection (<10 minutes), high sensitivity, and the ability to identify multiple pathogens simultaneously. These sensors are designed for respiratory pathogen detection. The sensors have three main regions: lysis, nucleic acid extraction, and amplification. The lysis region includes sample-loading reservoirs, while solid-phase extraction (SPE) is used in the nucleic acid extraction region. Extracted nucleic acids are collected in a lyophilized powder of Reverse

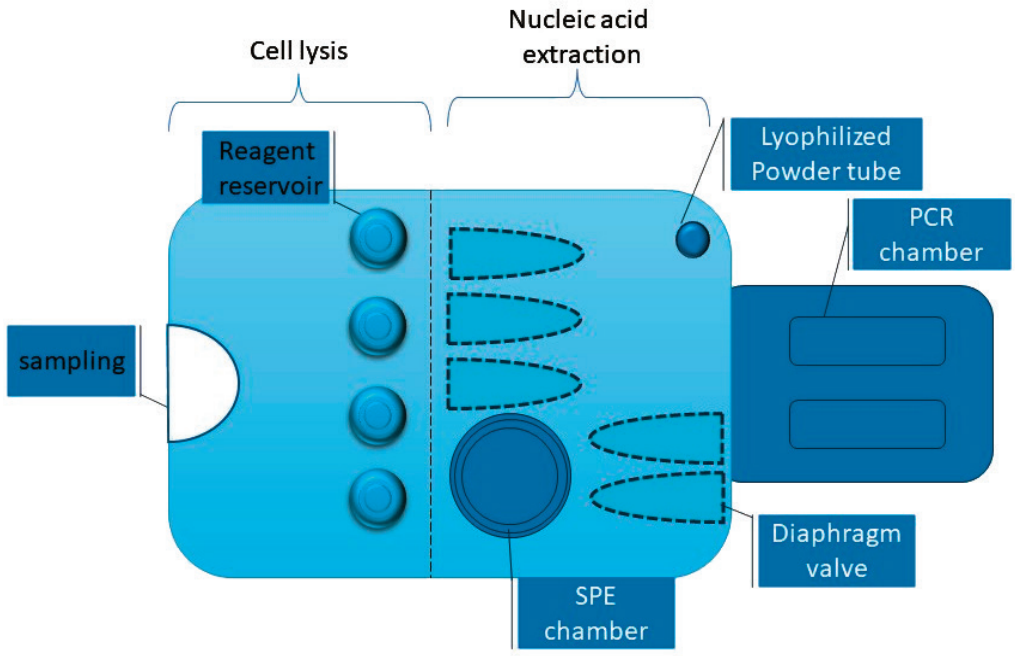

Figure 3. Operating procedure of the onestart system. A microfluidic chip, coupled with an amplification module, comprises a sample reservoir, three reagent reservoirs, an SPE chamber, six diaphragm valves, a lyophilized powder tube, and an amplification module housing 32 PCR chambers. The operational steps 1-4 represent the procedural guidelines for the Onestart system (Original: Prepared by the authors).

transcription polymerase chain reaction (RT-PCR) reagents tank to create the reaction mixture. The fluid transfer is controlled by six diaphragm valves. In the amplification region, the PCR solution with primers and probes is introduced under negative pressure from the lyophilized powder tank. The fully automated sensor is analyzed using a diagnostic device. Key advantages include low manufacturing cost, simultaneous detection of 21 pathogens, rapid processing time (about 1.5 hours), a LOD of 10^3, and a 95% detection limit. Required materials for sensor preparation include lysing buffer, washing buffer, magnetic beads, PCR buffer, DNA polymerase, RNase, deoxynucleoside triphosphate, magnesium chloride, fluorescence probe, primer, and positive/negative controls (**Fig. 3**) (56). **Table 3** shows examples of tests performed to detect airborne pathogens by the immunoassay method.

Introducing Epidax®29, an innovative and cost-effective microfluidic platform, designed like LEGO blocks, with a built-in temperature module, a detection module, and analysis software. It's easily adaptable for conducting COVID-19 screening using endpoint RT–PCR or RT-LAMP tests, as well as confirmatory tests using real-time RT–PCR (RT–qPCR). The platform's performance in detecting *SARS-CoV-2* viruses has been validated by comparing results from endpoint RT–PCR and RT–qPCR configured assays with those obtained from a commercial system. Notably, similar results were achieved while using only half the amount of reagents. Additionally, rapid *SARS-CoV-2* virus detection directly from 42 nasopharyngeal swab samples was achieved without the need for RNA extraction, reducing testing time to just one hour. Furthermore, *SARS-CoV-2* detection was successfully conducted in 54 clinical RNA extracts using a reconfigured RT-LAMP platform. The platform's modular design offers flexibility, allowing for the execution of various assay types to meet specific testing requirements and turnaround times (57).

4.3. Biosensors Based on the Method of Molecularly Imprinted Polymers

MIPs serve as an alternative to antibodies in pathogen detection. They were initially developed in 1970, forming a polymer matrix with selective binding sites for

Table 3. Applications of biosensors for detection of airborne pathogens by polymerase chain reaction method on a small scale.

Diagnostic method	Air sampler system	Target analyte	LOD	Time	Ref.
RT-PCR	Teflon fibers	*Rhinovirus*	TCID50	20 min – 4 h	(84)
PCR	Personal bio sampler	*Pseudomonas Bacillus* A/H5N1	10^3 PFUs² / m^3 air	3 h >	(85)
qPCR	Personal air sampler	*Bacteriophage* T4	24 PFUs liquid 200 PFUs / L air	1 h and 10 min	(86)
qPCR	Gas aerosol collector	*Anthrax bacterium* Hay bacillus spores	10^4 CFUs/mL liquid	>2 h	(87)
PCR	PCR chip	*E. coli* *Citrobacter koseri* *Staphylococcus aureus* *Klebsiella pneumoniae* *Pseudomonas aeruginosa*	10^3 CFUs /mL liquid	10 min	(88)

TCID50=50% tissue culture infectious dose, A/H5N1=Influenza A virus subtype H5N1, PFUs=plaque-forming unit, qPCR=Quantitative polymerase chain reaction

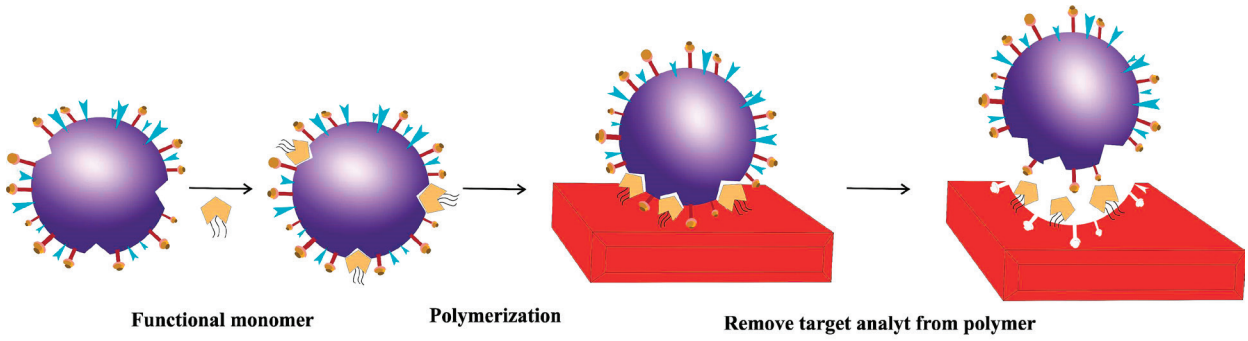

Figure 4. Template-based molecular imprinting: creating selective recognition polymers. Molecular imprinting technique used to create polymers with specific recognition features. By using a chosen molecule as a template, the resulting polymer matrix can selectively bind to the target molecule or similar molecules, thanks to the imprints left behind after removing the template (Original: Prepared by the authors).

target analytes. After analyte removal, hollow cavities matching the analyte's size and shape are formed. In virus detection, MIPs are attached to viral targets and assembled on a 2D surface connected to the polymer surface in contact with the sensor. To achieve selectivity, MIPs are combined with biosensors like optical detectors, SPR, and QCM (58). MIPs in Electrochemical Sensors (MIECS) cost-effectively provide fast and accurate information. Electrochemical sensors have many advantages, including detection features, low cost and miniaturization, high sensitivity, wide linear range, minimal energy requirements, portability, and ease of operation (59). MIPs are synthesized in a three-step process. Firstly, a functional monomer and a template molecule form a conjugate through covalent or non-covalent binding, known as covalent molding. The functional monomers have matching amino acid residues to the template. Next, polymerization creates a three-dimensional network that fixes the conjugate's structure. In the final step, the MIPs undergo thorough washing and testing with phosphate buffer, acetic acid solution, distilled water, alkaline, urea, acetic acid, and 20% tween to remove the template, resulting in complementary sites that replicate the size, shape,

Table 4. Detection of airborne pathogens by MIP method.

MIP	Monomer	Target analyte	LOD	Time	Ref.
MIP-QCM	Acrylic acid Acrylamide N-benzyl acrylamide	Liner epitope NS1 (dengue)	1-10 µg.L^{-1}	<1 h	(60)
MIP-QCM	Acrylamide Methacrylic acid Methyl methacrylate N-Vinylpyrrolidone	H5N1 H5N3 H6N1 H1N3 H1N1	10^5 particle.mL^{-1}	3-4 h	(66)
MIP-QCM	Polydopamine (PDA)	*HIV* 1Gp 41	2 ng.mL^{-1}	-	(89)
MIP-QCM	Acrylamide Methacrylic acid Methyl methacrylate N-Vinylpyrrolidone	*CSFV*	1/7 µg.mL^{-1}	-	(90)

H5N3=Influenza A H5N3, H6N1=Influenza A virus subtype H6N1, H1N3=Influenza A virus subtype H1N3, H1N1=Influenza A virus subtype H1N1, HIV 1Gp 41 = human immunodeficiency virus-1 glycoprotein 41, CSFV= Classical swine fever virus

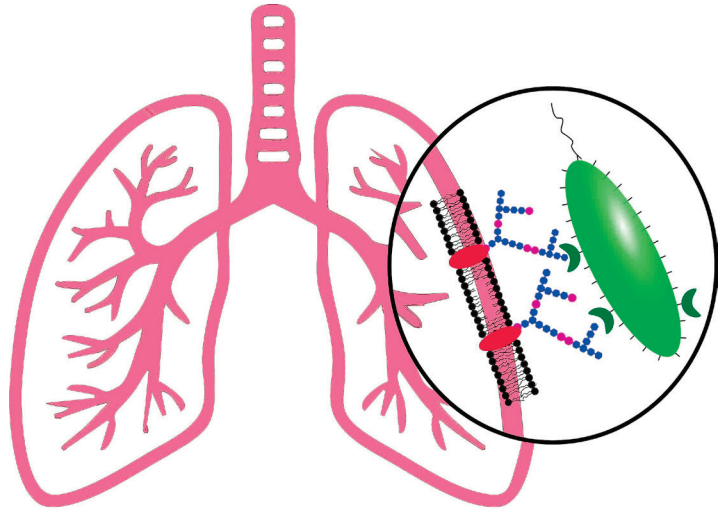

Figure 5. Bacterial lectins Interaction and mucosal receptors. Multivalent binding by oligosaccharides between bacterial and mammalian cell membranes. Colored squares represent different monosaccharide units, red circles represent mammalian respiratory lectin, and green half-circles represent pathogen lectin (Original: Prepared by the authors).

and chemical characteristics of the original template molecule (60). To maintain the morphology and stability of the printed sites, it is possible to use binders such as ethylene glycol dimethacrylate, divinylbenzene, and trimethylolpropane trimethacrylate, which are important compounds in the construction of MIP (61). These steps are shown in **Figure 4**.

In the field of molecular molding technology, calculations based on computer simulation with biomarkers of microbial target analytes such as atoms, molecules, or macromolecules such as surface proteins, surface polysaccharides, and surface glycopolysaccharides can

be used to facilitate the identification and tracking of airborne pathogens (62). Molecular imprinted polymer nanoparticles are more selective and specific because they have only one binding site for a target molecule, such as an enzyme or protein (63). The common biomarker molecules that are used to facilitate the identification of airborne pathogens in the MIP format are:

a. Small Molecule Biomarkers

N-Acyl homoserine lactone is a metabolite and small signaling molecule that can be used for various applications. In a study conducted by *Jiang et al.*, a magnetic MIP was developed for the selective detection of N-acyl homoserine lactone. They used methacrylic acid as a monomer and 2,5-dimethyl-4-hydroxy-3(2H)-furanone as an analog template to create the MIP system. With this approach, the MIP system demonstrated high selectivity and sensitivity toward N-acyl homoserine lactone detection (64).

b. Saccharide Biomarkers

Monosaccharides such as sialic acid and mannose are often used as saccharide targets. Glycans can recognize and differentiate different pathogens as well as cancer cells (62).

c. Toxins and Other Protein Biomarkers

For protein biomarkers, a simple way to increase the affinity of the target protein for its binding sites is to place specific charges in their specific binding sites. For this purpose, a monomer with a positive charge, such as 4-valent ammonium salts, holding a vinyl ring and an aromatic ring for MIP assembly for BSA, which holds the negative charge under decomposition conditions (pH 7.4 and isoelectric point 5.4), must be used. In this condition, an ionic bond is created between MIP and BSA (65).

d. Virus

MIPs can selectively recognize and bind to a virus based on its size, shape, and chemical functionality. However, the use of MIPs in virus detection and identification is an active area of research, and they may offer advantages over traditional methods based on morphology and surface features, such as higher sensitivity and specificity (66).

e. Surface Load of Bacteria

To detect the Covid-19 virus in the nasopharyngeal samples of patients, *Raziq et al.* developed MIP electrochemical sensors based on Sars nucleoprotein, which consists of S protein subunits as a suitable functional monomer on a gold-based thin film electrode using poly -M- diphenylene diamine. Finally, the performance of the sensor was measured by changes in electric potential with different concentrations of virus in the samples (67).

The MIP method can be combined with various identification methods, simplifying the process of identifying diverse analytes. Commercializing ideas in this field faces challenges due to insufficient research, limited production methods, and the high costs associated with commercial production (68). Some of the advantages of using the MIP-QCM sensor in virus detection are its high sensitivity, low technical dependencies, convenient data interpretation, low cost, short working time (20-30 minutes for each sample), and the possibility of identifying any target with any size. It is worth mentioning another merit: In 2017, research explored electrochemical biosensors that can be reused and stored at room temperature. The reversibility of MIP binding with the target analyte makes MIP sensors suitable for reusable sensing technologies. Some studies have shown the possibility of using MIP-based tools more than three times, with sensitivity remaining over 90% after washing seven times and reconnecting the target. However, the sensitivity of the sensor generally decreases after four weeks of storage at room temperature (69). Another study suggests that MIP sensors can be reused up to five times, with a stable connection affinity for approximately 30 days. During this time, the polymers only lost 10-20% of their binding affinity, primarily due to binding site occupation by pollutants. Polymers that were intact after washing and used again one month later showed no significant decrease in binding affinity (60). **Table 4** is a summary of the investigations carried out for the detection of airborne pathogens by the MIP method, along with suitable monomers and their detection limits.

4.4. Lectin Method

The mucosal surfaces of the respiratory, gastrointestinal, and urogenital tracts are the most common portals by which infectious bacteria enter the deeper tissues of a mammalian host. In numerous cases, the firm adhesion of bacteria is mediated by special protein molecules associated with proteinaceous organelles. The surface of the infectious bacteria employs lectins to combine with complementary structures on the mucosal surfaces known as receptors, either as glycoproteins or as glycolipids (70). Lectins are proteins that have

Table 5. Particular lectins of certain airborne infections.

Pathogen	Receptor	Receptor sequence	Ref.
Mycobacterium tuberculosis	Sialyl-Lewis X	3′-SLeX, α-NeuNAc-(2→3)-β-D-Gal-(1→4) (α-L-Fuc-[1→3])-D-GlcNAc	(91)
Streptococcus pneumoniae	Laminin Vitronectin Collagen IV Asialo-GM1 Asialo-GM2	GalNAcβ1-4Galβ1-4Glcβ1-1Cer Galβ1-3GalNAcβ1-4Galβ1-4Glcβ1-1Cer NeuAcα2-3Galβ1-4Glc NeuAcα2-6Galβ1-4Glc Galβ1-3GalNAcβ1-4(NeuAcα2-3) Galβ1-4Glcβ1-1Cer GalNAcβ1-3Galα1-4Galβ1-4Glcβ1-1Cer Galβ1-4Glcβ1-1Cer	(92)
	WEB2086	3-[4-(2-Chlorophenyl)-9-methyl-6H-thieno[3,2-f] [1,2,4] triazolo[4,3-a] [1,4] diazepin-2-yl]-1-(4-morpholinyl)-1-propanone	(93)
Bordetella pertussis	Asialo GM1* Chondroitin sulfate Heparan sulfate Dextran Sulfate LewisA, LewisB, LewisX	Galβ1-4Glc, GalNAcβ1-4Gal Gal (3SO4) β1-1Cer	(94)
Haemophilus influenzae	Dextran Sialyl-glycolipids Lewis A Fibronectin Laminin Collagen I Collagen II Asialo-GM1 Asialo-GM2 GM1, GM2 Gangliosides GM1, GM2, GM3	Galβ1-3GalNAcβ1-4Galβ1-4Glcβ1-1Cer GalNAcβ1-4Galβ1-4Glcβ1-1Cer Galβ1-3GalNAcβ1-4(NeuAcα2-3) Galβ1-4Glcβ1-1Cer NeuAcα2-3Galβ1-3GalNAcβ1-4(NeuAcα2-3) Galβ1-4Glcβ1-1Cer	(95)
Influenza A	Dextran Sulfate	NeuAc(α2-6) Gal, GP-2(NeuAca2-3Gal)	(96)
Mycoplasma pneumonia	Sulfated glycolipids Dextran Sulfate	NeuAcα2-3Galβ1-3GalNAc Gal (3SO4) β1-1Cer NeuAcα2-3Galβ1-4Glc	(72)
Pseudomonas aeruginosa	Sialyl-Lewis X Heparan sulfate Dextran Fibronectin Laminin Collagen II, I Cholesterol p-Nitrofenol Asialo-GM1 Asialo-GM2	Galα1-4Gal Galβ1-3GalNAcβ1-4(NeuAcα2-3) Galβ1-4Glcβ1-1Cer Galβ1-4GlcNAc Galβ1-4Glcβ1-1Cer GalNAcβ1-4Galβ1-4Glcβ1-1Cer	(97)
Staphylococcus aureus	Dextran Lewis A Heparin Heparan sulfate Fibronectin Laminin Collagen I Asialo-GM1 ، Asialo-GM2	GalNAcβ1-4Galβ1-4Glcβ1-1Cer	(72)
(SARS-CoV-2)	-	sialated complex fucosylated 2-antennae (FA2) in ACE2	(98)
MERS-COV	DPP4	dipeptidyl peptidase 4 α2,3-linked sialic acids 3 N-acetyl-D-lactosamine	(99)

WEB2086=Thieno-triazolodiazepine, DPP4= Dipeptidyl Peptidase-4

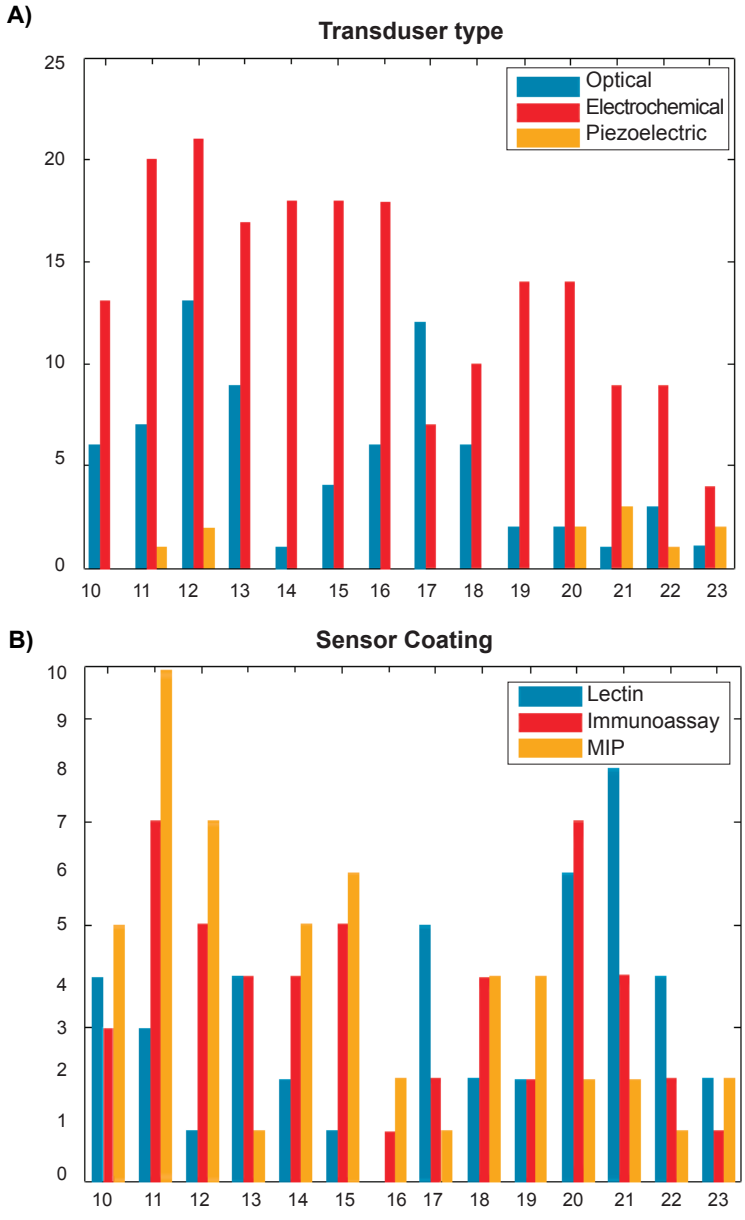

Figure 6. Analyzing trends of transducer and bio-elements. A) Number of studies published in PubMed based on classification of application of transducers for virus assays. **B)** The number of studies published in PubMed based on the classification of the use of bio-elements for the assay of viruses (Original: Prepared by the authors).

unique sugar specificity and can bind non-covalently and reversibly to carbohydrates and play several roles in the biological identification of cells, carbohydrates, and proteins. In other words, lectins are mediators for connecting bacteria, viruses, and fungi to their intended targets. Because of the wide variety of lectins, they have been used in many fields, such as molecular biology, pharmaceutical, and clinical medicine. As shown in **Figure 5**, lectins are normally present in the cytoplasmic membrane of living organisms and the oligosaccharide chains attached to them are exposed to the external environment of the cell, which specifically interacts with proteins on the surface of microorganisms (adhesion in bacteria or agglutinin in viruses) that are the cause of infection interact (71).

The most obvious example of the specificity of lectins

is the binding of airborne pathogens to lectins on the cell surfaces of the respiratory system (72). For example, *S. pneumoniae* binds to GlcNAc beta (1-3) Gal receptors on human epithelial cells, or *MERS* uses the N-terminal part of the S_1 subunit of the spike protein to bind to two molecules on the cell surface. The host uses dipeptidyl peptidase-4 (DPP4) and α2,3-sialic acids.

Table 5 shows several respiratory pathogens that bind to specific oligosaccharide structures (73).

Masarova *et al.* found that for the detection of two different species of *Salmonella*, two species of *E.coli*, *Klebsiella* and *Citrobacter*, lectins were covalently attached to lectin-based optical biosensors through amino groups, and after the lectins were attached to the sensor, the analyte-containing endotoxin or whole bacterial cells were injected into the surface (74).

5. Discussion

This comprehensive review article offers a captivating exploration of the dynamic world of biosensors, serving as an indispensable guide to the cutting-edge field of in situ detection of airborne pathogens. In this meticulously researched piece, we delve into the intriguing realm of biosensor technology, dissecting the advantages and limitations of diverse biosensor types, bioelements, and transducers. To provide readers with an up-to-the-minute understanding of the research landscape, we conducted a thorough analysis of the Pubmed database spanning from 2010 to 2023. Notably, our findings, showcased in **Figure 6A**, underscore the dominance of electrochemical techniques, possibly attributed to their cost-effectiveness and user-friendly nature. Nevertheless, the somewhat gradual adoption of piezoelectric sensors, exemplified by QCM, paves the way for further exploration and innovation in this domain. **Figure 6B** unveils a fascinating panorama of bio-recognition elements, revealing a rich tapestry of coating methods for sensors and a burgeoning interest in Lectin-based coatings in recent times. Amidst these revelations, we emphasize the pivotal role that the pathogen's type, size, and characteristics play in guiding the selection of the most suitable detection methodology. Join us on this enlightening journey through the realm of biosensors, where science and innovation converge to shape the future of pathogen detection. Since the antibodies of a specific microbial strain act specifically, antigen-based microbial detection approaches are limited to the presence of specific antibodies in the environment. High cost, maintenance, and stability of antibodies are among the challenges of antibody-based sensors. These various challenges have been overcome by exploiting robust molecular diagnostic schemes and replacing natural receptors with aptamers and synthetic templates such as MIPs (40). Due to the complexity of detecting pathogens based on their structural and biochemical characteristics, the design of biosensors based on genetics is a suitable alternative. The use of genetic materials in PCR biosensors is a powerful technology that makes approaches to identify unknown pathogens very flexible. Therefore, in complex samples such as air where there is no idea about the type of pathogens, genome-based approaches will be more useful for rapid and effective pathogen detection. However, PCR biosensors, due to a combination of miniaturization, ease of use, and a lack of strict standards, have led to the publication of poor data and inappropriate conclusions. Two biosensors based on antibody-antigen and PCR, despite having sufficient sensitivity and characteristics for pathogen identification, face challenges due to limitations such as low stability and high cost. Also, these diagnostic methods are often time-consuming and require laboratory equipment, an operator, and basic knowledge of the target structure (75). Therefore, recently, lectin and MIP-based biosensors have emerged as cost-effective and stable alternatives to antibodies and nucleic acids. They offer acceptable sensitivity and selectivity. MIP technology can combine with various identification methods, making it suitable for detecting analytes of any size without complex techniques. The commercial potential of MIP in diagnostics is highly promising and may revolutionize the market. However, challenges exist, such as the limited ability to detect small gas molecules and the constraints posed by pathogen mutations, and the emergence of new strains. Lectin diagnostics method identifies pathogens based on surface factors without advanced equipment. By mimicking pathogen binding to respiratory cell receptors, lectins offer unique binding to pathogen surface sugars. Despite being less specific than antibodies, lectins are affordable, stable, and suitable for applications in molecular biology, pharmaceuticals, and clinical medicine. This innovative diagnostic technique detects pathogen connections with the carbohydrate parts of lectins on a sensor surface in real-time using

recorded frequencies. Biosensors, which are gaining attention, can integrate with micro-sized bioaerosol collectors, enabling real-time detection and analysis of airborne pathogens simultaneously. Despite its limited availability, this system proves to be a powerful tool for identifying pathogens in the environment (76,77).

Biosensors have emerged as versatile tools in this context, offering significant advantages such as real-time monitoring, sensitivity, and specificity. In envisioning the possible future of biosensors for the detection of airborne pathogens, we anticipate the convergence of various cutting-edge technologies, like artificial intelligence to create highly sophisticated biosensors. This integrating enhances the capabilities and effectiveness of biosensors in several ways like, reduced false positives, real-time data analysis, pathogen presence or mutations, and automated decision-making. Biosensors also, will empower individuals to monitor their health by providing wearable and home-based devices that can detect airborne pathogens, supporting early intervention and personalized health management. The last but not least, they will be integrated into the Internet of Things (IoT) ecosystem, providing continuous data streams for cloud-based platforms. Big data analytics will enable predictive modeling and early warning systems (78).

In conclusion, airborne pathogen biosensors present clinicians with innovative tools for timely detection and response to infectious diseases, promising to save lives, reduce healthcare costs, and enhance global pandemic preparedness. Clinicians should stay informed about these advancements and consider integrating biosensors into routine monitoring for more effective infectious disease management.

Acknowledgment

This activity has been carried out in the form of a research plan approved by the IROST. Also, the authors of the article consider it necessary to thank Dr. Farzaneh Azizmohseni and Prof. Saeed Mirdamadi, scientific members of the Iranian Research Organization for Science and Technology, for some scientific consultations. A special acknowledgment is extended to the authors who devoted their creativity to crafting additional visuals (**Figures1, 2, 3, 4, 5, 6**), thereby enriching the overall content.

Conflict of interest:

The authors declare that they have no conflict of interest.

References

1. Qiu G, Gai Z, Tao Y, Schmitt J, Kullak-Ublick GA, Wang J. Dual-Functional Plasmonic Photothermal Biosensors for Highly Accurate Severe Acute Respiratory Syndrome Coronavirus 2 Detection. *ACS Nano*. 2020;**14**(5):5268–5277. doi:10.1021/acsnano.0c02439
2. Després VR, Alex Huffman J, Burrows SM, Hoose C, Safatov AS, Buryak G, *et al.* Primary biological aerosol particles in the atmosphere: A review. *Tellus B*. 2012;**64**(1).doi:10.3402/tellusb.v64i0.15598
3. Ma J, Du M, Wang C, Xie X, Wang H, Zhang Q. Advances in airborne microorganisms detection using biosensors: A critical review. *Front Environ Sci Eng*. 2021;**15**(3):1–19.doi:10.1007/s11783-021-1420-8
4. Miripour ZS, Sarrami-Forooshani R, Sanati H, Makarem J, Taheri MS, Shojaeian F, et al. Real-time diagnosis of reactive oxygen species (ROS) in fresh sputum by electrochemical tracing; correlation between COVID-19 and viral-induced ROS in lung/respiratory epithelium during this pandemic. *Biosens Bioelectron*. 2020;**165**(June):112435.doi:10.1016/j.bios.2020.112435
5. Jamison DT, Gelband H, Horton S, et al. E. Disease Control Priorities: Improving Health and Reducing Poverty. *IBRD*. 2017;9. doi:10.1596/978-1-4648-0527-1
6. Khan S, El R, Abad R, Bindajam A, Alqadhi S. Where we missed? Middle East Respiratory Syndrome (MERS-CoV) epidemiology in Saudi Arabia; 2012–2019. *Sci Total Environ*. 2020 ;747:141369. doi:10.1016/j.scitotenv.2020.141369
7. Helrich K. Official methods of analysis of the Association of Official Analytical Chemists. *AOAC*. 1990.
8. Hobson NS, Tothill I, Turner APF. Microbial detection. *Biosensors & bioelectronics*. 1996;**11**(5):455-477. doi:10.1016/0956-5663(96)86783-2
9. Yagupsky P, Nolte FS. Quantitative aspects of septicemia. *Clinical microbiology*. 1990;**3**(3):269-279.doi: 10.1128/CMR.3.3.269
10. Tietjen M, Fung DYC. Salmonellae and food safety. *Crit Rev Microbiol*. 1995;**21**(1):53–83. doi:10.3109/10408419509113534
11. Wang J, Yang L, Wang H, Wang L. Application of Microfluidic Chips in the Detection of Airborne Microorganisms. *Micromachines*. 2022;**13**(10):1–18.doi:10.3390/mi13101576
12. Pan H, Zhang Y, He GX, Katagori N, Chen H. A comparison of conventional methods for the quantification of bacterial cells after exposure to metal oxide nanoparticles. *BMC Microbiol.* 2014;14:222.doi: 10.1186/s12866-014-0222-6
13. Bhardwaj SK, Bhardwaj N, Kumar V, Bhatt D, Azzouz A, Bhaumik J, *et al.* Recent progress in nanomaterial-based sensing of airborne viral and bacterial pathogens. *Environ Int*. 2021;146:106183.doi:10.1016/j.envint.2020.106183
14. Cassedy A, Mullins E, O'Kennedy R. Sowing seeds for the future: The need for on-site plant diagnostics. *Biotechnol Adv*. 2020;39:107358.doi:10.1016/j.biotechadv.2019.02.01415.
15. Carroll A. World report on disability. *Ir Med J.* 2012;**105**(5).
16. Sivakumar R, Lee NY. Recent advances in airborne pathogen detection using optical and electrochemical biosensors. *Anal Chim Acta*. 2022;1234: 340297.doi:10.1016/j.aca.2022.340297
17. Martinelli F, Scalenghe R, Davino S, Panno S, Scuderi G, Ruisi P, *et al.* Advanced methods of plant disease detection. A review. *Agron Sustain Dev*. 2015;**35**(1):1–25.doi: 10.1007/s13593-014-0246-1
18. Lazcka O, Del Campo FJ, Munoz FX. Pathogen detection: A perspective of traditional methods and biosensors. *Biosens*

Bioelectron. 2007;**22**(7):1205-17. doi:10.1016/j.bios.2006.06.036
19. Fratamico PM, Strobaugh TP, Medina MB, Gehring AG. Detection of *Escherichia coli* 0157: H7 using a surface plasmon resonance biosenso*r*. *Biotechnology Techniques*.1998;12:571–576. doi:10.1023/A:1008872002336
20. Griffiths D, Hall G. Biosensors—what real progress is being made*? Trends Biotechnol*. 1993;**11**(4):122-130. doi: 10.1016/0167-7799(93)90086-O
21. Nguyen PQ, Soenksen LR, Donghia NM, Angenent-Mari NM, de Puig H, Huang A, *et al.* Wearable materials with embedded synthetic biology sensors for biomolecule detection. *Nat Biotechnol*. 2021;**39**(11):1366-1374.doi:10.1038/s41587-021-00950-3
22. Fronczek CF, Yoon J. Biosensors for Monitoring Airborne Pathogens. *J Lab Autom*. 2015;**20**(4):390-410.doi:10.1177/2211068215580935
23. Clark LC, Lyons C. Electrode Systems for Continuous Monitoring in Cardiovascular Surgery. *Ann N Y Acad Sci.* 1962;**31**(102):29-45. doi:10.1111/j.1749-6632.1962.tb13623.x
24. Skottrup PD, Nicolaisen M, Justesen AF. Towards on-site pathogen detection using antibody-based sensors. *Biosensors & bioelectronics*. 2008;**24**(3):339–348. doi:10.1016/j.bios.2008.06.045
25. Bigdeli A, Ghasemi F, Golmohammadi H, Abbasi-Moayed S, Nejad MAF, Fahimi-Kashani N, *et al.* Nanoparticle-based optical sensor arrays. *Nanoscale*. 2017;**9**(43):16546-16563. doi:10.1039/C7NR03311G
26. Fahimi-Kashani N, Hormozi-Nezhad MR. Gold-Nanoparticle-Based Colorimetric Sensor Array for Discrimination of Organophosphate Pesticides. *Anal Chem*. 2016;**88**(16):8099–8106.doi:10.1021/acs.analchem.6b01616
27. Fahimi-Kashani N, Shadabipour P, Hormozi-Nezhad MR. Colorimetric detection of glutathione based on transverse overgrowth of high aspect ratio gold nanorods investigated by MCR-AL*S*. *RSC Adv.* 2015;5:82906-82915. doi: 10.1039/C5RA14784K
28. Turner A. Biosensors for use in the food industry: a new rapid bioactivity monitor. 1986
29. Khater M, de la Escosura-Muñiz A, Merkoçi A. Biosensors for plant pathogen detection. *Biosens Bioelectron*. 2017;93:72–86. doi:10.1016/j.bios.2016.09.091
30. Liu H, Ge J, Ma E, Yang L. Advanced biomaterials for biosensor and theranostic*s*. *Biomaterials in Translational Medicine*. 2019;213–255. doi:10.1016/B978-0-12-813477-1.00010-4
31. He F, Xiong Y, Liu J, Tong F, Yan D. Construction of Au-IDE/CFP10-ESAT6 aptamer/DNA-AuNPs MSPQC for rapid detection of Mycobacterium tuberculosis. *Biosens Bioelectron*. 2016;**15**(77):799–804.doi:10.1016/j.bios.2015.10.054
32. Pohanka M. QCM immunosensor for the determination of Staphylococcus aureus antigen. *Chem Pap*. 2020;**74**(2):451–458. doi:10.1007/s11696-019-00889-5
33. Naresh V, Lee N. A review on biosensors and recent development of nanostructured materials-enabled biosensor*s*. *Sensors (Switzerland*). 2021;**21**(4):1–35. doi:10.3390/s21041109
34. Mavrikou S, Moschopoulou G, Tsekouras V, Kintzios S. Development of a portable, ultra-rapid and ultra-sensitive cell-based biosensor for the direct detection of the SARS-COV-2 S1 spike protein antigen. *Sensors (Switzerland)*. 2020;**20**(11):3121.doi:10.3390/s20113121
35. Yu Y, Chen Z, Jian W, Sun D, Zhang B, Li X. Biosensors and Bioelectronics Ultrasensitive electrochemical detection of avian in fl uenza A (H7N9) virus DNA based on isothermal exponential ampli fi cation coupled with hybridization chain reaction of DNAzyme nanowires. *Biosens Bioelectron*. 2015;**15**(64):566–571.doi:10.1016/j.bios.2014.09.080
36. Wu Z, Zhou C, Chen J, Xiong C, Chen Z, Pang D, *et al.* Biosensors and Bioelectronics Bifunctional magnetic nanobeads for sensitive detection of avian in- fl uenza A (H7N9) virus based on immunomagnetic separation and enzyme-induced metallizatio*n*. *Biosens Bioelectron*. 2015;68:586–592. doi:10.1016/j.bios.2015.01.051
37. Aydin M, Aydin EB, Sezgintürk MK. Advances in immunosensor technology. *Adv Clin Chem*. 2021;102:1–62. doi:10.1016/bs.acc.2020.08.001
38. Son SU, Jang S, Lim J, Seo SB, Kang T, Jung J, et al. Conductive Thread-Based Immunosensor for Pandemic Influenza A (H1N1) Virus Detection. *ACS*. 2023;**15**(6). doi:10.1021/acsami.2c19403
39. Eun H, Schuck A, Hi S, Lee Y, Kang M, Kim Y. Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID- 19 . *DIM*. 2020; doi:10.2478/dim-2020-0012
40. Denmark DJ, Mohapatra S, Mohapatra SS. Point-of-Care Diagnostics: Molecularly Imprinted Polymers and Nanomaterials for Enhanced Biosensor Selectivity and Trans-ductio*n*. *EuroBiotech J*. 2020;**4**(4):184–206. doi:10.2478/ebtj-2020-0023
41. Norouzi S, Dashtian K, Amourizi F, Zare-dorabei R. Red-emissive carbon nanostructure-anchored molecularly imprinted Er-BTC MOF: a biosensor for visual anthrax monitoring. *RSC*. 2023;148:3379–3391. doi:10.1039/D3AN00865G
42. Hassan SU, Donia A, Sial U, Zhang X, Bokhari H. Glycoprotein- and lectin-based approaches for detection of pathogens. *Pathogens*. 2020;**9**(9):1–22. doi:10.3390/pathogens9090694
43. Bojar D, Meche L, Meng G, Eng W, Smith DF, Cummings RD, *et al.* A Useful Guide to Lectin Binding: Machine-Learning Directed Annotation of 57 Unique Lectin Specificitie*s*. *ACS chemical biology*. 2022;**17**(11):2993–3012. doi:10.1021/acschembio. 1c00689
44. Priyadarshi N, Ambule MD, Kaushal S, Kumar A, Sagar P, Srivastava AK, *et al.* Nanoglycocluster based diagnostic platform for colorimetric detection of bacteria; A comparative study analysing the effect of AuNPs size, linker length, and glycan diversity. *Biosens Bioelectron*. 2022;201(January):113969. doi:10.1016/j.bios.2022.113969
45. Busby M, Xue C, Li C, Farjoun Y, Gienger E, Yofe I, *et al.* Systematic comparison of monoclonal versus polyclonal antibodies for mapping histone modifications by ChIP - se*q*. *Epigenetics Chromatin*. 2016;1–16. doi: 10.1186/s13072-016-0100-6
46. Puthussery J V., Ghumra DP, McBrearty KR, Doherty BM, Sumlin BJ, Sarabandi A, *et al.* Real-time environmental surveillance of SARS-CoV-2 aerosols. *Nat Commun*. 2023;**14**(1):3692.doi:10.1038/s41467-023-39419-z
47. Sivagnanam V, Bouhmad A, Lacharme F, Vandevyver C, Gijs MAM. Sandwich immunoassay on a microfluidic chip using patterns of electrostatically self-assembled streptavidin-coated bead*s*. *Microelectron Eng*. 2009;**86**(4–6):1404–1406. doi:10.1016/j.mee.2008.11.087
48. Shamsi MH, Choi K, Ng AHC, Wheeler AR. A digital microfluidic electrochemical immunoassay. *Lab Chip*. 2014;**14**(3):547–554. doi: 10.1039/C3LC51063H

49. Ng AHC, Choi K, Luoma RP, Robinson JM, Wheeler AR. Digital microfluidic magnetic separation for particle-based immunoassays. *Anal Chem*. 2012;**84**(20):8805–8812. doi:10.1021/ac3020627
50. Vergauwe N, Witters D, Ceyssens F, Vermeir S, Verbruggen B, Puers R, *et al.* A versatile electrowetting-based digital microfluidic platform for quantitative homogeneous and heterogeneous bio-assays. *J Micromech Microeng*. 2011;**21**(5):054026. doi:10.1088/0960-1317/21/5/054026
51. Vashist SK, Luong JHT. Point-of-care technologies enabling next-generation healthcare monitoring and management. *Springer Cham*. 2019;1–225.doi:10.1007/978-3-030-11416-9_1
52. Tong R, Zhang L, Song Q, Hu C, Chen X, Lou K, *et al.* A fully portable microchip real-time polymerase chain reaction for rapid detection of pathogen. *Electrophoresis*. 2019;**40**(12–13):1699–1707. doi:10.1002/elps.201900090
53. Kopp MU, De Mello AJ, Manz A. Chemical amplification: continuous-flow PCR on a chip. *Science*. 1998;**280**(5366):1046–1048. doi:10.1126/science.280.5366.1046
54. Yamanaka K, Saito M, Kondoh K, Hossain MM, Koketsu R, Sasaki T, *et al.* Rapid detection for primary screening of influenza A virus: Microfluidic RT-PCR chip and electrochemical DNA sensor. *Analyst*. 2011;**136**(10):2064-2068. doi: 10.1039/C1AN15066A
55. Fronczek CF, Yoon J-Y. Biosensors for monitoring airborne pathogens. *J Lab Autom*. 2015;**20**(4):390–410. doi:10.1177/2211068215580935
56. Huang F, Zhang Y, Lin J, Liu Y. Biosensors Coupled with Signal Amplification Technology for the Detection of Pathogenic Bacteria: A Review. *Biosensors*. 2021;**11**(6):190. doi:10.3390/bios11060190
57. Nguyen PQM, Wang M, Ann Maria N, Li AY, Tan HY, Xiong GM, *et al.* Modular micro-PCR system for the onsite rapid diagnosis of COVID-19. *Microsystems Nanoeng*. 2022;**8**(1). doi:10.1038/s41378-022-00400-3
58. Birnbaumer GM, Lieberzeit PA, Richter L, Schirhagl R, Milnera M, Dickert FL, *et al.* Detection of viruses with molecularly imprinted polymers integrated on a microfluidic biochip using contact-less dielectric microsensors. *Lab Chip*. 2009;**9**(24):3549–3556. doi:10.1039/B914738A
59. Cui B, Liu P, Liu X, Liu S, Zhang Z. Molecularly imprinted polymers for electrochemical detection and analysis: Progress and perspectives. *JMR&T*. 2020;**9**(6):12568–12584. doi:10.1016/j.jmrt.2020.08.052
60. Tai D-F, Lin C-Y, Wu T-Z, Huang J-H, Shu P-Y. Artificial receptors in serologic tests for the early diagnosis of dengue virus infection. *Clin Chem.* 2006;**52**(8):1486–1491. doi:10.1373/clinchem.2005.064501
61. Vasapollo G, Sole R Del, Mergola L, Lazzoi MR, Scardino A, Scorrano S, *et al.* Molecularly imprinted polymers: Present and future prospective. *Int J Mol Sci*. 2011;**12**(9):5908-5945. doi:10.3390/ijms12095908
62. Piletsky S, Canfarotta F, Poma A, Bossi AM, Piletsky S. Molecularly imprinted polymers for cell recognition. *Trends Biotechnol.* 2020;**38**(4):368–387. doi:10.1016/j.tibtech.2019.10.002
63. Malik AA, Nantasenamat C, Piacham T. Molecularly imprinted polymer for human viral pathogen detection. *Mater Sci Eng C*. 2017;77:1341–1348. doi:10.1016/j.msec.2017.03.209
64. Jiang H, Jiang D, Shao J, Sun X. Magnetic molecularly imprinted polymer nanoparticles based electrochemical sensor for the measurement of Gram-negative bacterial quorum signaling molecules (N-acyl-homoserine-lactones). *Biosens Bioelectron*. 2016;75:411–419. doi:10.1016/j.bios.2015.07.045
65. Ferreira NS, Moreira APT, de Sá MHM, Sales MGF. New electrochemically-derived plastic antibody on a simple conductive paper support for protein detection: Application to BSA. *Sensors Actuators B Chem.* 2017;243:1127–1136. doi:10.1016/j.snb.2016.12.074
66. Wangchareansak T, Thitithanyanont A, Chuakheaw D, Gleeson MP, Lieberzeit PA, Sangma C. A novel approach to identify molecular binding to the influenza virus H5N1: Screening using molecularly imprinted polymers (MIPs). *Medchemcomm*. 2014;**5**(5):617–621. doi: 10.1039/C3MD00272A
67. Raziq A, Kidakova A, Boroznjak R, Reut J, Öpik A, Syritski V. Development of a portable MIP-based electrochemical sensor for detection of SARS-CoV-2 antigen. *Biosens Bioelectron*. 2021;178:113029. doi: 10.1016/j.bios.2021.113029.
68. Lowdon JW, Diliën H, Singla P, Peeters M, Cleij TJ, van Grinsven B, *et al.* MIPs for commercial application in low-cost sensors and assays–An overview of the current status quo. *Sensors Actuators B Chem.* 2020;325:128973. doi: 10.1016/j.snb.2020.128973
69. Manickam P, Pasha SK, Snipes SA, Bhansali S. A reusable electrochemical biosensor for monitoring of small molecules (cortisol) using molecularly imprinted polymers. *JES*. 2016;**164**(2):B54. doi: 10.1149/2.0781702jes
70. Rosenberg E, DeLong EF, Thompson F, Lory S, Stackebrandt E. The prokaryotes: Human microbiology. *Springer*. 2013;1–554. doi: 10.1007/978-3-642-30144-5
71. Mi F, Guan M, Hu C, Peng F, Sun S, Wang X. Application of lectin-based biosensor technology in the detection of foodborne pathogenic bacteria: A review. *Analyst*. 2021;**146**(2):429–443. doi: 10.1039/D0AN01459A
72. Krivan HC, Roberts DD, Ginsburg V. Many pulmonary pathogenic bacteria bind specifically to the carbohydrate sequence GalNAcβ1-4Gal found in some glycolipids. *PNAS* 1988;**85**(16):6157–6161. doi: 10.1073/pnas.85.16.6157
73. Thomas RJ. Receptor mimicry as novel therapeutic treatment for biothreat agents. *Bioeng Bugs.* 2010;**1**(1):17–30. doi: 10.4161/bbug.1.1.10049
74. Masarova J, Dey ES, Danielsson B. Optical lectin based biosensor as tool for bacteria identification. *Polish J Microbiol*. 2004;**53**(SUPPL.):23–7.
75. Jyoti A, Tomar RS. Detection of pathogenic bacteria using nanobiosensors. *Environ Chem Lett*. 2017;**15**(1):1–6. doi: 10.1007/s10311-016-0594-y
76. Vishweswaraiah RH, Tenguria S, Chandrasekhar B, Harshitha CG, Gandhi K, Kumar N, *et al.* Monitoring of Microbial Safety of Foods Using Lectins: A Review. *JFST*. 2022;**2**(April):1–11. doi: 10.3389/frfst.2022.842063
77. Parisi OI, Francomano F, Dattilo M, Patitucci F, Prete S, Amone F, *et al.* The Evolution of Molecular Recognition: From Antibodies to Molecularly Imprinted Polymers (MIPs) as Artificial Counterpart. *J Funct Biomater*. 2022;**13**(1):12. doi: 10.3390/jfb13010012
78. Kim ER, Joe C, Mitchell RJ, Gu MB. Trends in Biotechnology Biosensors for healthcare : current and future perspectives. *Trends Biotechnol*. 2023;**41**(3):374–395. doi: 10.1016/j.tibtech.2022.12.005
79. Ren J, He F, Yi S, Cui X. A new MSPQC for rapid growth and detection of Mycobacterium tuberculosis. *Biosens Bioelectron.* 2008;**24**(3):403–409. doi: 10.1016/j.bios.2008.04.018

80. Noi K, Iijima M, Kuroda S, Ogi H. Ultrahigh-sensitive wireless QCM with bio-nanocapsules. *Sensors Actuators B Chem*. 2019;293:59–62. doi: 10.1016/j.snb.2019.04.150
81. Nidzworski D, Pranszke P, Grudniewska M, Król E, Gromadzka B. Universal biosensor for detection of influenza virus. Biosens Bioelectron. 2014;59:239–242. doi: 10.1016/j.bios.2014.03.050
82. Shen F, Tan M, Wang Z, Yao M, Xu Z, Wu Y, *et al.* Integrating silicon nanowire field effect transistor, microfluidics and air sampling techniques for real-time monitoring biological aerosols. *ACS*. 2011;**45**(17):7473–7480. doi: 10.1021/es1043547
83. Jing W, Jiang X, Zhao W, Liu S, Cheng X, Sui G. Microfluidic platform for direct capture and analysis of airborne mycobacterium tuberculosis. *Anal Chem*. 2014;**86**(12):5815–5821. doi: 10.1021/ac500578h
84. Myatt TA, Johnston SL, Rudnick S, Milton DK. Airborne rhinovirus detection and effect of ultraviolet irradiation on detection by a semi-nested RT-PCR assay. *BMC Public Health*. 2003;3:1–7. doi: 10.1186/1471-2458-3-5
85. Agranovski IE. Personal sampler for viable airborne microorganisms: Main development stages. *Clean*. 2007;**35**(1):111–117. doi: 10.1002/clen.200600020
86. Usachev E V., Agranovski IE. Internally controlled PCR system for detection of airborne microorganisms. *J Environ Monit.* 2012;**14**(6):1631-1637. doi: 10.1039/C2EM30019B
87. Inami H, Tsuge K, Matsuzawa M, Sasaki Y, Togashi S, Komano A, *et al.* Semi-automated bacterial spore detection system with micro-fluidic chips for aerosol collection, spore treatment and ICAN DNA detection. *Biosens Bioelectron.* 2009;**24**(11):3299-3305. doi: 10.1016/j.bios.2009.04.025
88. J Jiang X, Jing W, Zheng L, Liu S, Wu W, Sui G. A continuous-flow high-throughput microfluidic device for airborne bacteria PCR detection. *Lab Chip*. 2014;**14**(4):671–676. doi: 10.1039/C3LC50977J
89. Lu CH, Zhang Y, Tang SF, Fang Z Bin, Yang HH, Chen X, et al. Sensing HIV related protein using epitope imprinted hydrophilic polymer coated quartz crystal microbalance. *Biosens Bioelectron*. 2012;**31**(1):439–444. doi: 10.1016/j.bios.2011.11.008
90. Klangprapan S, Choke-arpornchai B, Lieberzeit PA, Choo wongkomon K. Heliyon Sensing the classical swine fever virus with molecularly imprinted polymer on quartz crystal microbalance. *Heliyon*. 2020;**6**(6):e04137. doi: 10.1016/j.heliyon.2020.e04137
91. Matos R, Fonseca KL, Mereiter S, Maceiras AR, Gomes J, Vilaplana C, *et al*. Mycobacterium tuberculosis infection up-regulates sialyl lewis x expression in the lung epithelium. *Microorganisms*. 2021;**9**(1):1–14. doi: 10.3390/microorganisms9010099
92. Krivan HC, Ginsburg V, Roberts DD. Pseudomonas aeruginosa and Pseudomonas cepacia isolated from cystic fibrosis patients bind specifically to gangliotetraosylceramide (asialo GM1) and gangliotriaosylceramide (asialo GM2). *ABB*. 1988;**260**(1):493–496. doi: 10.1016/0003-9861(88)90473-0
93. Cundell DR, Gerard C, Idanpaan-Heikkila I, Tuomanen EI, Gerard NP. PAF receptor anchors Streptococcus pneumoniae to activated human endothelial cells. *Adv Exp Med Biol*. 1997;416:89–94.doi: 10.1007/978-1-4899-0179-8_16
94. Brennan MJ, Hannah JH, Leininger E. Adhesion of Bordetella pertussis to sulfatides and to the GalNAcβ4Gal sequence found in glycosphingolipids. *J Biol Chem*.1991;**266**(28):18827–18831.doi:10.1016/S0021-9258(18)55138-3
95. Van Alphen L, Eijk P, Geelen-Van Den Broek L, Dankert J. Immunochemical characterization of variable epitopes of outer membrane protein P2 of nontypeable Haemophilus influenzae. *Infect Immun*. 1991;**59**(1):247–252. doi: 10.1128/iai.59.1.247-252.1991
96. Suzuki Y, Nagao Y, Kato H, Suzuki T, Matsumoto M, Murayama J ichiro. The hemagglutinins of the human influenza viruses A and B recognize different receptor microdomains. *BBA Biomembr*. 1987;**903**(3):417–424. doi: 10.1016/0005-2736(87)90048-4
97. Thomas R, Brooks T. Common oligosaccharide moieties inhibit the adherence of typical and atypical respiratory pathogens. *J Med Microbiol*. 2004;**53**(9):833–840. doi: 10.1099/jmm.0.45643-0
98. Nguyen K, Chakraborty S, Mansbach RA, Korber B, Gnanakaran S. Exploring the Role of Glycans in the Interaction of SARS-CoV-2 RBD and Human Receptor ACE2. *Viruses*. 2021;**13**(5):927. doi: 10.3390/v13050927
99. Li W, Hulswit RJG, Widjaja I, Raj VS, McBride R, Peng W, *et al.* Identification of sialic acid-binding function for the Middle East respiratory syndrome coronavirus spike glycoprotein. *PNAS*. 2017;**114**(40):E8508-E8517. doi: 10.1073/pnas.1712592114