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Chapter 18

Electrochemical virus detections with nanobiosensors

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Abbreviations

| Abbreviation | Description |
|--------------|-------------|
| Au           | gold        |
| AuNPs        | gold nanoparticles |
| Au@Pd/MoS²@MWCNTs | gold@palladium nanoparticles loaded by molybdenum disulfide functionalized multiwalled carbon nanotubes |
| bi-MBs       | bifunctional magnetic nanobeads |
| CIMC         | carbon nanotubes—iron oxides magnetic composites |
| CNTs         | carbon nanotubes |
| Cu-apoferritin | apoferritin-encapsulated Cu |
| CuNPs        | copper nanoparticles |
| GO           | graphene oxide |
| GQDs         | graphene quantum dots |
| HAU          | hemagglutination units |
| HBV          | Hepatitis B virus |
| HIV          | human immunodeficiency virus |
| HPV          | Human papillomavirus |
| MWCNT        | multiwalled carbon nanotubes |
| PANi–MWCNT   | polyaniline–multiwalled carbon nanotube |
| PFU          | plaque forming units |
| rGO          | reduced graphene oxide |
| SWCNTs       | single-walled carbon nanotubes |
| TCID₅₀       | 50% tissue culture infective dose |
18.1 Introduction

18.1.1 Viruses

Viruses can be regarded as simple structures, which have genetic information (genome) and can replicate themselves through hosts [1]. These are small intracellular agents that contain only one type of nucleic acid (RNA or DNA) and are not replicated outside the host cell. Viruses cannot replicate on their own. However, it is a compulsory intracellular parasite because it can replicate in a host cell. When they cannot find a host cell, it is transformed into a crystalline structure and can remain for a long time. The genetic materials of the viruses called genome may consist of single- or double-stranded DNA or RNA. The genetic existence of viruses, which is either DNA or RNA, is surrounded by a sheath made of a protein called capsid. Therefore viruses are composed of nucleoproteins [2] and replication process of viruses that takes place in a host is exceptional for retroviruses [3]. For example, the genome of human immunodeficiency virus (HIV) has RNA, but after an interaction with a host cell, it creates a DNA copy [3]. Viruses replicate themselves using the host cell’s metabolism and may mutate during copying. The mutation causes an increase in genetic diversity. Thus viruses can easily adapt to different environmental conditions. As was mentioned earlier, a virus uses host cells to create viral proteins and new virus particles; those new particles are named as virions, which leave the host cell and can infect other cells [1]. Bacteriophage is a type of virus which infects bacteria [1]. Viruses do not have an enzyme system. In their structure, digestive enzymes can only be found to dissolve the membrane of the cell (host cell) into which they will enter. Viruses are not affected by antibiotics because they do not have enzyme systems [4,5]. There are wide varieties of virus families that are related to different human diseases, for example, Herpesviridae, Parvoviridae, and Adenoviridae that are DNA viruses, and Retroviridae, Astroviridae, and Rhabdoviridae that are RNA viruses [6].

18.1.2 Effects of viruses

Viruses can infect all types of the life forms. Viral infections have been shown to be the cause of an acute disease that does not require hospitalization in developed countries and the cause of death and permanent disability among developing countries, especially among infants and children. For instance, varicella-zoster virus, which is a member of Herpesviridae family, causes chickenpox disease generally in children and herpes zoster in adults [6]. Viruses as well as viral infections can be transferred between people directly, but also contaminated water and/or food consumption is another way for infection [7]. Viral gastroenteritis, considered the cause of deaths of almost 1 million children under 5 years of age every year, is a very common foodborne infection [7]. On the other hand, the transmission of Hepatitis B virus (HBV) is only possible with the contact with body fluids of an infected person [8]. Viruses infect not only humans but also plants and animals. Citrus tristeza virus which is a member of Closteroviridae family infects citrus species and can cause serious diseases in trees that result with fruit loss and death of citrus trees [9]. Rabies virus from Rhabdoviridae family is a causing agent for rabies which is a zoonotic disease (a disease that can be transferred from animals into humans), and it is considered a serious risk to human and animal health by World Health Organization (WHO) [10]. Some data suggest that the broad spectrum of already established viral diseases can be extended to involve other serious human diseases, such as juvenile diabetes, rheumatoid arthritis, various neurological and immunological disorders, and some tumors [11].

18.1.3 Methods used for the determination of viruses

Many techniques have been developed to identify viral samples. The most common conventional methods for detecting viruses are time-consuming, expensive, often poor reproducible and required specialist facilities, and trained personnel. Simple instrumentation, the rapid and low-cost detection of viruses, in this case, is of great interest because such a method can expose the threat quickly before spreading.

The most commonly used methods for measuring viruses can be divided into broad categories in the following subsections.

18.1.3.1 Measurement of viral proteins and nucleic acid

Polymerase chain reaction (PCR): PCR is a very important method in molecular biology and biotechnology. It allows increasing extremely small amounts of DNA such as a single gene sequence to a million copies in vitro conditions using enzymes [12,13]. By this means enough amount of DNA is provided for further analyses from a template [13].
In addition to a template DNA, primers, Taq polymerase, nucleotides, and a thermocycler are necessary for PCR process [13]. PCR is a significant technique for not only measuring viral nucleic acids but also for medical diagnosis, plant industry, environmental studies, and gene therapy [13]. PCR is one of the most commonly used methods for the detection of viral nucleic acids. Using PCR, we can determine the identity and/or quantity of viral genomes of virions and infected cells [12,14]. PCR, as a sensitive method, allows searching multiple possible viruses in samples and recognizing virus groups through common sequences [14]. Despite all those advantages, it is really hard to prevent patient samples which will be used for diagnostic PCR analysis from contamination and that can be considered a setback [14].

PCR analysis, also known as reverse transcription PCR (RT-PCR), can also be used to identify viral RNA by adding an initial step in which RNA is converted to DNA [15]. Reverse transcription is carried out by using an enzyme called reverse transcriptase [16]. This conversion step is important because it provides obtaining a DNA more stable than RNA and not easily denatured like RNA for PCR process [16].

Immunoblotting: Immunoblotting, also known as Western blotting, is used for identifying proteins and protein on a membrane, and protein concentration changes in samples with antibodies [17]. The immunoblotting technique determines specific viral proteins insulated from a cell, tissue, organ, or body fluid. With immunoblotting method the infection stage of patient can be determined depending on which antibody is developed against which antigen [12]. Although the difficulty and cost of interpreting the results of immunoblotting results in a decrease in the overall use of this technique, immunoblots are still widely used for diagnostic and research purposes [12,18].

Immunoprecipitation (IP): IP is the method of precipitating a protein antigen out of solution using an antibody that specifically binds to that specific protein. This technique can be used to isolate and concentrate a particular protein from a sample containing thousands of different proteins [19]. It is a helpful method because it provides purification of viruses which cannot be purified with standard methods, and it also allows quick purification of intact virions from small tissues for transmission electron microscopy (TEM) analysis [20]. Nevertheless, virus-specific antibodies are essential for IP and that can be considered a disadvantage [20].

Enzyme-linked immunosorbent assay (ELISA): Immunoassays, the most popular type of which is ELISA, provide quantification and identification of various antigens [21]. ELISAs involve simple enzyme assays with specificity of antibodies using antigens or antibodies linked to an easily assayed enzyme. The basic principle of ELISA technique is radioimmunoassay process that involves a tagged antibody in order to detect antigens [14,21]. An enzyme bound with a substrate, a fluorescent molecule, or a radioactive isotope can be described as the tag [14]. ELISA has been used in various fields such as environmental studies in order to detect pollutants, food industry in order to detect toxins or allergens, and medical studies in order to detect pharmaceuticals, disease markers [22]. When we approach ELISA in terms of viruses, it can provide the detection of a virus or an antibody from a sample of a patient infected by viruses [14]. The quantity of viruses from a cell culture/sample or a specific antibody to a specific viral pathogen can be detected using ELISA [14]. Those studies are very crucial for diagnostics [22]. ELISA is a much faster method than immunoblotting to detect a specific viral protein. These are considered highly sensitive methods that can detect very low amounts of protein. On the other hand, ELISA tests can sometimes be quite expensive due to the cost of reagents being used [23]. Direct ELISA, indirect ELISA, sandwich ELISA, and competitive ELISA are the different types of ELISA tests which are used for different scientific fields [14,21,22].

Hemagglutination assay (HA): Basically, hemagglutination can be described as the aggregation of red blood cells (RBCs) due to the presence of hemagglutinating agents such as viruses [24]. Some viruses, such as influenza virus, rabies virus, rubella virus, mumps virus, and measles virus, have hemagglutinin surface proteins that attach to surface glycoproteins of RBCs [25]. HA is a method which relies on the fact that many viruses contain proteins that can bind and agglutinate RBCs. The principle of this assay is simple; however, sample preparation is considered laborious and presents some drawbacks [26]. HA is one of the most widely used techniques in order to detect the presence and quantity of viruses in various samples [24,25]. However, it cannot give information about the level or measure of viral infectivity [24]. HA is also used for detecting the antibody levels against specific viruses in patient samples. The presence of specific antibodies will prevent the hemagglutination of RBCs by binding the viruses [25]. The results of HAs are given as hemagglutination unit (HAU) [27]. In an assay, in various samples, the amount of viruses in the one that can agglutinate all RBCs is described as 1 HAU [27].

18.13.2 Direct counting of viral particles

Flow cytometry (FCM): FCM is a commonly used technique in biology, microbiology, virology, and immunology [28]. FCM technique involves investigating cells, cell populations, and antigens from human samples such as several body fluids [28,29]. Nowadays, with current technological improvements, FCM method provides the determination of
particles that have sizes ranging from 100 to 1000 nm such as viruses/viral particles [28]. FCM has become an important device in virology, due to its applications in viral replication and viral—cell interactions, as well as its capacity to quantify proteins [30,31]. FCM is used for the diagnosis of viral diseases [29].

Transmission electron microscopy: TEM which is a significant method for diagnostic area can be described as a microscopy technique in which electrons pass through various samples and compose an image of the sample [32]. It allows showing very small materials and due to that, it is used in medical sciences, virology, physical sciences, etc. [32,33]. Viruses are very small, and most of them can only be viewed by TEM. Therefore TEM has made significant contributions to virology such as the discovery of many viruses, diagnosis of various viral infections, and basic research of virus—host cell interactions [34]. Despite being a relatively quicker method and providing qualitative and quantitative information about virions, as a disadvantage, this method has a high detection limit and can only be applied to high virus concentrations ($\geq 10^7$ particles/mL) [33].

18.1.3.3 Methods of virus identification

Microscopy in cell culture: Cell culture means growing living cells outside of living organisms in controlled conditions [25]. In order to produce a cell culture the most significant thing is doing all the work under sterile conditions [14]. First step of producing a cell culture is removing and mincing the required tissue. After that, different enzymes such as collagenase are applied to the tissue for degradation of extracellular matrix and releasing cells. Then centrifugation step is applied. Later, cells and growth media are combined with culture dishes and contained in an incubator with humidity, 37°C temperature and 5% CO$_2$. Lastly, cells grow and divide by linking to the dish [14]. Cell culture-based virus isolation has been accepted as a “gold standard” in the detection and identification of viruses and is the technique by which all other test methods have been compared [35].

Immunofluorescence assay (IFA): IFA is a diagnostic technique that uses the interaction between viruses and specific antibodies [14,25]. IFA can be considered a relatively quick method, and it is easy to apply without special technicians, it provides the certain identification of the virus [25]. It is one of the commonly used techniques for the rapid detection of virus infections by identifying virus antigens. IFA staining usually gives very rapid, sensitive, and specific virus identification in about 1—2 hours. Unfortunately, the IFA technique may not be able to verify the identity of all virus strains and may be quite expensive due to the cost of the antibodies used [36]. Before the availability of ELISA tests, IFA was used for diagnostics, but now it is only used for research studies [27].

18.1.3.4 Measurement of viral infectivity

Viral plaque assay: Viral plaque analysis is one of the most commonly used methods in virology to determine viral titer, and this technique is thought to be effective only for viruses that can infect single-celled cells and replicate cells. With this method, it is possible to determine infectious dose; in other words, the quantitative amount of infectious virus particles [27,37]. The results are expressed as plaque forming units (PFU) [27]. This method usually requires 4—10 days depending on the virus being analyzed and is considered time-consuming [38]. Viral plaque assay results can change depending on the assay conditions and the PFU results that were found may not always show the certain amount of infectious viral particles [37].

Quantal assays—TCID$_{50}$, LD$_{50}$, EID$_{50}$. Procedures, such as TCID$_{50}$, LD$_{50}$, and EID$_{50}$ assays, are used to determine the infectious titer of virus types that can cause cytopathic effects in tissue culture over a period of 5—20 days.

Immunofluorescence foci assay: The immunofluorescence foci assay is a quick method of virus titration that allows the measurement of virus in cell lines, which does not promote plaque occurrence or do not exhibit detectable cytopathic effect (CPE) [39].

18.1.4 Electrochemical studies and advantages

The purpose of this review is to discuss the methods used to detect viruses and to summarize the studies on electrochemical nanobiosensors. Rapid assessment of pathogenicity and virulence is the key to taking appropriate health measures in outbreaks. The most important precondition for the fight against viruses is the early isolation and detection of the presence of viral nucleic acid. In conventional methods for detecting viruses, equipment and personnel are required, and furthermore, the diagnosis of infection takes longer. Given these challenges, it is important to find rapid methods for detecting the virus in an easy, inexpensive, sensitive, and selective way in the environment, body fluids, and tissues.

The use of nanoparticles (NPs) in combination with electrochemical detection is promising in detecting viruses. The biosensor is an analytical device used for the detection of analytes that combine a biological component with a
physicochemical detector [40]. A biosensor may be defined as an analytical device comprising a transducer portion and a biological element [41—43]. Compared to conventional techniques, electrochemical nanobiosensors are faster, practical, precise, selective, and economical. The NP-based biosensor has high specificity and can easily be used, having low cost and precision required for rapid and reproducible detection of pathogenic microorganisms in clinical specimens [44—46].

18.2 The most observed viruses in humans

Viral diseases continue to be one of the most important causes of morbidity and premature death in the human population worldwide. In addition, there is a constant threat of the emergence of new viruses that affect us [47,48]. Viruses that cause major diseases in humans are as follows:

**Blood and lymphoid system**: Herpesvirus, Paramyxovirus, Parvovirus, Retrovirus  
**Eye**: Adenovirus, Herpesvirus  
**Fetus (infection in utero)**: Herpesvirus, Togavirus  
**Gastrointestinal tract**: Adenovirus, Astrovirus, Calicivirus, Reovirus  
**Genital tract**: Herpesvirus, Papillomavirus  
**Heart**: Picornavirus  
**Liver**: Picornavirus, Hepadnavirus, Flavivirus  
**Multisystem/hemorrhagic fevers**: Arenavirus, Bunyavirus, Filovirus, Flavivirus  
**Nervous system**: Bunyavirus, Flavivirus, Herpesvirus, Paramyxovirus, Picornavirus, Rhabdovirus  
**Respiratory tract**: Adenovirus, Coronavirus, Orthomyxovirus, Paramyxovirus, Picornavirus  
**Skin**: Herpesvirus, Papillomavirus  
**Testes**: Paramyxovirus

**Herpesvirus**: Herpesviruses are one of the most well-known viruses among all because they can cause infections for a wide variety of animals from birds to humans [49,50]. The virions of herpesviruses are enveloped, spherical and have double-stranded DNA [51]. Herpesviruses can affect skin, nervous system, genital tract, etc. and cause several well-known diseases in humans such as chickenpox, genital herpes, and cold sore [49,50]. Moreover, they are also related with human cancers such as nasopharyngeal carcinoma and lymphoma (Epstein—Barr virus; a species of Herpesvirus) [50]. Those are the types of Herpesviruses that cause infections in humans: *Rhabdovirus* also known as Kaposi’s sarcoma herpes virus that infects B lymphocytes and epithelial cells and causes lymphoma and sarcoma; *Simplex virus* also known as Herpes simplex virus that infects epithelial cells and causes genital and oral herpes; *Varicellovirus* also known as Varicella-zoster virus that infects epithelial cells and causes chickenpox; *Cytomegalovirus* that infects epithelial cells, monocytes, endothelial cells and causes congenital defects; *Lymphocryptovirus* also known as Epstein—Barr virus that infects B lymphocytes and epithelial cells and causes Burkitt’s lymphoma, Hodgkin’s lymphoma, and nasopharyngeal carcinomas [49,52].

**Paramyxovirus**: Paramyxovirus virions are enveloped, spherical with viral RNA [53]. They are responsible for wide variety of diseases in human beings ranging from mumps and measles to aseptic meningitis [54,55]. In addition to this, Canine morbillivirus that is a member of Paramyxoviridae causes canine distemper disease in some animals [54]. Primary viruses from Paramyxoviridae that infects humans are given next: mumps virus is responsible for mumps disease that is characterized by parotitis and can be very serious in the adulthood. Newcastle disease virus is the cause of virulent Newcastle disease which affects avian species but also it can transmit to humans [53]. Measles virus is an extremely contagious virus which is responsible for measles disease that affects skin, respiratory, and immune systems [56]. The virus infects immune and epithelial cells and measles symptoms are often confused with common cold [56]. Nowadays, there are vaccines available against most of the Paramyxoviruses such as measles, mumps, canine distemper, and Newcastle disease [54].

**Parvovirus**: Parvoviruses are one of the smallest viruses of all with an enveloped and icosahedral virion that has single-stranded DNA [57,58]. They can affect a wide variety of creatures ranging from humans to mice and mosquitoes [57]. Adeno-associated virus is considered the prototype of parvoviruses, and it infects humans but does not cause any diseases, only mild infections [57]. In other respects, Adeno-associated virus is used as therapeutic gene delivery vector [58]. B19 virus is a parvovirus which is the cause of erythema infectiosum that infects erythrocytes in children [57]. Minute virus of mice infects T lymphocytes of mice and causes very infectious disease especially in laboratory mice [59,60]. Canine parvovirus is the reason of gastroenteritis which is a fatal disease for dogs [57]. Human bocavirus is a
parovirus that infects humans and causes respiratory infections with mild symptoms, especially in summertime. It was first isolated both in bovine and canine [57].

Retrovirus: Retrovirus virions are enveloped with RNA that plays a role as a template for synthesis of double-stranded DNA and that is the origin of “retro” name of virus [61]. Retroviruses are related with transmissible cancers, for example, HIV [61]. Avian leucosis virus uses chickens as hosts, and this infection can result with tumors in lymphoid [62]. Nowadays, it is still a serious threat for poultry industry, in addition to this, researches about the interaction between avian leucosis virus and immune system are really promising for the prevention and treatment of human retroviral diseases such as acquired immune deficiency syndrome (AIDS) [63]. HIV is the cause of AIDS which was first notified in 1981, and it is associated with Kaposi’s sarcoma, non-Hodgkin’s lymphoma, and invasive cervical cancer [62,64]. With current vaccination and antiviral drug therapy, it is possible to protect from infection and prevent the progress of disease [62]. Human T-cell leukemia virus which is a RNA virus infects mainly T-cells and causes an endemic disease. It is also related with T-cell tumors [61].

Adenovirus: Adenovirus is an icosahedral, nonenveloped tumor virus with a double-stranded DNA [65,66]. Adenovirus was first isolated from adenoid tissue of a human [65]. Human adenovirus with its subgroups of A, C, and E causes infections with mild symptoms such as respiratory infections, gastroenteritis, and conjunctivitis in humans [65,66]. In addition to these, adenoviruses cause tumor in rodents but not in humans because when an adenovirus infects a human, the virus can complete its full life cycle in order to create a new virus [66]. But in rodents, such as mice, the virus cannot complete its life cycle at the late phase and that results with cell transformation [66].

Togavirus: Togaviruses are small, icosahedral, enveloped viruses with single-stranded RNA genome [57,67]. *Sindbis virus* and *Semliki Forest virus* from Togaviruses which can infect birds and rodents are not serious pathogens for humans, but they are significant veterinary pathogens. Among all togaviruses, only Rubella virus causes an important infection in humans, which is German measles [57,67]. Transmission of togaviruses occurs with mosquitoes [57,67]. *Chikungunya virus* is a novel virus that uses primates and mosquitoes as hosts and causes fever, arthritis, and rash in humans [57]. Its geographical distribution involves Africa, India, and Southeast Asia [67]. *Venezuelan equine encephalitis virus* (VEEV) is a zoonotic virus whose hosts are birds, horses, mosquitoes, and humans [57,67]. VEEV causes fever and encephalitis in humans, and its transmission cycle consists of mosquito—horse—mosquito and spreads throughout humans [57,67].

Astrovirus: Astroviruses from Astroviridae family have nonenveloped, icosahedral, single-stranded RNA virions [68]. First observation of Astroviruses goes back to 1975; they were found in the feces of infants with diarrhea [68,69]. After that, with the improvement in the identification methods for viruses such as immunoassays and PCR, they have been described as the most common viral gastroenteritis (community or hospital acquired) agent in children younger than 2 years of age after rotavirus and calicivirus [68–70]. Astroviruses are transmitted by the fecal–oral route, and their infections are not common in adults [69]. Astroviruses-related gastroenteritis causes only mild symptoms, and it can be treated with hydration and electrolyte replacement without further medical treatment [70].

Calicivirus: Caliciviruses from family of Caliciviridae are small, icosahedral, nonenveloped, and single-stranded RNA viruses, which were first identified using immunoelectron microscopy in 1972 [71]. Nowadays, caliciviruses are considered the primal causing agent of gastroenteritis with astroviruses and rotaviruses [71]. They can affect both adults and younger children and cause severe childhood diarrhea [71].

Rotavirus: Rotaviruses are large, icosahedral, nonenveloped, single-stranded RNA viruses, and they are members of Reoviridae family [57]. First observation and identification of rotavirus was in young children with gastroenteritis in 1973 by electron microscopy [72]. They are the leading agent of gastroenteritis that especially occurs in winter in the children under 5 years of age worldwide [57]. Rotavirus infections cause vomiting and diarrhea which result with dehydration, if not treated carefully, it can prove fatal for children [57]. Currently, Rotarix and RotaTeq are available rotavirus vaccines; nonetheless, there are no therapeutic antiviral drugs against rotavirus infection [72].

Papillomavirus: Papillomaviruses are small, nonenveloped, icosahedral, double-stranded DNA viruses from Papillomaviridae family [73,74]. Their first identification goes back to the 1930s [75]. They can affect a wide variety of creatures from humans to monkeys and rabbits [73]. In humans, they infect genital tract causing cervical and vaginal cancers, respiratory tract, eye, mouth, and skin causing skin warts and skin cancer [75]. Human papillomavirus (HPV) is a carcinogenic virus that can be mucosal or cutaneous [73]. Gardasil and Cervarix are available HPV vaccines for prophylaxis [73]. For the clinical diagnosis of HPV infections, Pap smear procedure is used, which examines HPV-related changes and malignancies in cells. Routine screening is really important for early diagnosis and treatment [75].

Picornavirus: Picornavirus is a small, nonenveloped, icosahedral RNA virus, which belongs to Picornaviridae family [76]. They can affect both animals and humans, picornavirus infections may be related with gastrointestinal tract, respiratory tract, muscles, and neuronal tissues [77]. Foot and mouth disease virus infects livestock such as cows, goats,
sheep, etc. and causes foot and mouth disease by affecting epithelial cells [77]. Encephalomyocarditis is a disease which is caused by encephalomyocarditis virus (EMCV). EMCV infects heart and central nervous system in humans [77]. Poliovirus is one of the first human viruses, the structure of which was examined by X-ray crystallography [76]. It is the causative agent of poliomyelitis in humans which is a paralytic disease resulting from the destruction of neurons in the spinal cord [77]. Rhinovirus infects upper and lower airway tract in humans and causes colds and respiratory diseases [76,77]. Hepatitis A virus was first identified as the agent of hepatitis A in 1973 [76]. It infects parenchymal cells of liver in humans [76].

**Orthomyxovirus:** Orthomyxoviruses are spherical, enveloped, single-stranded RNA viruses. Influenza viruses A, B, C, and D are the most significant types of orthomyxoviruses, and they cause infections in a wide variety of creatures from humans to birds. While influenza B virus can only infect humans, influenza A virus can infect not only humans but also pigs, horses, whales, seals, etc. In order to make a further categorization, subtypes can be formed based on the hosts of viruses. RT-PCR is the current detection method for the identification of influenza viruses. Influenza virus related influenza symptoms are described as sudden onset of fever, headache, malaise, sore throat, myalgia, and nonproductive cough. However, as a common diagnostic mistake, all respiratory illnesses might be considered as flu. For sensitive and accurate diagnosis of influenza, RT-PCR is used. Influenza viruses affect epithelial cells in the upper and lower respiratory tract, and this infection is extremely contagious due to quick spread potential by coughing and sneezing of infected people. There are two types of available therapeutic antiviral drugs: neuraminidase inhibitors (oseltamivir and zanamivir) and drugs related with the interference of the function of viral envelope (amantadine and rimantadine). There are also prophylactic live attenuated vaccines such as LAIV4 and FluMist [78,79].

**Coronavirus:** Coronaviruses are large, enveloped, spherical, single-stranded RNA viruses. Majority of coronaviruses are the causative agents of acute/chronic, lethal, zoonotic diseases of respiratory or enteric tracts such as otitis media, severe acute respiratory syndrome (SARS), and Middle East respiratory syndrome (MERS) by infecting epithelial cells. Transmission of SARS and MERS occurs with close contact. RT-PCR is used for diagnostic analysis of coronaviruses [80–82].

**Rhabdovirus:** Rhabdoviruses are long, enveloped, single-stranded RNA viruses from Mononegavirales [83]. Rabies virus and Vesicular stomatitis virus (VSV) are most important rhabdoviruses [83,84]. Even though VSV, which is the causative agent of vesicular stomatitis, a zoonotic disease, is not considered an important pathogen for humans, it has gained significance due to its newly discovered oncolytic activity and possible use for cancer therapy [84]. Rabies virus was first studied by Louis Pasteur in 1885 even before the detailed studies on viruses have started and he developed a postexposure vaccine [85]. Rabies virus is the only significant human pathogen of rhabdoviruses [83,85]. It infects the central nervous system of humans and animals and causes fatal disease, rabies, leading to fatal encephalomyelitis [83]. At the onset of the rabies the symptoms are mild and flu-like, but in the later phases of disease, symptoms get more severe such as paralysis, anxiety, insomnia, and hydrophobia; at this stage the recovery is almost impossible [83]. There are currently available postexposure vaccines for humans, domestic, and wildlife animals [84].

**Hepadnavirus:** Hepadnaviruses are small, spherical, enveloped DNA viruses from Hepadnaviridae family [86]. HBV, as the smallest human DNA virus and the causative agent of acute viral hepatitis with chronic liver disease and hepatocellular carcinoma, is the most important hepadnavirus [86–88]. Transmission route of HBV is through body fluids, such as blood, saliva, and vaginal fluids [87]. Recombinant vaccines for hepatitis B prophylaxis is first injected after birth and then during childhood [87]. Vaccines provide high ratio of protection and immunity against HBV, and they decrease the transmission and prevalence of HBV worldwide [87].

**Flavivirus:** Flaviviruses are enveloped, icosahedral, single-stranded RNA viruses which include Dengue virus (DENV) and hepatitis C virus (HCV) [89,90]. Important flaviviruses that cause infections in humans are listed next: mosquitoes are the transmission agent of yellow fever virus (YFV) to humans [90]. YFV causes hemorrhagic fever with accompanying symptoms, such as vomiting, back pain, and photophobia, and patients to look yellow [89–91]. DENV is classified into four types, and the transmission of all these to humans takes place through mosquitoes [90]. DENV infection results with hemorrhagic fever and dengue shock syndrome [90]. With early diagnosis and accurate treatment, fatality rate can be decreased [90]. Japanese encephalitis virus (JEV) is also transmitted to humans through mosquitoes, such as YFV and DENV, and it is the main cause of encephalitis in Asia [89,90]. Vaccines against JEV are available in Asia and Australia [90]. HCV, which causes acute/chronic hepatitis and liver cancer resulting immunosuppression, was first discovered in 1989 [89]. Ribavirin, sofosbuvir, alpha interferon, and boceprevir are the currently used antiviral drugs for HCV; nonetheless, there is no available preventive vaccine [89]. Zika virus (ZIKV) was first isolated in 1947, but the first ZIKV outbreak took place in 2007. After that, by the end of 2016, ZIKV cases have started to spread rapidly and WHO declared Public Health Emergency of International Concern. General symptoms of ZIKV infections are
vomiting, edema, myalgia, headache, and fever. Researches on the development of vaccines against ZIKV are still an ongoing process [90].

### 18.3 Nanobiosensor

Biosensor-related research has received high attention over the last three decades. Biosensors have some advantages, such as affordable, fast responsive, and easy to operate analytical-friendly techniques. Therefore they present a wide area of detection and diagnosis suited for health-care analysis. Biosensors are commonly defined as analytical devices composed of a biological recognition system [92] and a physicochemical transducer [93]. Biosensors have highly selective properties due to possibility of tailoring the specific interaction of compounds by immobilizing biological recognition elements on the sensor [94]. Typically biosensors comprises three components: a bioreceptor or biological identification component, a signal transducer, and an amplifier [94] (Fig. 18.1).

A biosensor is an analytical device, which converts biological response into a quantifiable and processable signal [96]. Immobilizing a biologically sensitive material on the surface of a biosensor is a new approach in biosensor technology. Bioreceptor elements are generally considered as biomarker, enzymes, microorganism, nucleic acids, tissues, virus, bacteria, and antigens [97]. The most common traditional techniques, such as electrochemical [cyclic voltammetry (CV), amperometric, impedance spectroscopy, potentiometric], optical, and various field-effect transistor-based methods, are described [96,98]. Nanomaterials (NMs) bring new possibilities for the development of electrochemical biosensors. Incorporation of NMs with promising novel approaches in biosensor design provides construction of biosensors and development of novel electrochemical assays [99,100]. In addition, the advanced nanoscale biosensor can be utilized to achieve high sensitivity and selectivity of biological sensing for analytical purposes in various fields of research and technology [92,95]. NMs have great potential due to its promoting electron transfer reactions, high surface area and electrical conductivity, good chemical stability, and mechanical robustness [101]. Moreover, they can be used to enhance electrochemical reaction and promote signal of biorecognition system [100] (Figs. 18.2 and 18.3).

**FIGURE 18.1** The schematic diagram of target analytes, biorecognition elements, and detection of a typical nanobiosensor. Reprinted with permission from R. Shandilya, A. Bhargava, N. Bunkar, R. Tiwari, I.Y. Goryacheva, P.K. Mishra, Nanobiosensors: point-of-care approaches for cancer diagnostics, Biosens. Bioelectron. 130 (2019) 147–165. Available from: https://doi.org/10.1016/j.bios.2019.01.034 [95].
Various NMs, such as magnetic NPs (iron oxide NPs), metal NPs (gold and silver NPs), carbon-based nanotubes and carbon allotropes, nanowire, and quantum dots with different biological recognition elements (enzymes, nucleic acids, antibodies, antigens, peptide), provide many opportunities for enhancing the performance of nanobiosensor [104,105].

The electrochemical nanobiosensors were used in versatile areas of cancer diagnostics and detection of infectious microorganisms, virus, etc. [100].
18.3.1 Substrates

In sensing substrates, molecular recognition processes play a central role in biosensors. Substrates of biosensors enhance the performance of the biosensors. Moreover, the sensing substrates improve the biosensing sensitivity, specificity, stability, and response dynamics [106]. There are three main engineering techniques to construct highly efficient sensing substrates: nanostructured sensing substrates, molecule-mediated interface, and DNA nanostructure—functionalized sensing interface [106]. Nanostructured sensing substrates are generally used for ultrasensitive detection of nucleic acids and proteins. Molecule-mediated interface is especially applied for small molecules.

The biosensors have a wide range of analytes from small molecules to proteins, such as enzymes, antibodies, or oligonucleotides. Biological materials can be immobilized on nanostructured electrodes surface. For example, oligonucleotides are interacted with electron surface for designing biosensors genomic analysis [107].

Immunosensors are based on a working principle—the specific antigen—antibody interaction connected with different transducers. Most of the immunosensors are based on a direct and indirect format and labeled methods. The specific antigens are first immobilized on the electrode surface, and then the analyte (antibody) is added on antigen linked electrode surface. Therefore the specific antigen selectively recognizes and binds the antibody, and the specific antigen—antibody complex can be evaluated using secondary antibody labeled with an enzyme [108].

Electrochemical design of nucleic acids biosensor is closely related to DNA sequencing methods based on genomics [109]. The application of nucleic acids as a bioreceptor manages analysis of RNA/DNA-based biosensors. Moreover, nucleic acid bioreceptors are also employed for detection of pathogens regards to complementary base pairs [110].

Biosensors are advantageous in relation to other PCR product-analysis techniques because they can add speed and precision to the molecular assay and can also perform simultaneous analysis of multiple analytes [111].

18.4 Methods

Biosensors can be mainly classified as optical, electrochemical, and mass spectrometric. Among biosensors, electrochemical biosensors with a volumetric transducer displayed a great potential in the detection of biomolecules [112]. Electrochemical biosensors are widely used for the detection of various analytes because of their rapid response, great sensitivity, simplicity, cost-effective, miniaturization, and portable.

Fabrication of biosensors using the techniques of square wave voltammetry (SWV), CV, and electrochemical impedance spectroscopy (EIS) allows rapid biosensing for different types of analytes.

EIS has enlighten at surface area and interaction modification agents and the electrode surface [113]. Because of occurrence of an electrochemical reaction at the electrode surface upon interaction with target molecule, impedance biosensors have been widely used for the environmental monitoring of disrupting chemicals and drugs, interaction between antibody and antigen, and DNA strains [114]. The EIS measurement studies the dielectric parameters of a biological system in wide frequencies. The EIS provides information about surface adsorption, ion exchange, diffusion, and charge transfer [114].

In another electrochemical technique, quantitative analysis using SWV is one of the most promising mechanisms in the fabrication of biosensors due to their ability to perform more sensitive answer for rapid biosensing when compared to differential pulse voltammetry (DPV) techniques.

In pulse methods the procedures are based on the application of pulse changes of potential, and the current response is measured at a suitable time relative to the time of the pulse [115].

All pulse techniques are based on the difference in the rate of the decay of the charging and the faradaic currents related a potential step or pulse.

The working electrode (WE) represents the fundamental component in electrochemical studies. The most commonly used WE materials are metal electrodes (Pt, Au, Hg, etc.) and carbon electrodes. It can be worked in more negative potential area by using carbon electrodes as well as good anodic potential windows. The most common form of carbon electrode is glassy carbon electrode. Moreover, carbon paste electrodes are also useful in many applications [116].

Siuzdak et al. worked on pathogen-detection methods. The nanocrystalline boron-doped diamond-based electrode (B:NCD) was used as platform of biosensor. The modified material is a highly promising material for the third-generation biosensor due to its chemical inertiess, wide potential window, low background current, biocompatibility, and high stability [117].

H5N1, Avian influenza virus, is determined by different methods such as the immunochromatography, the reverse-transcription PCR (RT-PCR), ELISA, serological methods [9], quartz crystal microbalance, surface plasmon resonance, and fluorescence. However, the electrochemical detection method received high attention because of providing low
| Target                          | Biosensor type       | Nanomaterial                          | LOD                | Linear range                   | Application               | Reference |
|--------------------------------|----------------------|---------------------------------------|--------------------|--------------------------------|---------------------------|-----------|
| Influenza virus M1 protein     | Electrochemical      | Nanocrystalline boron-doped diamond   | $5 \times 10^{-4}$ g/mL | —                              | Saliva                    | [117]     |
| Avian influenza virus           | Voltammetric         | Porous AuNPs                          | 0.15 pM            | 1 pM–100 nM                    | Chicken serum             | [118]     |
| HBV antigen                    | Voltammetric         | Nanoporous gold                       | 0.064 pg/mL        | 1 pg/mL–1 ng/mL                | Human serum               | [124]     |
| Chikungunya virus DNA          | Electrochemical      | Gold shells–coated magnetic nanocubes | 0.1 nM             | 0.1 nM–100 μM                  | Serum                     | [119]     |
| Human enterovirus 71           | Voltammetric         | Dual-labeled magnetic nanobeads       | 0.01 ng/mL         | —                              | —                         | [125]     |
| HBV-genomic DNA                | Voltammetric         | AuNPs                                 | 0.15 ng/μL         | 1.55–6.68 ng/μL                | Blood plasma              | [120]     |
| HBV surface antigen            | Voltammetric         | Fe$_3$O$_4$–Au nanocomposites         | 10 fg/μL           | 0.1–10 000 pg/μL               | Serum                     | [121]     |
| Influenza A virus (relied on neuraminidase activity) | Electrochemical      | Graphene–gold hybrid nanocomposite    | $10^{-8}$ U/mL     | $10^{-8}$–$10^{-1}$ U/mL       | Egg sample               | [45]      |
| HBV DNA                        | Voltammetric         | GQDs                                  | 1 nM               | 10–500 nM                      | —                         | [122]     |
| HPV DNA                        | Electrochemical      | Gold nanotubes                        | 1 fM               | 0.01 pM–1 μM                   | —                         | [114]     |
| Citrus tristeza virus DNA      | Electrochemical      | AuNPs                                 | 100 nM             | 0.1–10 μM                      | Plant sample              | [126]     |
| Avian leukosis virus subgroup J | Voltammetric         | Nanocellulose–Au composite            | $10^{1.98}$ TCID$_{50}$/mL | $10^{2.08}$–$10^{3.0}$ TCID$_{50}$/mL | —                        | [123]     |
| Herpes virus 5 DNA             | Voltammetric         | Zn–Ag nanoblooms                      | 97 copies/mL       | $113$–$10^3$ copies/mL         | Urine                     | [127]     |
| HBV surface antigen            | Photoelectrochemical | AuNPs/ZnAgInS quaternary quantum dots nanocomposite | 0.5 pg/μL         | 0.005–30 ng/μL                  | Clinical serum samples    | [128]     |
| Influenza virus H9N2            | Chronoamperometric   | AuNPs                                 | 16 HAU             | —                              | —                         | [129]     |
| HBV core antigen               | Electrochemical      | AuNPs–rGO                             | 3.8 ng/mL          | 3.91–125 ng/mL                 | Human serum               | [130]     |
| Hepatitis B antigen            | Amperometric         | Au@Pd/MoS$_2$@MWCNTs                  | 26 fg/μL           | 0.1–500 pg/μL                  | Human serum               | [131]     |
| Cotton leaf curl DNA           | Voltammetric         | MWCNTs–CuNPs                          | 0.01 ng/μL         | —                              | —                         | [132]     |
| Khokran virus DNA              | Voltammetric         | GO-AuNPs                              | 0.01 ng/mL         | 0.05–150 ng/mL                 | Human serum               | [133]     |
| HBV surface antigen            | Electrochemical      | Carboxylated CNTs                     | —                  | —                              | Blood and saliva          | [134]     |
| Zika virus-specific antibodies  | Electrochemical      | Boehmite nanoparticles                | 1.9 pM             | 10 pM–1 μM                      | Human serum               | [136]     |
| Dengue virus 2 NS1 antibody     | Electrochemical      | CNTs                                  | $10^{-12}$ g/mL    | $10^{-12}$–$10^{-5}$ g/mL      | Blood plasma              | [135]     |
| Hepatitis C virus RNA           | Amperometric         | Nanoliposomes                         | 1.9 pM             | 10 pM–1 μM                      | Human serum               | [137]     |
| Hepatitis C virus core antigen  | Voltammetric         | Boehmite nanoparticles                | 10 fg/μL           | 0.08–110 pg/μL                  | Human serum               | [137]     |

(Continued)
| Target                                      | Biosensor type          | Nanomaterial                          | LOD            | Linear range         | Application                        | Reference |
|---------------------------------------------|-------------------------|---------------------------------------|----------------|----------------------|------------------------------------|-----------|
| Odontoglossum ringspot virus                | Electrochemical impedance | AuNPs                                 | 0.345 ng/mL    | 0.5–50,000 ng/mL     | Orchid leaves sample               | [138]     |
| Hepatitis C virus core antigen              | Voltammetric            | MWCNTs—chitosan nanocomposite         | 1.67 fg/mL     | 5 fg/mL–1 pg/mL      | Human serum                        | [139]     |
| HPV-16 L1 protein                           | Voltammetric            | Porous rGO                             | 1.75 pM        | 3.5–35.3 pM          | Human serum and saliva             | [140]     |
| Dengue virus NS1 antigen                    | Voltammetric            | Hydroxyapatite nanoparticles           | 12.8 μg/mL     | 25–100 μg/mL         | Human serum                        | [141]     |
| HBV DNA                                    | Voltammetric            | Bi-FMNs with monolayer AuNPs          | 7.8 fg/mL      | 0.01–1.5 pg/mL       | Chicken serum and liver            | [142]     |
| H7N9 Avian influenza virus                  | Voltammetric            | MoS 2@Cu 2O–Pt nanohybrid             | 0.15 pg/mL     | 0.5 pg/mL–200 ng/mL  | Human serum                        | [143]     |
| Hepatitis B surface antigen                 | Voltammetric            | AuNPs                                 | 3.8 × 10⁻¹⁰ M  | 5 × 10⁻¹⁷–1 × 10⁻¹⁶ M| –                                  | [144]     |
| Zika virus                                  | Voltammetric            | Vanadium oxide nanobelts              | 1.3 fg/mL      | 10 fg/mL–100 ng/mL   | Human serum                        | [145]     |
| Avian influenza virus DNA                   | Voltammetric            | Meso/macroporous cobalt (II) oxide nanoflakes | 86.4 aM   | 1 fM–1 nM            | Cultured samples, human subjects   | [146]     |
| Capsicum chlorosis virus                   | Amperometric            | AuNP–MWCNT                            | 1:800,000 dilution| –                  | Bovine serum                       | [147]     |
| Avian influenza virus H7                   | Voltammetric            | CNTs                                  | 0.43 ng/mL     | 1–25 ng/mL           | –                                  | [148]     |
| Hepatitis C virus core antigen              | Voltammetric            | Nation@TiO 2 nanocomposite            | 25 fg/mL       | 0.1–250 pg/mL        | Human serum                        | [149]     |
| HPV DNA                                    | Electrochemical impedance | Au nanosheets                        | 0.15 pM        | 1 pM–1 µM            | –                                  | [150]     |
| White spot syndrome virus structural protein| Voltammetric            | GO                                    | 1.36 × 10⁻³ copies/µL| –                  | Shrimp, fish intestine, fish muscles| [151]     |
| HIV p24                                    | Voltammetric            | MWCNTs                                | 0.083 pg/cm³   | 1 × 10⁻⁴–2 ng/cm³    | Human serum                        | [152]     |
| Japanese encephalitis virus                | Electrochemical impedance | Carbon nanoparticles                  | 0.36 ng/mL     | 1–20 ng/mL           | Human serum                        | [153]     |
| Influenza virus H1N1                       | Chronoamperometric      | rGO                                   | 10² PFU/mL     | 10²–10⁸ PFU/mL       | –                                  | [154]     |
| Dengue virus                               | Electrochemical impedance | GO-polymer composite                  | 0.12 PFU/mL    | 1–2 × 10³ PFU/mL     | –                                  | [155]     |
| Hepatitis C virus DNA                      | Electrochemical impedance | MB@SiNPs                              | 90 copies/mL   | 100–10⁶ copies/mL    | Real patient samples               | [156]     |
| Dengue virus                               | Voltammetric, electrochemical impedance | Manganese(III) oxide nanofiber | 120 × 10⁻²¹ M | 1 aM–1 µM            | Whole blood serum                  | [157]     |
| Disease/Pathogen                                      | Detection Method                  | LOD Quantity                  | Range Quantity                  | Sample Type               | Reference |
|------------------------------------------------------|-----------------------------------|------------------------------|--------------------------------|---------------------------|-----------|
| HBV core antigen                                     | Voltammetric AgNPs/GQD-SH nanocomposite | 3 fg/mL                      | 0.05 pg/mL – 60 pg/mL          | Human serum               | [160]     |
| HBV surface antigen                                  | Voltammetric Fe$_3$O$_4$ magnetic nanoparticles | 0.19 pg/mL                   | 0.3 – 1000 pg/mL              | Human serum               | [161]     |
| Dengue virus DNA                                      | Voltammetric ZnO/Pt-Pd nanocomposite | $4.3 \times 10^{-5}$ M       | $1 \times 10^{-6} – 100 \times 10^{-6}$ M | –                        | [162]     |
| Dengue virus serotype 2 DNA                          | Electrochemical Cu$_2$CdSnS$_4$ quaternary alloy nanostuctures | 16.9 nM                      | –                             | –                         | [163]     |
| HBV core antigen                                     | Amperometric GO/Ferrocene–chitosan nanocomposite | 0.1 ng/mL                    | 0.1 – 350 ng/mL               | Human serum               | [165]     |
| HIV envelope glycoprotein                             | Voltammetric AgNPs-Graphene        | 1.6 pg/mL                    | $1.6 \times 10^{-3} – 16$ ng/mL | –                        | [167]     |
| Hepatitis B core protein antibodies H1N1, H5N1 and H7N9 influenza viruses | Voltammetric Hyaluronic acid–CNT hybrid film | 0.03 ng/mL                   | Up to 6 ng/mL                | –                         | [8]       |
| HBV DNA                                              | Voltammetric Zeolite nanocrystals and MWCNT nanocomposite | 111 copies/mL               | $10^3 – 10^{5.1}$ copies/mL | Real patient samples      | [173]     |
| Rotavirus                                             | Voltammetric AuNPs                 | 167 PFU/mL                   | $500 – 5 \times 10^5$ PFU/mL  | –                        | [170]     |
| HBV DNA                                              | Electrochemical impedance          | 2.3 PFU/mL                   | $4.6 – 4.6 \times 10^4$ PFU/mL | –                        | [171]     |
| HBV DNA                                              | Electrochemical impedance          | 3.1 $\times 10^{-13}$ M      | $8.3 \times 10^{-13} – 6.4 \times 10^{-7}$ M | Real patient samples      | [172]     |
| Influenza virus H5N1/ H1N1                           | Voltammetric GO                    | 8.3 pM                       | 25 – 500 pM                   | –                        | [176]     |
| Influenza virus                                      | Voltammetric PNP–porous ZnO spheres | 0.76 pg/mL                   | 0.001 – 60 ng/mL              | Human serum               | [177]     |
| Cucumber mosaic virus                                 | Chronoamperometric AuNPs          | 0.1 mg/mL                    | –                             | –                        | [178]     |
| Avian influenza virus H5N1                            | Amperometric Pyrene succinimidyl ester functionalized graphene | –                            | –                             | –                        | [179]     |
| Adenovirus type 5                                     | Electrochemical impedance          | AuNPs                        | 30 virus particles/mL         | 10 – $10^6$ virus particles/mL | –         | [180]     |
| Avian influenza A virus H7N9                          | Voltammetric Bi-MBs               | 6.8 pg/mL                    | 0.01 – 20 ng/mL               | –                        | [181]     |
| HBV DNA                                              | Voltammetric Magnetite nanoparticles | $3.3 \times 10^{-13}$ M     | $7.8 \times 10^{-13} – 8.8 \times 10^{-9}$ M | Urine and blood plasma   | [182]     |

(Continued)
| Target                             | Biosensor type       | Nanomaterial                          | LOD             | Linear range                  | Application                  | Reference |
|-----------------------------------|----------------------|---------------------------------------|-----------------|------------------------------|-----------------------------|-----------|
| Avian influenza virus H5N1 DNA    | Voltammetric         | VS$_2$ nanoflower-graphene--AuNPs     | $5.2 \times 10^{-4}$ M | $5 \times 10^{-12} – 1 \times 10^{-10}$ M | --                          | [183]    |
| HIV DNA                           | Voltammetric         | GR/AuNC                               | 30 aM           | 0.1 fM–100 nM                | Human serum                 | [184]    |
| Dengue virus DNA                  | Voltammetric         | SiNWs                                 | $1.63 \times 10^{-12}$ M | $1 \times 10^{-11} – 1 \times 10^{-7}$ M | --                          | [185]    |
| Dengue virus NS1 protein          | Voltammetric         | Carboxylated CNTs                     | 0.035 μg/mL     | 0.1–2.5 μg/mL                | Serum                       | [186]    |
| Avian influenza A virus H7N9      | Amperometric         | Tetrahedral nanostructure             | 97 fM           | 1 pM–2.5 nM                  | --                          | [187]    |
| HBV DNA                           | Voltammetric         | AuNRs                                 | $2 \times 10^{-12}$ M | $1 \times 10^{-12} – 1 \times 10^{-6}$ M | --                          | [188]    |
| Avian influenza virus H5N1        | Amperometric         | Carbon nano-onions                    | 0.5 nM          | 0.5–20 nM                    | Clinical samples from cervical scraps | [190] |
| HPV oncogene                      | Electrochemical      | AuNPs                                 | $8 \times 10^{-4}$ HAU/200 μL | --                          | --                          | [191]    |
| Avian influenza virus H5N1        | Voltammetric         | CIMC–AuNPs                            | 110 TCID$_{50}$/mL | $10^{2.05} – 10^{4.50}$ TCID$_{50}$/mL | Normal avian serum          | [192]    |
| Avian leukosis virus subgroup J   | Pathogen virus DNA   | MWCNT                                 | $1.2 \times 10^{-12}$ M | --                          | --                          | [193]    |
| HBV surface antigen               | Voltammetric         | Fe$_3$O$_4$ nanoparticles              | 0.06 ng/mL      | 1–250 ng/mL                  | Human serum                 | [194]    |
| Influenza virus type A            | Voltammetric         | AuNPs                                 | --              | --                           | --                          | [195]    |
| Avian influenza virus subtype H5  | Voltammetric         | GO                                    | $2^{-15}$ HAU/50 μL | $2^{-15} – 2^{-8}$ HAU/50 μL | --                          | [196]    |
| HBV DNA                           | Voltammetric         | AuNPs                                 | $7.6 \times 10^{-12}$ M | $5.7 \times 10^{-11} – 6.6 \times 10^{-6}$ M | Urine                       | [197]    |
| Influenza virus                   | Voltammetric         | Cds QDs                               | 0.06 mM         | 0.06–0.5 mM                  | Real patient samples        | [198]    |
| Avian leukemia virus subgroup J   | Voltammetric         | GQDs and Cu-apoferritin               | 115 TCID$_{50}$/mL | $10^{2.08} – 10^{4.50}$ TCID$_{50}$/mL | --                          | [199]    |
| HBV surface antigen               | Voltammetric         | Magnetic NPs                          | 0.9 pg/mL       | 0.001–0.015 ng/mL            | Human serum                 | [200]    |
| Dengue 2 and Dengue 3 viruses     | Electrochemical      | Nanoporous alumina                    | 0.23 PFU/mL for dengue 2 and 0.710 PFU/mL for dengue 3 | 1–900 PFU/mL | Human serum | [201] |
| HBV and HPV DNAs                  | Electrochemical      | SWCNT arrays and AuNPs                | $10^{-18}$ M for HBV and HPV | $1 \times 10^{-18} – 1 \times 10^{-16}$ M for HBV and HPV | --                          | [202]    |
| HIV                               | Voltammetric         | AuNPs                                 | 600 fg/mL       | 600 fg/mL–375 pg/mL          | --                          | [203]    |
| Dengue virus DNA                  | Electrochemical      | Nanoporous alumina                    | $2.7 \times 10^{-12}$ M | $2.7 \times 10^{-12} – 1 \times 10^{-6}$ M | --                          | [204]    |
| Hepatitis C virus nonstructural 5 A protein | Chronoamperometric | Au–MoO$_3$/chitosan nanocomposite     | 1 ng/mL         | 1–50 μg/mL                   | Human serum                 | [205]    |
| Pathogen                        | Detection Method          | Antigen/Structure                          | Concentration Range          | Matrix                  | Reference |
|--------------------------------|---------------------------|--------------------------------------------|-----------------------------|-------------------------|-----------|
| Japanese encephalitis virus    | Voltammetric              | Polyaniline nanowires                      | 10 ng/mL                    | 10–500 ng/mL            | [206]     |
| HIV p24 antigen                | Voltammetric              | AuNPs–Fe₃O₄ NPs                           | 0.5 pg/mL                   | 0.001–10 ng/mL          | Human serum | [207]     |
| Murine norovirus               | Voltammetric              | AuNPs                                     | 10 aM                       | 20–120 aM               | Human serum | [208]     |
| Hepatitis C virus core antigen | Voltammetric              | MWCNTs                                    | 0.01 pg/mL                  | 0.25–300 pg/mL          | Human serum | [209]     |
| Dengue virus nonstructural protein 1 | Voltammetric              | CNT                                        | 12 ng/mL                    | 40 ng/mL–2 μg/mL        | Blood serum | [210]     |
| HBV DNA                        | Voltammetric              | PtNPs–MWCNTs                              | 5.56 × 10⁻¹² M              | 1.13 × 10⁻¹³–1.13 × 10⁻⁹ M | –         | [211]     |
| Avian leukosis virus subgroup J | Voltammetric              | Fe₃O₄ core/Ni–Al layered double hydroxides shell nanospheres | 180 TCID₅₀/mL | 10²⁻¹²–10⁵.5⁰ TCID₅₀/mL | –         | [212]     |
| Dengue type 2 virus            | Voltammetric              | Nanoporous alumina                        | 1 PFU/mL                    | 1–10⁹ PFU/mL            | Infected Aedes aegypti mosquito sample | [213] |
| Dengue virus serotype 2        | Electrochemical impedance | Nanoporous alumina                        | 1 PFU/mL                    | 1–900 PFU/mL            | –         | [214]     |
| Hepatitis C virus core antigen | Voltammetric              | AuNPs–ZrO₂NPs                             | 0.17 ng/mL                  | 2–512 ng/mL             | Human serum | [215]     |
| Dengue virus RNA               | Voltammetric              | Nanoporous alumina                        | 9.55 × 10⁻¹² M              | 9.55 × 10⁻¹²–10⁻⁶ M     | –         | [216]     |
| HIV-1                          | Voltammetric              | Fe₃O₄ nanoparticles                        | 50 pM                       | 50–300 pM               | –         | [217]     |
| HPV-16 antibody                | Voltammetric              | PAN–MWCNT                                 | 490 pM                      | 10–50 nM                | –         | [218]     |
| Plum pox virus                 | Voltammetric              | AuNPs                                     | 10 pg/mL                    | 10–200 pg/mL            | –         | [219]     |
| Avian influenza virus H5N1 gene| Voltammetric              | MWCNTs–AuNPs                              | 4.3 × 10⁻¹³ M               | 5 × 10⁻¹²–1 × 10⁻⁹ M    | –         | [220]     |

Bi-FMNs, bifunctional fluorescence magnetic nanospheres; Bi-MBs, bifunctional magnetic nanobeads; CIMC, carbon nanotubes–iron oxides magnetic composites; CNTs, carbon nanotubes; GO, graphene oxide; GQDs, graphene quantum dots; HIV, human immunodeficiency virus; HBV, Hepatitis B virus; HPV, human papillomavirus; HAU, hemagglutination units; MWCNT, multiwalled carbon nanotubes; SWCNTs, single-walled carbon nanotubes; NPs, nanoparticles; PFU, human papillomavirus.
cost, small sample volume without amplification step, and user-friendly interface and portability [118]. Lee et al. reported the H5N1 detection with 1 pM of limit of detection (LOD). CV was applied to confirm the HA protein binding to multifunctional DNA structure on pAuNPs-modified electrode.

Hepatitis B e antigen (HBeAg) immunosensor was developed using electrochemical techniques. Cocatalysis of horseradish peroxidase (HRP) and nanoporous gold are used as modifier agents. The developed immunosensor gives a good linear relation between peak current and concentration of HBeAg (1 pg/mL to 1 ng/mL as well as 0.064 pg/mL of LOD).

The electrochemical DNA biosensing device becomes effective tool because of the properties such as rapid response time, high specificity, sensitivity, and user friendly. Electrochemical paper analytical device (ePADs) makes a great contribution on the sensor, because of paper being an inexpensive substrate. Singhal et al. describe their study about the fabrication of ePADs, by diagnosing the target DNA of Chikungunya virus (CHIKV) [119].

Electrical and optical methods were used in the study by Oliveira et al. [120]. Genomic DNA is detected in blood plasma of patients with hepatitis B without PCR amplification. The linear range of HBV-genomic DNA concentration was found as 1.55–6.68 ng/μL with LOD of 0.15 ng/μL.

HBV surface antigen (HBsAg) immunosensor was developed by Alizadeh et al. Hemin/G-quadruplex/Fe3O4–AuNPs and H-amino-rGO–Au were used as modifier agents [121]. The HBsAg immunosensor was also applied in spiked human serum sample.

Smart electrochemical platform was formed by Wiang et al. An ultrasensitive label-free electrochemical biosensor using graphene quantum dots for detecting HBV DNA was made. The proposed sensor exhibits high sensitivity with a detection limit of 1 nM, and the linear detection range is from 10 to 500 nM [122].

EIS detection is one of the main concepts in label-free biosensing which are nucleotides (DNA/RNA), enzymes, aptamers, and antibodies detection. Moreover, EIS measurement is a nondestructive and relatively facile system. Shariati et al. developed a biosensor of HPV DNA. Impedimetric HPV DNA biosensor by AuNTs-polycarbonate electrode was fabricated. Biosensor in label-free detection showed the good linear ranges of 0.01–1 mM [114].

Nanocelluloses could be used to immobilize antibodies, enzymes, and noble metal NPs, all of which could enhance electrochemical immunosensor performance. Surprisingly, very little work has been reported on the application of nanocelluloses in electrochemical immunoassays. Liu et al. aim to develop a sensitive sandwich-type electrochemical immunosensor for the measurement of Avian leukosis virus subgroup J [123].

### 18.5 Conclusion

In this chapter, we tried to collect and describe all reported biosensors for viruses by electrochemical methods. Generally, measurements depend on the affinity interaction between antibody and antigen. The most used methods were observed as amperometry, voltammetry, and impedance spectroscopy methods. The developed biosensors with viruses can be used with integrated substrates (metallic- or carbon-based electrodes) for clinical, environmental, and industrial applications. Some selected applications were summarized and listed in Table 18.1.

### References

[1] D.P. Clark, N.J. Pazdernik, Viruses, Mol. Biol. (2013) e517–e522. Available from: https://doi.org/10.1016/B978-0-12-378594-7.00056-1.

[2] D. Stuart, Viruses, Curr. Opin. Struct. Biol. 3 (1993) 167–174. Available from: https://doi.org/10.1016/S0959-440X(05)80148-4.

[3] J. Heritage, Viruses, in: Handb. Water Wastewater Microbiol., Academic Press, Elsevier, 2003. https://doi.org/10.1016/B978-0-12-470100-7.00033-0.

[4] K.M. Smith, Modern Virology, Nature Publishing Group, Springer, 2003. https://doi.org/10.1038/175012a0.

[5] M.B.A. Oldstone, History of virology, in: Encyclopedia of Microbiology (Fourth Edition), 2014, pp. 608–695.

[6] H.R. Gelderblom, Structure and classification of viruses, Med. Microbiol. (1996). Available from: http://www.ncbi.nlm.nih.gov/pubmed/21413309.

[7] H. Appleton, Viruses, in: Food Technol., Elsevier, 2003, pp. 88–95.

[8] D.G.A. Cabral, E.C.S. Lima, P. Moura, R.F. Dutra, A label-free electrochemical immunosensor for hepatitis B based on hyaluronic acid-carbon nanotube hybrid film, Talanta 148 (2016) 209–215. Available from: https://doi.org/10.1016/j.talanta.2015.10.083.

[9] H. Haji-Hashemi, P. Norouzi, M.R. Safarnejad, M.R. Ganjali, Label-free electrochemical immunosensor for direct detection of Citrus tristeza virus using modified gold electrode, Sens. Actuators, B: Chem. 244 (2017) 211–216. Available from: https://doi.org/10.1016/j.snb.2016.12.135.

[10] Y. Guo, M. Duan, X. Wang, J. Gao, Z. Guan, M. Zhang, Early events in rabies virus infection—attachment, entry, and intracellular trafficking, Virus Res. 263 (2019) 217–225. Available from: https://doi.org/10.1016/j.virusres.2019.02.006.

[11] J.W. St Gome, A Biological Perspective of Slow Virus Infection and Chronic Disease, The Western Journal of Medicine, 1978.
[42] D. Nidzworski, K. Siuzdak, P. Niedzialkowski, R. Bogdanowicz, M. Sobaszek, J. Ryl, et al., A rapid-response ultrasensitive biosensor for influenza virus detection using antibody modified boron-doped diamond, Sci. Rep. 7 (2017) 1–10. Available from: https://doi.org/10.1038/s41598-017-15806-7.

[43] L.M. Fernando, M.K. Vasher, E.C. Alocilja, A DNA-based nanobiosensor for the rapid detection of the dengue virus in mosquito, Int. Sch. Sci. Res. Innov. 9 (2015) 822–825.

[44] Y. Tepeli, A. Ülkü, Electrochemical biosensors for influenza virus a detection: the potential of adaptation of these devices to POC systems, Sens. Actuators B. Chem. 254 (2018) 377–384. Available from: https://doi.org/10.1016/j.snb.2017.07.126.

[45] U. Anik, Y. Tepeli, M. Sayhi, J. Nsiri, M.F. Diouani, Towards the electrochemical diagnostic of influenza virus: development of a graphene-Au hybrid nanocomposite modified influenza virus biosensor based on neuraminidase activity, Analyst 143 (2018) 150–156. Available from: https://doi.org/10.1039/c7an01537b.

[46] L. Krejcova, D. Hynck, P. Michealik, V. Milosavljevic, P. Kopel, O. Zitka, et al., Electrochemical sensors and biosensors for influenza detection, Int. J. Electrochem. Sci. 9 (2014) 3440–3448.

[47] M. Woolhouse, F. Scott, Z. Hudson, R. Howey, M. Chase-Topping, Human viruses: discovery and emergence, Philos. Trans. R. Soc. Lond. B. Biol. Sci. 367 (2012) 2864–2871. Available from: https://doi.org/10.1098/rstb.2011.0354.

[48] L.H. Taylor, S.M. Latham, M.E. Woolhouse, Risk factors for human disease emergence, Philos. Trans. R. Soc. Lond. B. Biol. Sci. 356 (2001) 983–989. Available from: https://doi.org/10.1098/rstb.2001.0888.

[49] J. Louten, Herpesviruses, in: Essent. Hum. Virol., Academic Press, Elsevier, 2016, pp. 235–246. Available from: https://doi.org/10.1016/B978-0-12-800947-5.00013-2.

[50] W.-S. Ryu, Herpesviruses, in: Mol. Virol. Hum. Pathog. Viruses, Academic Press, Elsevier, 2017, pp. 125–139. Available from: https://doi.org/10.1016/B978-0-12-800838-6.00009-6.

[51] J.L. Brunson, M.V. Khoretzenko, K.Y. Stokes, Herpesviruses, Vascular Responses to Pathogens, Elsevier, Inc, 2016, pp. 123–136. Available from: https://doi.org/10.1016/B978-0-12-801078-5.00010-8.

[52] C.J. Burrell, C.R. Howard, F.A. Murphy, Herpesviruses, in: Fenner White’s Med. Virol., Academic Press, Elsevier, 2017, pp. 237–261. Available from: https://doi.org/10.1016/B978-0-12-375156-0.00017-5.

[53] A. Scheid, Paramyxoviridae, Perspect. Med. Virol. 3 (1987) 233–252. Available from: https://doi.org/10.1016/0168-7069(87)70098-3.

[54] T.G. Morrison, Paramyxoviruses, infection and immunity, in: Encycl. Immunol., second ed., Academic Press, Elsevier, 1998, pp. 1909–1916.

[55] J.-Y. Han, J.R. Romero, Aseptic and viral meningitis, Princ. Pract. Pediatr. Infect. Dis. (2017) 301–305.e2. Available from: https://doi.org/10.1097/0000421-000034-8.

[56] H.Y. Naim, Measles virus; informations, Hum. Vaccine Immunother. 11 (2015) 21–26. Available from: https://doi.org/10.4161/hv.34298.

[57] W.-S. Ryu, Other DNA viruses, in: Mol. Virol. Hum. Pathog. Viruses, Academic Press, Elsevier, 2017, pp. 125–139. Available from: https://doi.org/10.1016/B978-0-12-800838-6.00009-6.

[58] D.G. Baker, Natural pathogens of laboratory animals: their effects on research, Clin. Microbiol. Rev. 11 (1998) 231–266. Available from: http://books.google.com/books?id=EeHcWppSwG4C&printsec=frontcover%5Cnpapers://f7bdc8ea-3a41-4131-ba77-e128607ec597/Paper/p517.

[59] D.G. Brownstein, A.L. Smith, E.A. Johnson, D.J. Pintel, L.K.A.Y. Naeger, P. Tattersall, The pathogenesis of infection with minute virus of mice depends on expression of the small nonstructural protein NS2 and on the genotype of the allotropic determinants VP1 and VP2, J. Virol. 66 (1992) 3118–3124.

[60] S. Payne, Family Retroviridae, in: Viruses, Academic Press, Elsevier, 2017, pp. 287–301. Available from: https://doi.org/10.1016/b978-0-12-803109-4.00036-2.

[61] J. Kam, Retroviruses, in: Brenner’s Encycl. Genet., second ed., Academic Press, Elsevier, 2013, pp. 211–215. Available from: https://doi.org/10.1016/B978-0-12-374984-0.01323-1.

[62] M. Feng, X. Zhang, Immunity to Avian leucosis virus: where are we now and what should we do? Front. Immunol. 7 (2016) 1–8. Available from: https://doi.org/10.3389/fimmu.2016.00624.

[63] J.C. Castelli, J.A. Levy, HIV (Human Immunodeficiency Virus), third ed., Elsevier, Inc, 2018. Available from: https://doi.org/10.1016/b0-12-227555-1/00103-9.

[64] B. Harrach, Adenoviruses: general features, Encycl. Virol., Elsevier, Inc, 2008, pp. 1–9. Available from: https://doi.org/10.1016/b978-012374410-4.00680-4.

[65] W.-S. Ryu, Adenoviruses, in: Mol. Virol. Hum. Pathog. Viruses, Academic Press, Elsevier, 2017, pp. 111–124. Available from: https://doi.org/10.1016/B978-0-12-800838-6.00008-4.

[66] W. Faber, H. de Vries, Togaviruses, in: Mucocutaneous Manifestations Viral Dis., CRC Press, Taylor and Francis Group, 2013, pp. 447–465. Available from: https://doi.org/10.3109/9781420073133-25.

[67] C.J. Burrell, C.R. Howard, F.A. Murphy, Astroviruses, in: Fenner White’s Med. Virol., Academic Press, Elsevier, 2017, pp. 473–476. Available from: https://doi.org/10.1016/B978-0-12-375156-0.00034-S.

[68] J.E. Tate, Astroviruses, in: Princ. Pract. Pediatr. Infect. Dis., Elsevier, 2018, p. 1224–1226.e1. Available from: https://doi.org/10.1016/B978-0-323-40181-4.00240-1.

[69] M.V. Yates, Astroviruses, Microbiol. Waterborne Dis., second ed., Elsevier, 2014, pp. 479–491. Available from: https://doi.org/10.1016/B978-0-12-415846-7.00024-X.

[70] C.J. Burrell, C.R. Howard, F.A. Murphy, Caliciviruses, in: Fenner White’s Med. Virol., Academic Press, Elsevier, 2017, pp. 465–471. Available from: https://doi.org/10.1016/B978-0-12-415846-7.00028-7.
[105] P.P. Waifalkar, A.D. Chougale, P. Kollu, P.S. Patil, P.B. Patil, Magnetic nanoparticle decorated graphene based electrochemical nanobiosensor for H$_2$O$_2$ sensing using HRP, Colloids Surf. B: Biointerfaces 167 (2018) 425–431. Available from: https://doi.org/10.1016/j.colsurfb.2018.04.042.

[106] M. Li, M. Lv, L. Wang, C. Fan, X. Zuo, Engineering electrochemical interface for biomolecular sensing, Curr. Opin. Electrochem. 14 (2019) 71–80. Available from: https://doi.org/10.1016/j.coelec.2019.01.001.

[107] K.J. Stine, Biosensor applications of electrodeposited nanostructures, Appl. Sci. 9 (2019) 797. Available from: https://doi.org/10.3390/app9040797.

[108] A. Florea, G. Melinte, I. Simon, C. Cristea, Electrochemical biosensors as potential diagnostic devices for autoimmune diseases, Biosensors, 2019, pp. 1–15. <https://doi.org/10.3390/bios9010038>.

[109] E. Palčček, M. Bartošík, Electrochemistry of nucleic acids, Chem. Rev. 112 (2012) 3427–3481. Available from: https://doi.org/10.1021/cr200305p.

[110] A. Saadati, S. Hassanpour, M. de la Guardia, J. Mosafer, M. Hashemzaei, A. Mokhtarzadeh, et al., Recent advances on application of peptide nucleic acids as a bioreceptor in biosensors development, TrAC—Trends Anal. Chem. 114 (2019) 56–68. Available from: https://doi.org/10.1016/j.trac.2019.02.030.

[111] B.C. Janegitz, J. Cancino, V. Zacolotto, Disposable biosensors for clinical diagnosis, J. Nanosci. Nanotechnol. 14 (2014) 378–389. Available from: https://doi.org/10.1166/jnn.2014.9234.

[112] A. Roointan, T. Ahmad, S. Ibrahim, K. Khadim, B. Ahmed, S. Abraham, et al., Early detection of lung cancer biomarkers through biosensor technology: a review, J. Pharm. Biomed. Anal. 164 (2019) 93–103. Available from: https://doi.org/10.1016/j.jpba.2018.10.017.

[113] S. Wu, W. Ye, M. Yang, M. Taghipoor, R. Meissner, J. Brugger, et al., Impedance sensing of DNA immobilization and hybridization by microfabricated alumina nanopore membranes, Sens. Actuators B: Chem. 216 (2015) 105–112. Available from: https://doi.org/10.1016/j.snb.2015.03.094.

[114] M. Shariati, M. Ghorbani, P. Sasanpour, A. Karimizefreh, An ultrasensitive label free human papilloma virus DNA biosensor using gold nanotubes based on nanoporous polycarbonate in electrical alignment, Anal. Chim. Acta 1048 (2018) 31–41. Available from: https://doi.org/10.1016/j.aca.2018.09.062.

[115] B. Uslu, S.A. Ozkan, Electroanalytical methods for the determination of pharmaceuticals: a review of recent trends and developments, Anal. Lett. 44 (2011) 2644–2702. Available from: https://doi.org/10.1080/000271911.553010.

[116] C. Working, Electrodes—Chemistry LibreTexts, n.d. https://chem.libretexts.org/Booksheles/Analytical_Chemistry/Supplemental_Modules_(Analytical_Chemistry)/Analytical_Sciences_Digital_Library/JASDL/Courseware/Analytical_Electrochemistry%3A_The_Basic_Concepts/05_Experimental_Hardware/C_Wor kin_ Electrodes.

[117] K. Siuzda k, P. Niedziolkowski, M. Sobaszek, T. Łe ąga, M. Sawczak, E. Czaczyk, et al., Biomolecular influenza virus detection based on the electrochemical impedance spectroscopy using the nanocrystalline boron-doped diamond electrodes with covalently bound antibodies, Sens. Actuators, B: Chem. 280 (2019) 263–271. Available from: https://doi.org/10.1016/j.snb.2018.10.005.

[118] T. Lee, S.Y. Park, H. Jang, G.H. Kim, C. Park, M. Mohammadniaei, et al., Fabrication of electrochemical biosensor consisted of multifunctional DNA structure/porous au nanoparticle for avian influenza virus (H5N1) in chicken serum, Mater. Sci. Eng. C. 99 (2018) 511–519. Available from: https://doi.org/10.1016/j.msec.2019.02.001.

[119] C. Singhal, A. Dubey, A. Mathur, C.S. Pandir, J. Narang, Paper based DNA biosensor for detection of chikungunya virus using gold shells coated magnetic nanocubes, Process Biochem. 74 (2018) 35–42. Available from: https://doi.org/10.1016/j.procbio.2018.08.020.

[120] D.A. Oliveira, J.V. Silva, J.M.R. Flauzino, A.C.H. Castro, A.C.R. Moço, M.M.C.N. Soares, et al., Application of nanomaterials for the electrical and optical detection of the hepatitis B virus, Anal. Biochem. 549 (2018) 157–163. Available from: https://doi.org/10.1016/j.abb.2018.03.023.

[121] N. Alizadeh, R. Hallaj, A. Salimi, Dual amplified electrochemical immunosensor for hepatitis B virus surface antigen detection using hemin/ G-quadruplex immobilized onto Fe$_3$O$_4$-AuNPs or (hemin-amino-rGO-Au) nanohybrid, Electroanalysis 30 (2018) 402–414. Available from: https://doi.org/10.1002/elan.201700727.

[122] Q. Xiang, J. Huang, H. Huang, W. Mao, Z. Ye, A label-free electrochemical platform for the highly sensitive detection of hepatitis B virus DNA using graphene quantum dots, RSC Adv. 8 (2018) 1820–1825. Available from: https://doi.org/10.1039/c7ra11945c.

[123] C. Liu, J. Dong, G.L.N. Waterhouse, Z. Cheng, S. Ai, Electrochemical immunosensor with nanocellulose-Au composite assisted multiple signal amplification for detection of Avian leu ksis virus subgroup, J. Biosens. Bioelectron. 101 (2018) 110–115. Available from: https://doi.org/10.1016/j.bios.2017.10.007.

[124] Y. Zhang, Y. Gao, X. Zhang, H. Wang, T. Xia, C. Bian, Electrochemical biosensor for HBe antigen detection based on a signal amplification strategy: the co-catalysis of horseradish peroxidase and nanoporous gold, Sens. Actuators B: Chem. 284 (2019) 296–304. Available from: https://doi.org/10.1016/j.snb.2018.12.157.

[125] Y.H. Hou, J.J. Wang, Y.Z. Jiang, C. Lv, L. Xia, S.L. Hong, et al., A colorimetric and electrochemical immunosensor for point-of-care detection of enterovirus 71, Biosens. Bioelectron. 99 (2018) 186–192. Available from: https://doi.org/10.1016/j.bios.2017.07.035.

[126] M. Khater, A. de la Escosura-Muniz, D. Quesada-González, A. Merkoçi, Electrochemical detection of plant virus using gold nanoparticle-modified electrodes, Anal. Chim. Acta 1046 (2018) 123–131. Available from: https://doi.org/10.1016/j.aca.2018.09.031.

[127] J. Narang, C. Singhal, A. Mathur, S. Sharma, V. Singla, C.S. Pandir, Portable bioactive paper based genosensor incorporated with Zn-Ag nanoblooms for herpes detection at the point-of-care, Int. J. Biol. Macromol. 107 (2018) 2559–2565. Available from: https://doi.org/10.1016/j.ijbiomac.2017.10.146.
[128] Y. Hu, Y. Huang, Y. Wang, C. Li, W.L. Wong, X. Ye, et al., A photoelectrochemical immunosensor based on gold nanoparticles/ZnAgInS quaternary quantum dots for the high-performance determination of hepatitis B virus surface antigen, Anal. Chim. Acta 1035 (2018) 136–145. Available from: https://doi.org/10.1016/j.aca.2018.06.019.

[129] M. Sayhi, O. Ouerghi, K. Belgacem, M. Arbi, Y. Tepeli, A. Ghram, et al., Electrochemical detection of influenza virus H9N2 based on both immunomagnetic extraction and gold catalysis using an immobilization-free screen printed carbon microelectrode, Biosens. Bioelectron. 107 (2018) 170–177. Available from: https://doi.org/10.1016/j.bios.2018.02.018.

[130] M.F. Abd Muain, K.H. Cheo, M.N. Omar, A.S. Amir Hamzah, H.N. Lim, A.B. Salleh, et al., Gold nanoparticle-decorated reduced-graphene oxide targeting anti hepatitis B virus core antigen, Bioelectrochemistry 122 (2018) 199–205. Available from: https://doi.org/10.1016/j.bioelechem.2018.04.004.

[131] Z. Gao, Y. Li, X. Zhang, J. Feng, L. Kong, P. Wang, et al., Ultrasensitive electrochemical immunosensor for quantitative detection of HBeAg using Au@Pd/MoS2@MWCNTs nanocomposite as enzyme-mimetic labels, Biosens. Bioelectron. 102 (2018) 189–195. Available from: https://doi.org/10.1016/j.bios.2017.11.032.

[132] M.A. Tahir, S.Z. Bajwa, S. Mansoor, R.W. Briddon, W.S. Scheffler, et al., Evaluation of carbon nanotube based copper nanoparticle composite for the efficient detection of agroviruses, J. Hazard. Mater. 346 (2018) 27–35. Available from: https://doi.org/10.1016/j.jhazmat.2017.12.007.

[133] F. Zhao, Y. Bai, R. Zeng, L. Cao, J. Zhu, G. Han, et al., An electrochemical immunosensor with graphene-oxide-ferrocene-based nanocomposites for hepatitis B surface antigen detection, Electroanalysis 30 (2018) 2774–2780. Available from: https://doi.org/10.1002/elan.201800476.

[134] G. Cabral-Miranda, A.R. Cardoso, L.C.S. Ferreira, M.G.F. Sales, M.F. Bachmann, Biosensor-based selective detection of antibodies in infected individuals, Biosens. Bioelectron. 113 (2018) 101–107. Available from: https://doi.org/10.1016/j.bios.2018.04.058.

[135] Q. Palomar, C. Gondran, R. Marks, S. Cosnier, M. Holzinger, Impedimetric quantification of anti-dengue antibodies using functional carbon nanotube deposits validated with blood plasma assays, Electrochim. Acta 274 (2018) 84–90. Available from: https://doi.org/10.1016/j.electacta.2018.04.099.

[136] H. Tu, K. Lin, Y. Lun, L. Yu, Magnetic bead/capture DNA/glucose-loaded nanoliposomes for amplifying the glucometer signal in the rapid screening of hepatitis C virus RNA, Anal. Bioanal. Chem. 410 (2018) 3661–3669. Available from: https://doi.org/10.1007/s00216-018-1055-1.

[137] A. Valipour, M. Roushani, Using boehmite nanoparticles as an undercoat, and riboflavin as a redox probe for immunosensor designing: ultrasensitive detection of hepatitis C virus core antigen, Anal. Bioanal. Chem. 5 (2018) 353–361.

[138] Y.-S. Jian, C.-H. Lee, F.-J. Jan, G.-J. Wang, Detection of Odontoglossum ringspot virus infected Phalaenopsis using a nano-structured biosensor, J. Electrochem. Soc. 165 (2018) H449–H454. Available from: https://doi.org/10.1149/2.0351809jes.

[139] K. Ghanbari, M. Roushani, A nanohybrid probe based on double recognition of an aptamer MIP grafted onto a MWCNTs-Chit nanocomposite for sensing hepatitis C virus core antigen, Sens. Actuators B: Chem. 258 (2018) 1066–1071. Available from: https://doi.org/10.1016/j.snb.2017.11.145.

[140] F. Chekin, K. Bagga, P. Subramanian, R. Iijie, S.K. Singh, S. Kurungot, et al., Nucleic aptamer modified porous reduced graphene oxide/ MoS2 based electrodes for viral detection: application to human papillomavirus (HPV), Sens. Actuators B: Chem. 262 (2018) 991–1000. Available from: https://doi.org/10.1016/j.snb.2018.02.065.

[141] S. Solanki, A. Soni, M.K. Pandey, A. Biradar, G. Sumana, Langmuir-Blodgett nanoassemblies of the MoS2-X composite at the air-water interface for dengue detection, ACS Appl. Mater. Interfaces 10 (2018) 3020–3028. Available from: https://doi.org/10.1021/acsami.7b14391.

[142] A. Erdem, G. Congur, Hydroxyapatite nanoparticles modified graphite electrodes for electrochemical DNA detection, Electroanalysis 30 (2018) 67–74. Available from: https://doi.org/10.1002/ela.201700462.

[143] Z. Wu, W.J. Gao, Y.Y. Bai, L. Zhang, J. Hu, D.W. Pang, et al., Digital single virus electrochemical enzyme-linked immunoassay for ultrasensitive H7N9 avian influenza virus counting, Anal. Chem. 90 (2018) 1683–1690. Available from: https://doi.org/10.1021/acs.analchem.7b03281.

[144] F. Li, Y. Li, J. Feng, Z. Gao, H. Lv, X. Ren, et al., Facile synthesis of MoS2@CuO-Pt nanohybrid as enzyme-mimetic label for the detection of the hepatitis B surface antigen, Biosens. Bioelectron. 100 (2018) 512–518. Available from: https://doi.org/10.1016/j.bios.2017.09.048.

[145] C. Tancharoen, W. Sukjee, C. Thepparit, T. Jaimipuk, P. Aeunwarakul, A. Thitithanyanont, et al., An electrochemical biosensor based on surface imprinting for Zika virus detection in serum, ACS Sensors 4 (2018). Available from: https://doi.org/10.1021/acssensors.8b00885.

[146] B. Kaur, K. Malecka, D.A. Cristaldi, C.S. Chay, I. Mames, H. Radecka, et al., Approaching single DNA molecule detection with an ultrasensitive electrochemical genosensor based on gold nanoparticles and cobalt-porphyrin DNA conjugates, Chem. Commun. 54 (2018) 3573–3575. Available from: https://doi.org/10.1039/c8cc05362f.

[147] A. Valipour, M. Roushani, A glassy carbon immunoelectrode modified with vanadium oxide nanobelts for ultrasensitive voltammetric determination of the core antigen of hepatitis C virus, Microchim. Acta 184 (2017) 4477. Available from: https://doi.org/10.1007/s00705-2017-3293-5.

[148] J. Mohammadi, A. Moattari, N. Sattarrahmad, N. Pirbonyeh, H. Yadeegari, H. Heli, Electrochemical biosensing of influenza A subtype genome based on meso/macroporous cobalt(II) oxide nanoflakes-applied to human samples, Anal. Chim. Acta 979 (2017) 51–57. Available from: https://doi.org/10.1016/j.aca.2017.05.010.

[149] A. Sharma, A. Kaushal, S. Kulshrestha, A nano-Au/C-MWCNT based label free amperometric immunosensor for the detection of capsicum chlorosis virus in bell pepper, Arch. Virol. 162 (2017) 2047–2052. Available from: https://doi.org/10.1007/s00705-017-3293-5.

[150] J. Tian, D. Wang, Y. Zheng, T. Jing, A high sensitive electrochemical avian influenza virus H7 bio sensor based on CNTs/MoSX aerogel, Int. J. Electrochem. Sci. 12 (2017) 2658–2668. Available from: https://doi.org/10.20964/2017.04.30.
[151] A. Valipour, M. Roushani, TiO2 nanoparticles doped with Celestine Blue as a label in a sandwich immunoassay for the hepatitis C virus core antigen using a screen printed electrode. Microchim. Acta 184 (2017) 2015–2022. Available from: https://doi.org/10.1007/s00604-017-2190-7.

[152] A. Karimizereh, F.A. Mahyari, M. VaezJalali, R. Mohammadmour, P. Sasanpour, Impedimetric biosensor for the DNA of the human papilloma virus based on the use of gold nanosheets. Microchim. Acta 184 (2017) 1729–1737. Available from: https://doi.org/10.1007/s00604-017-2173-8.

[153] A. Natarajan, K.S.S. Devi, S. Raja, A. Senthil Kumar, An elegant analysis of white spot syndrome virus using a graphene oxide/methylene blue based electrochemical immunosensor platform. Sci. Rep. 7 (2017) 1–11. Available from: https://doi.org/10.1038/srep46169.

[154] Y. Ma, X.L. Shen, Q. Zeng, H.S. Wang, L.S. Wang, A multi-walled carbon nanotubes based molecularly imprinted polymers electrochemical sensor for the sensitive determination of HIV-p24, Talanta 164 (2017) 121–127. Available from: https://doi.org/10.1016/j.talanta.2016.11.043.

[155] H.C. Lai, S.F. Chin, S.C. Pang, M.S. Henry Sum, D. Perera, Carbon nanoparticles based electrochemical biosensor strip for detection of Japanese encephalitis virus, J. Nanomater. 2017 (2017) 1–8. Available from: https://doi.org/10.1155/2017/3615707.

[156] R. Singh, S. Hong, J. Jang, Label-free detection of influenza viruses using a reduced graphene oxide-based electrochemical immunosensor integrated with a microfluidic platform. Sci. Rep. 7 (2017) 1–11. Available from: https://doi.org/10.1038/srep42771.

[157] K. Navakul, C. Warakulwit, Pa-thai Yenchitsomanus, A. Panya, P.A. Lieberzeit, C. Sangma, A novel method for dengue virus detection and antibody screening using a graphene-polymer based electrochemical biosensor, Nanomed. Nanotechnol. Biol. Med. 13 (2017) 549–557. Available from: https://doi.org/10.1016/j.nano.2016.08.009.

[158] A. Valipour, M. Roushani, Using silver nanoparticle and thiol graphene quantum dots nanocomposite as a substratum to load antibody for detection of hepatitis C virus core antigen: electrochemical oxidation of riboflavin was used as redox probe, Biosens. Bioelectron. 89 (2017) 946–951. Available from: https://doi.org/10.1016/j.bios.2016.09.086.

[159] N. Alizadeh, R. Hallaj, A. Salimi, A highly sensitive electrochemical immunosensor for hepatitis B virus surface antigen detection based on hemin/G-quadruplex horseradish peroxidase-mimicking DNAzyme-signal amplification, Biosens. Bioelectron. 94 (2017) 184–192. Available from: https://doi.org/10.1016/j.bios.2017.02.039.

[160] C. Singhal, A. Ingle, D. Chakraborty, A.K. PN, C.S. Pandir, J. Narang, Impedimetric genosensor for detection of hepatitis C virus (HCV1) DNA using viral probe on methylene blue doped silica nanoparticles, Int. J. Biol. Macromol. 98 (2017) 84–93. Available from: https://doi.org/10.1016/j.ijbiomac.2017.01.093.

[161] S. Tripathy, S.R. Krishna Vanjari, V. Singh, S. Swaminathan, S.G. Singh, Electrosprun manganese(III) oxide nanofiber based electrochemical DNA-nanobiosensor for zeptomolar detection of dengue consensus primer, Biosens. Bioelectron. 90 (2017) 372–387. Available from: https://doi.org/10.1016/j.bios.2016.12.008.

[162] A. Valipour, M. Roushani, Using silver nanoparticle and thiol graphene quantum dots nanocomposite as a substratum to load antibody for detection of hepatitis C virus core antigen: electrochemical oxidation of riboflavin was used as redox probe, Biosens. Bioelectron. 89 (2017) 946–951. Available from: https://doi.org/10.1016/j.bios.2016.09.086.

[163] A. Nehra, W. Chen, D.S. Dimitrov, A. Puri, K.P. Singh, Graphene oxide-polycarbonate track-etched nanosieve platform for sensitive detection of H1N1, H5N1, and H7N9 virus using ZnO nanorods for sensitivity enhancement, Sens. Actuators B: Chem. 228 (2016) 36–42. Available from: https://doi.org/10.1016/j.snb.2015.07.068.

[164] A. Valipour, M. Roushani, TiO2 nanoparticles doped with Celestine Blue as a label in a sandwich immunoassay for the hepatitis C virus core antigen using a screen printed electrode. Microchim. Acta 184 (2017) 2015–2022. Available from: https://doi.org/10.1007/s00604-017-2190-7.

[165] F. Zhao, L. Cao, Y. Liang, Z. Wu, Z. Chen, R. Zeng, Label-free amperometric immunosensor based on graphene oxide and ferrocene-chitosan nanocomposites for detection of hepatitis B virus antigen, J. Biomed. Nanotechnol. 13 (2017) 1300–1308. Available from: https://doi.org/10.1016/j.jbionano.2017.2415.

[166] A. Nehra, W. Chen, D.S. Dimitrov, A. Puri, K.P. Singh, Graphene oxide-polycarbonate track-etched nanosieve platform for sensitive detection of human immunodeficiency virus envelope glycoprotein, ACS Appl. Mater. Interfaces 9 (2017) 32621–32634. Available from: https://doi.org/10.1021/acsami.7b12103.

[167] J. Huang, Z. Xie, Z. Xie, S. Luo, L. Xie, L. Huang, et al., Silver nanoparticles coated graphene electrochemical sensor for the ultrasensitive analysis of avian influenza virus H7, Anal. Chim. Acta 913 (2016) 121–127. Available from: https://doi.org/10.1016/j.aca.2016.01.050.

[168] J.H. Han, D. Lee, C.H.C. Chew, T. Kim, J.J. Pak, A multi-virus detectable microfluidic electrochemical immunosensor for simultaneous detection of H1N1, H5N1, and H7N9 virus using ZnO nanorods for sensitivity enhancement, Sens. Actuators B: Chem. 228 (2016) 36–42. Available from: https://doi.org/10.1016/j.snb.2015.07.068.

[169] E. Eksin, A. Erdem, Chitosan-carbon nanofiber modified single-use graphite electrodes developed for electrochemical detection of DNA hybridization related to hepatitis B virus, Electroanalysis 28 (2016) 2514–2521. Available from: https://doi.org/10.1002/elan.201501113.

[170] X.G. Eng, F.Z. Hang, Q.G. Ao, Y.L. Ei, sensitive impedimetric immunoassay of Japanese encephalitis virus based on enzyme biocatalyzed precipitation on a gold nanoparticle-modified screen-printed carbon electrode, Anal. Sci. 32 (2016) 1105–1109. Available from: https://doi.org/10.2116/analsci.32.1105.

[171] A. Attar, J. Mandli, M.M. Ennaji, A. Amine, Label-free electrochemical impedance detection of rotavirus based on immobilized antibodies on gold sononanoparticles, Electroanalysis 28 (2016) 1839–1846. Available from: https://doi.org/10.1002/elan.201600179.

[172] J. Narang, C. Singhal, N. Malhotra, S. Narang, A.K. PN, R. Gupta, et al., Impedimetric genosensor for ultratrace detection of hepatitis B virus DNA in patient samples assisted by zeolites and MWCNT nano-composites, Biosens. Bioelectron. 86 (2016) 566–574. Available from: https://doi.org/10.1016/j.bios.2016.07.013.

[173] C.C. Chen, Z.L. Lai, G.J. Wang, C.Y. Wu, Polymerses chain reaction-free detection of hepatitis B virus DNA using a nanostructured impedance biosensor, Biosens. Bioelectron. 77 (2016) 603–608. Available from: https://doi.org/10.1016/j.bios.2015.10.028.
[174] S. Karash, R. Wang, L. Kelso, H. Lu, T.J. Huang, Y. Li, Rapid detection of avian influenza virus H5N1 in chicken tracheal samples using an impedance aptasensor with gold nanoparticles for signal amplification, J. Virol. Methods 236 (2016) 147–156. Available from: https://doi.org/10.1016/j.jviromet.2016.07.018.

[175] M.H. Mashhadizadeh, R.P. Talemi, Synergistic effect of magnetite and gold nanoparticles onto the response of a label-free impedimetric hepatitis B virus DNA biosensor, Mater. Sci. Eng. C 59 (2016) 773–781. Available from: https://doi.org/10.1016/j.msec.2015.10.082.

[176] M. Veerapanidand, R. Hunter, S. Neethirajan, Dual immunosensor based on methylene blue-electroadsorbed graphene oxide for rapid detection of the influenza A virus antigen, Talanta 155 (2016) 250–257. Available from: https://doi.org/10.1016/j.talanta.2016.04.047.

[177] Z. Yang, Y. Zhuo, R. Yuan, Y. Chai, A nanohybrid of platinum nanoparticles-porous ZnO—hemin with electrocatalytic activity to construct an amplified immunosensor for detection of influenza, Biosens. Bioelectron. 78 (2016) 321–327. Available from: https://doi.org/10.1016/j.bios.2015.10.073. Available from: doi:.

[178] A.R. Rafidah, S. Faridah, A.A. Shahrul, M. Mazidah, I. Zamri, Chronoamperometry measurement for rapid cucumber mosaic virus detection in plants, Procedia Chem. 20 (2016) 25–28. Available from: https://doi.org/10.1016/j.proche.2016.07.003.

[179] S.S. Low, J.S.Y. Chia, M.T.T. Tan, H.-S. Loh, P.S. Khiew, A. Singh, et al., A proof of concept: detection of avian influenza H5 gene by a graphene-enhanced electrochemical genosensor, J. Nanosci. Nanotechnol. 16 (2016) 2438–2446. Available from: https://doi.org/10.1166/jnn.2016.11714.

[180] D. Lin, T. Tang, D. Jed Harrison, W.E. Lee, A.B. Jemere, A regenerating ultrasensitive electrochemical impedance biosensor for the detection of adenovirus, Biosens. Bioelectron. 68 (2015) 129–134. Available from: https://doi.org/10.1016/j.bios.2014.12.032.

[181] Z. Wu, C.H. Zhou, J.J. Chen, C. Xiong, Z. Chen, D.W. Pang, et al., Bifunctional magnetic nanobeads for sensitive detection of avian influenza A (H7N9) virus based on immunomagnetic separation and enzyme-induced metallization, Biosens. Bioelectron. 68 (2015) 586–592. Available from: https://doi.org/10.1016/j.bios.2015.01.051.

[182] M.H. Mashhadizadeh, R.P. Talemi, Simple in situ functionalizing of magnetite nanoparticles by 4-nitrobenzenediazonium for construction of a sensitive electrochemical DNA biosensor for detection of a DNA sequence related to Hepatitis B virus, J. Iran. Chem. Soc. 12 (2015) 1747–1756. Available from: https://doi.org/10.1007/s13738-015-0649-1.

[183] L.X. Fang, J.T. Cao, K.J. Huang, A sensitive electrochemical biosensor for specific DNA sequence detection based on flower-like VS2, graphene and Au nanoparticles signal amplification, J. Electroanal. Chem. 746 (2015) 1–8. Available from: https://doi.org/10.1016/j.jelechem.2015.03.026.

[184] Y. Wang, X. Bai, W. Wen, X. Zhang, S. Wang, Ultrasensitive electrochemical biosensor for HIV gene detection based on graphene stabilized gold nanoclusters with exonuclease amplification, ACS Appl. Interfaces 7 (2015) 18872–18879. Available from: https://doi.org/10.1021/acsi.1500585.

[185] J.I.A. Rashid, N.A. Yusof, J. Abdullah, U. Hashim, R. Hajian, A. Novel Disposable, Biosensor based on SiNWs/AuNPs modified-screen printed electrode for dengue virus DNA oligomer detection, IEEE Sens. J. 15 (2015) 4420–4421. Available from: https://doi.org/10.1109/JSEN.2015.2417911.

[186] M.M.S. Silva, A.C.M.S. Dias, B.V.M. Silva, S.L.R. Gomes-Filho, L.T. Kubota, M.O.F. Goulart, et al., Electrochemical detection of dengue virus NS1 protein with a poly(allylamine)/carbon nanotube layered immunoelectrode, J. Chem. Technol. Biotechnol. 90 (2015) 194–200. Available from: https://doi.org/10.1002/jctb.4305.

[187] S. Dong, R. Zhao, J. Zhu, X. Lu, Y. Li, S. Qiu, et al., Electrochemical DNA biosensor based on a tetrahedral nanostructure probe for the detection of avian influenza A (H7N9) virus, ACS Appl. Mater. Interfaces 7 (2015) 8834–8842. Available from: https://doi.org/10.1021/acsami.5b01438.

[188] Z. Shakoori, S. Salimian, S. Kharrazzi, M. Adabi, R. Saber, Electrochemical DNA biosensor based on gold nanorods for detecting hepatitis B virus, Anal. Bioanal. Chem. 407 (2015) 455–461. Available from: https://doi.org/10.1007/s00216-014-8303-9.

[189] F.S. Diba, S. Kim, H.J. Lee, Amperometric bioaffinity sensing platform for avian influenza virus proteins with aptamer modified gold nanoparticles on carbon chips, Biosens. Bioelectron. 72 (2015) 355–361. Available from: https://doi.org/10.1016/j.bios.2015.05.020.

[190] J.P. Bartolome, L. Echegoyen, A. Fragoso, Reactive carbon nano-onion modified glassy carbon surfaces as DNA sensors for human papilloma virus oncogene detection with enhanced sensitivity, Anal. Chem. 87 (2015) 6744–6751. Available from: https://doi.org/10.1021/acsanalchem.5b00924.

[191] Y. Fu, Z. Callaway, J. Lum, R. Wang, J. Lin, Y. Li, Exploiting enzyme catalysis in ultra-low ion strength media for impedance biosensing of avian influenza virus using a bare interdigitated electrode, Anal. Chem. 86 (2014) 1965–1971. Available from: https://doi.org/10.1021/ac502550f.

[192] X. Wang, L. Wang, W. Yang, S. Ai, A multiple-promoted silver enhancement strategy in electrochemical detection of target virus, Sens. Actuators B: Chem. 194 (2014) 276–282. Available from: https://doi.org/10.1016/j.snb.2013.12.068.

[193] V. Van Thu, P.T. Dung, L.T. Tam, P.D. Tam, Biosensor based on nanocomposite material for pathogenic virus detection, Colloids Surf. B: Biointerfaces 115 (2014) 176–181. Available from: https://doi.org/10.1016/j.colsurfb.2013.11.016.

[194] Q. Cheng, J.F. Li, L. Zhang, L. Liu, Functional magnetic nanoparticles for clinical application: electrochemical immunoassay of hepatitis B surface antigen and α-fetoprotein, Anal. Lett. 47 (2014) 592–605. Available from: https://doi.org/10.1080/00032719.2013.848362.

[195] H.E. Lee, Y.O. Kang, S.H. Choi, Electrochemical-DNA biosensor development based on a modified carbon electrode with gold nanoparticles for influenza a (H1N1) detection: effect of spacer, Int. J. Electrochem. Sci. 9 (2014) 6793–6808. Available from: https://doi.org/10.1371/journal.pone.0120026.

[196] Z. Xie, J. Huang, S. Luo, Z. Xie, L. Xie, J. Liu, et al., Ultrasensitive electrochemical immunoassay for avian influenza subtype H5 using nanocomposite, PLoS One 9 (2014) 96–99. Available from: https://doi.org/10.1371/journal.pone.0094685.
Nanosensors for healthy cities

[197] M.H. Mashhadizadeh, R. Pourtaghavi Talemi, A highly sensitive and selective hepatitis B DNA biosensor using gold nanoparticle electrodeposition on an Au electrode and mercaptobenzaldehyde, Anal. Methods 6 (2014) 8956–8964. Available from: https://doi.org/10.1039/c4ay01465k.

[198] L. Krejcova, L. Nejdl, M.A.M. Rodrigo, M. Zurek, M. Matousek, D. Hynek, et al., 3D printed chip for electrochemical detection of influenza virus labeled with CdS quantum dots, Biosens. Bioelectron. 54 (2014) 421–427. Available from: https://doi.org/10.1016/j.bios.2013.10.031.

[199] X. Wang, L. Chen, X. Su, S. Ai, Electrochemical immunosensor with graphene quantum dots and apoferritin-encapsulated Cu nanoparticles double-assisted signal amplification for detection of Avian leukosis virus subgroup, J. Biosens. Bioelectron. 47 (2013) 171–177. Available from: https://doi.org/10.1016/j.jbioss.2013.03.021.

[200] S. Nourani, H. Ghourchian, S.M. Boutorabi, Magnetic nanoparticle-based immunosensor for electrochemical detection of hepatitis B surface antigen, Anal. Biochem. (2013). Available from: https://doi.org/10.1016/j.ab.2013.06.011.

[201] A.E.K. Peh, S.F.Y. Li, Dengue virus detection using impedance measured across nanoporous alumina membrane, Biosens. Bioelectron. (2013). Available from: https://doi.org/10.1016/j.bios.2012.10.054.

[202] S. Wang, L. Li, H. Jin, T. Yang, W. Bao, S. Huang, et al., Electrochemical detection of hepatitis B and papilloma virus DNAs using SWCNT array coated with gold nanoparticles, Biosens. Bioelectron. (2013). Available from: https://doi.org/10.1016/j.bios.2012.08.021.

[203] J.H. Lee, B.K. Oh, J.W. Choi, Electrochemical sensor based on direct electron transfer of HIV-1 virus at Au nanoparticle modified ITO electrode, Biosens. Bioelectron. (2013). Available from: https://doi.org/10.1016/j.bios.2013.06.010.

[204] J. Deng, C.S. Toh, Impedimetric DNA biosensor based on a nanoporous alumina membrane for the detection of the specific oligonucleotide sequence of dengue virus, Sensors (Switzerland) 13 (2013) 7774–7785. Available from: https://doi.org/10.3390/s1309060774.

[205] M. Liang, L. Wang, C. Ma, M. Zhang, G. Xie, Sandwich immunosensor for hepatitis C virus non-structural 5A protein using a glassy carbon electrode modified with an Au-MoO3/chitosan nanocomposite, Anal. Lett. 46 (2013) 1241–1254. Available from: https://doi.org/10.1080/00032719.2012.755684.

[206] N. Van Hieu, T. Trung, M.A. Tuan, T.Q. Hue, C. Van Tuan, Polyaniline nanowires-based electrochemical immunosensor for label free detection of Japanese encephalitis virus, Anal. Lett. 46 (2013) 1229–1240. Available from: https://doi.org/10.1080/00032719.2012.755688.

[207] Y. Cao, Q. Jiang, T. Li, X. Du, N. Gan, F. Hu, An ultrasensitive electrochemical immunosensor for HIV p24 based on Fe3O4@SiO2 nanomagnetic probes and nanogold colloid-labeled enzyme–antibody copolymer as signal tag, Materials (Basel) 6 (2013) 1255–1269. Available from: https://doi.org/10.3390/ma6041255.

[208] A. Giamberardino, M. Labib, E.M. Hassan, J.A. Tetro, S. Springthorpe, S.A. Sattar, et al., Ultrasensitive norovirus detection using DNA aptamer technology, PLoS One 8 (2013) 1–9. Available from: https://doi.org/10.1371/journal.pone.0079087.

[209] Y. Jiang, H. Xiang, M. Liang, Y. Li, L. Wang, C. Ma, et al., Multispecific-HRP-DNA-coated CMWNTs as signal labels for an ultrasensitive hepatitis C virus core antigen electrochemical immunosensor, Biosens. Bioelectron. 47 (2013) 467–474. Available from: https://doi.org/10.1016/j.bios.2013.03.058.

[210] A.C.M.S. Dias, S.L.R. Gomes-Filho, M.M.S. Silva, R.F. Dutra, A sensor tip based on carbon nanotube-ink printed electrode for the dengue virus NS1 protein, Biosens. Bioelectron. 44 (2013) 216–221. Available from: https://doi.org/10.1016/j.bios.2012.12.033.

[211] S.Y. Niu, Y.Q. Qin, B. Han, Electrochemical DNA biosensor improved by imidazo[4,5-f]1,10-phenanthroline iron(iii) as an indicator based on pt-nanoparticles and carbon nanotubes modified electrode, Asian J. Chem. 25 (2013) 4375–4379.

[212] K. Shang, J. Zhu, X. Meng, Z. Cheng, S. Ai, Multifunctional Fe3O4 core/Ni-Al layered double hydroxides shell nanospheres as labels for ultra-sensitive electrochemical immunosassay of subgroup J of Avian leukosis virus, Biosens. Bioelectron. (2012). Available from: https://doi.org/10.1016/j.bios.2012.04.035.

[213] M.S. Cheng, J.S. Ho, C.H. Tan, J.P.S. Wong, L.C. Ng, C.S. Toh, Development of an electrochemical membrane-based nanobiosensor for ultrasensitive detection of dengue virus, Anal. Chim. Acta (2012). Available from: https://doi.org/10.1016/j.aca.2012.03.017.

[214] B.T.T. Nguyen, A.E.K. Peh, C.Y.L. Chee, K. Fink, V.T.K. Chow, M.M.L. Ng, et al., Electrochemical impedance spectroscopy characterization of nanoporous alumina dengue virus biosensor, Biologicalchemistry (2012). Available from: https://doi.org/10.1016/j.bioelechem.2012.04.006.

[215] C. Ma, M. Liang, G. Xie, B. Liu, H. Xiang, W. Zhang, Label-free sandwich type of immunosensor for hepatitis C virus core antigen based on the use of gold nanoparticles on a nanostructured metal oxide surface, Microchim. Acta 178 (2012) 331–340. Available from: https://doi.org/10.1007/s00604-012-0842-1.

[216] V. Rai, H.C. Hapuarachchi, L.C. Ng, S.H. Soh, Y.S. Leo, C.S. Toh, Ultrasensitive cDNA detection of dengue virus RNA using electrochemical nanoporous membrane-based biosensor, PLoS One 7 (2012) 1–7. Available from: https://doi.org/10.1371/journal.pone.0042346.

[217] L.D. Tran, B.H. Nguyen, N. Van Hieu, H.V. Tran, H. Le Nguyen, P.X. Nguyen, Electrochemical detection of short HIV sequences on chitosan/Fe3O4 nanoparticle based screen printed electrodes, Mater. Sci. Eng. C (2011). Available from: https://doi.org/10.1016/j.msec.2010.11.007.

[218] L.D. Tran, B.H. Nguyen, Q.P. Do, H. Le Nguyen, Development of interdigitated arrays coated with functional polyaniline/MWCNT for electrochemical biodetection: application for human papilloma virus, Talanta (2011). Available from: https://doi.org/10.1016/j.talanta.2011.06.048.

[219] U. Jarocka, M. Wasowicz, H. Radecka, T. Malinowski, L. Michalczyk, J. Radecki, Impedimetric immunosensor for detection of plum pox virus in plant extracts, Electroanalysis 23 (2011) 2197–2204. Available from: https://doi.org/10.1007/s00604-011-00152.

[220] X. Liu, Z. Cheng, H. Fan, S. Ai, R. Han, Electrochemical detection of avian influenza virus H5N1 gene sequence using a DNA aptamer immobilized onto a hybrid nanomaterial-modified electrode, Electroc. Acta 56 (2011) 6266–6270. Available from: https://doi.org/10.1016/j.electacta.2011.05.055.