Chapter 19
Nano-Biosensing Devices Detecting Biomarkers of Communicable and Non-communicable Diseases of Animals

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Abstract  Diseases are either communicable or non-communicable. Communicable diseases or infectious diseases are caused by interactions between two living organisms whereas non-communicable diseases are either hereditary or due to the living environment of animals. Animals are very susceptible to various types of infections and pathogens may live outside or inside their body very conveniently. Epidemic diseases affect animal herd, livestock and the leading cause of animal mortality which may result in significant losses to the agricultural economy. Animal diseases are a matter of concern due to the direct effect on the economy as well as the possibility of pathogen transmission in humans. The accurate detection of animal diseases is an important factor to control diseases in livestock and in wild animals. Disease diagnosis in animals is very challenging and based on the variety of examinations and tests. In this context, nano-biosensors exhibit better disease detection capacity than conventional methods. Nano-biosensors show high sensitivity, stability, reproducibility with a lower limit of detection. This chapter emphasized the insight of communicable and non-communicable animal diseases and their detection through nano-biosensing devices. Some important animal diseases are discussed along with a description of developed nano-biosensors for them. Nano-biosensor functionalized with disease-related biomarkers performed better than any other conventional methods in various aspects.

Keywords  Biosensor · Communicable diseases · Non-communicable diseases · Animal diseases · Nanotechnology
19.1 Introduction

19.1.1 Overview (History of Animal Diseases)

Animals are an important part of our ecosystem and their existence either directly or indirectly affects the life of humans in various aspects and vice versa. Like humans, animals also suffer with several types of communicable and non-communicable diseases. Sometimes there are some common diseases also found in humans and animals as well as they can play a role of a disease carrier for each other’s, for example, anthrax, brucellosis, giardiasis, and swine flu. Health risk of animal population may have an impact on food supply chains which is a threat to human health with long lasting effects and to economy as well. For the animal disease control which are communicable to man from livestock as well as wildlife animals, several organization including WHO conduct various programmes. These diseases known as zoonoses, comprised of existing infectious disease along with newly identified infectious disease to monitor the impact on human health.

History related to animal diseases describes that human and animal diseases developed parallely. Aristotle, the father of Biology and Hippocrates, the father of medicines, demonstrate animals and man’s diseases symptomatology as well as therapy in their writing. Ancient literature are evident to animal and human diseases which include Egyptian, Roman, and Greeks monographs. In history, agriculture, domesticated animals were focused particularly. After the discovery of microorganisms by Pasteur, animal diseases became a matter of concern for veterinarians because of their direct effect on human health by consuming animal origin foods like meat and dairy products. After that basic research and zoonoses have been started for the detection and treatment of animal diseases (Charles et al. 2018).

19.1.2 Communicable and Non-Communicable Diseases

Any disease either in animals or in humans may be communicable and non-communicable. The communicable term implies for interaction or communication between two living things which are known as host and parasite. The parasite exists in host cells and lives at the expense of their cellular machinery. Parasites are certain microorganisms such as virus, bacteria, protozoans, arthropods, and fungi, which are unable to survive on their own, so they depend on host organism for food, multiplication, or some other requirements. The disease-causing ability of a parasite is known as pathogenicity whereas ability to cause infection is known as virulence. The virulence property of a parasite is differed from one host to other, that it can be virulent for one but not to other hosts. Most of the parasite occurred in the atmosphere as an inactive form until they find appropriate conditions to establish themselves inside host cells. For example, Clostridium and Bacillus bacteria occurred as an inactive form known as spores for several years even in harsh environmental conditions.
The host cell defense system i.e. immune system provides a variety of mechanical and chemical barriers against infection, and to establish disease in the host body, it is essential to cross all these barriers. In animals, communicable diseases can be spread through direct contact of animals, waste of sick animals, unhygienic housing of animals, and presence of microorganisms in feed and water. Certain types of lice, mites, ticks, and fleas present inside or outside of body, also play a role in spreading of diseases, for example, plague (Heymann 2008). Some common types of communicable diseases and their host animals are represented in Fig. 19.1.

Non-communicable diseases, as the name suggested, not communicate from one animal to another and do not involve any virulent pathogens. Non-communicable diseases are caused by hereditary factors, poor feed, lack of nutrients, and environmental factors in surroundings. Sometimes it also caused by cuts, burns, certain toxic agents (insecticides, pesticides, fungicides, fluorine, and herbicides), or poisonous plants, and broken bones. Sometimes humans are responsible for some metabolic diseases in animals by injecting chemicals which causes the unsuitable alteration in body environment such as oxytocin is very commonly used in dairy animals to get more milk due to which contraction of uterus takes place and causes immense pain to the animal. Any disturbance in normal physiological conditions to maintain homeostasis and stability, leads to metabolic diseases. Non-communicable diseases are chronic and can be acute as well which causes a huge loss in milk, meat, and wool
production. The working capacity and rate of reproduction of livestock can also be affected (Habib and Saha 2010).

19.1.3 Conventional Approaches for Detection of Animal Diseases

Since it is impossible for a veterinarian to interrogate the animal, diagnosis of the animal disease includes a number of tests and examinations based on inspection of behaviour, palpation percussion, smells, eye examination, appearance, etc. Diseases like pullorum can be detected by agglutination test, tuberculin skin test for tuberculosis, faeces and eggs examination can be done in lab for early detection of diseases. Determination of chemicals, toxins in blood, or body fluids are performed for several years for a diagnosis of a variety of animal diseases.

19.1.4 Nano Biosensors and Its Applications

To control certain chronic communicable and non-communicable diseases, early and fast detection is essential in a population of animals such as a herd of cattle. In recent times, every year newly emerging diseases threaten animal health are a matter of concern. For the early stage detection of diseases in the case of animals, there is currently a lack of authentication and cost-effective diagnostics. Considering biosensing technologies, as they have the potential to overcome these problems by developing novel diagnostic tools because of their high sensitivity to detect disease-related biomarkers with a low limit of detection. The available conventional sensors are used in livestock monitoring and also as a tool for the assessment and monitoring in health monitoring and disease detection. These sensors when integrated with wireless data transfer through a server or with cloud-based systems, enabling access to the analyzed data from any internet enabled device. Applications of nanobiosensor not only help in the reduction of the current costs for reagents, handling samples, time of analysis, and cost of transportation but also helps in adapting and promoting the handling of livestock. Biosensor is a simple, miniaturized analytical device which is utilized for rapid and efficient diagnosis of infectious diseases and has the ability for real-time analysis (Sagadevan and Periasamy 2014).

19.1.5 Biomarkers and Their Utilization in Biosensors

Biomarkers are typical indicators for biological, pathogenic, or pharmacologic processes which are used to identify an event or physiologic process of interest. For
animal medicine, these biomarkers help in the early detection of several cardiopulmonary diseases, confirmation of doubtful processes (normal or abnormal), and contribute to the establishment of prognosis to decide a specific treatment (Fry and Dunbar 2007; Carretón et al. 2013). Also, they are used to detect the course of therapy or to predict safety or drug response. Biosensor consists of analytes, bio-recognition element (a biological element to detect analyte), and transducer surface (physico-chemical detector component) to convert any biological signal to a measurable electric signal. Biomarkers play a key role in the fabrication of biosensors to detect several important diseases like cancer, Alzheimer, organ health monitoring after a transplant, diabetes, neurological disorders, etc. Biomarkers exploit in biosensors could be antigen-antibody, dopamine, uric acid, hydrogen peroxide, ascorbic acid, hormones, microRNA, enzymes, or whole cell (bacteria/viruses) (Zetterberg et al. 2019; Dahal 2019; Viitanen et al. 2014; Scherr et al. 2016; Pereira et al. 2016; Çolak et al. 2013; Alcaraz et al. 2016; Fei et al. 2016; Peng et al. 2017). Some major diseases of animals along with their biomarkers are given in Table 19.1.

**19.1.6 How Can Animal Diseases Affect Human Health?**

In most of the cases, human infectious diseases which include disease agents and pathogens are acquired from animal species. Several diseases such as SARS, Nipah virus, avian influenza, cat scratch disease, West Nile disease, mad cow disease etc. are associated with animals. Recent pandemic Covid 19 is also acquired from bat species. So, humans and animal’s diseases are directly proportional to each other in about 60–75% cases (Wang and Anderson 2019).

**19.2 Communicable and Non-Communicable Diseases of Animals**

**19.2.1 Communicable Diseases of Animals**

**Aflatoxicosis:** Aflatoxicosis is a widespread disease in animals and affects several animal species including cattle, chicks, ducklings, turkeys, horses, and pigs. Disease is caused by a mycotoxin which is produced by *Aspergillus flavus*, a most popular form of fungus. The feed items like millets, maize, soybeans, and peanuts, contaminated with fungi are source of disease. Aflatoxin is a highly toxic metabolite and mainly affects the liver through ingestion of contaminated feeds. The disease is characterized by drop in egg production particularly in poultry birds, loss of weight, and sometimes hepatocellular tumors appeared in severe conditions. Aflatoxicosis is associated with great economic loss as it reduced productivity by many folds, for
| S. No | Animal disease | Disease causing pathogen | Host | Symptoms | Associated Biomarkers |
|-------|----------------|--------------------------|------|----------|-----------------------|
| 1.    | Aflatoxicosis  | Aspergillus flavus       | Cattle, chicks, ducklings, turkeys, horses, pigs | Drop in egg production, weight loss, hepatic cellular tumors | Aflatoxin B1, B2, G1, G2, M1, P1, Quinine N-7 guanine (AFB1-N7-Gua) |
| 2.    | African swine fever | DNA virus of Arboviridae family | Domestic and wild pigs | High fever, loss of appetite, vomiting, diarrhea, loss of weight, respiratory signs, chronic skin ulcers | SCD163 & E75CV (strain of virus), ASFV DNA |
| 3.    | Anthrax         | Bacillus anthracis       | Cattle | Fever, difficulty in breathing, loss of appetite, Crepitation swelling | Calcium dipicolinate, dipicolinic acid,|
| 4.    | Avian influenza | Avian influenza A viruses | Birds, poultry | Cough, cold, fever, headache, shortness of breath, and sore throat | AIV H5-hemagglutinin, IL-6, microRNA |
| 5.    | Bluetongue      | Bluetongue virus (BTV)   | Ruminants | Eye nasal discharge, high fever, drooling, inflammation | VP-7 |
| 6.    | Bovine leukosthenia | Clostridium botulinum | Cattle and avian species | Hindlimb weakness, paralysis, death | Botulinum neurotoxin serotype A |
| 7.    | Brucellosis     | Brucella                 | Goats, sheep, cows, ruminants like deer, bison and elk | Stillbirth or abortion | S19 and RB51 (continued) |
| S. No | Animal disease | Causing pathogen | Host | Symptoms | Associated Biomarkers |
|-------|----------------|-----------------|------|----------|----------------------|
| 8.    | Ehrlichiosis   | *Ehrlichia, Anaplasma, and Neorickettsia of Anaplasmataceae family* | Cannines | fever, Reticuloendothelial hyperplasia, lymphadenopathy, Splenomegaly, loss of stamina, stiffness, and edema of limbs | IgM and IgG antibodies, antigenic proteins P28-19, and *Ehrlichia* Hsp60 |
| 9.    | Hendra virus disease | *Hendra virus* | fruit bats, horses, humans | fever, cough, headache, tiredness, meningitis, coma | microRNA, physiological biomarkers like glucose, triglycerides, urea, protein etc. |
| 10.   | Hydatid        | *Echinococcus granulosus* tapeworm | Dogs | weight loss, weakness and loss of appetite, allergy | interferon-gamma, IL-4, IL-10, specific IgE, total IgG, Glutathione S-Transferase, microRNA |
| 11.   | Listeriosis    | Listeria monocytogenes | Animals, fishes, crustacean, birds and humans | encephalitis, meningitis, meningoencephalitis, stillbirth, abortion septicaemia, perinatal infections | invasion-associated protein, hemolysin, BE-LisAll |
| 12.   | Newcastle      | Newcastle disease virus | domestic poultry and other species of birds | Respiratory disease, diarrhea, depression, or nervous manifestations | Nucleoprotein, glycoprotein, antibodies |
| 13.   | Nipah         | Nipah virus     | Fruit bat, Pigs, humans | Barking pig syndrome, encephalitic syndrome | Nipah virus G-protein |
example, milk production can be reduced by 15% or more (Dalvi 1986; Solis-Cruz et al. 2019).

**African swine fever**: African swine fever (ASF) is a severely contagious viral disease affecting domestic and wild pigs. It is caused by a DNA virus of *Asfarviridae* family which also responsible for infection in ticks of *Ornithodoros* genus. ASF associated with serious loss in production (pork, lard, leather, glue, fertilizer, and a variety of medicines produces through pigs) and economy. The virus is transmitted through a contaminated feed to animals and fomites such as shoes, knives, cloth, equipment, and vehicles, i.e. non-living things. The virus shows high resistant capacity for harsh environmental conditions. ASF has been reported in Europe, South America, Asia, Africa, and Caribbean. Symptoms of ASF include acute and chronic forms. Acute forms indicated by high fever, loss of appetite, vomiting, diarrhoea, haemorrhages in the skin, and death within few days (6–20 days). Chronic forms are characterized by loss of weight, respiratory signs, chronic skin ulcers, intermittent fever, and arthritis. Chronic forms are less intense clinically and can persist for longer period with low mortality rate (Dixon et al. 2019).

**Anthrax**: A large spore forming *Bacillus anthracis* bacteria is responsible for anthrax disease. It is an extremely infectious and fatal disease that causes acute mortality in cattles. The bacterial toxin is highly potent which immediately shows ill effects and a high mortality rate. After exposure to this bacterial infection, symptoms usually appear within 3–7 days and animal death occurred usually within 2 days. Cattles usually get infections by grazing and inhaling the spores of bacteria which are colourless, odourless, and tasteless. The infected animal usually expresses sudden symptoms such as fever, difficulty in breathing, loss of appetite, Crepitation swelling over the shoulder hip, and back, which is followed by death. This is a highly dangerous disease and exhibit potential loss of economy (Doganay and Demiraslan 2015).

**Avian influenza**: Avian influenza or bird flu is caused by avian influenza A viruses which naturally occur among wild water birds. The virus generally infects birds, poultry, animals, and sometimes human beings may also get infected through contaminated poultry. Although humans rarely get infected with this virus, however virus can change itself and gain the ability to infect humans and spread among them. Influenza virus have the quality to change themselves time to time and certain strains spread easily in human populations. Symptoms arise within 2–8 days and include cough, cold, fever, headache, shortness of breath, and sore throat. The disease refers to high mortality rate in humans also (Li et al. 2019). In recent times poultry business is one of the major areas of interest because of high demand in food industries. But avian influenza is one of the big challenges as it may cause major economic loss. Recent advancement makes possible to detect and continuously monitoring of disease through biosensors, wearable sensors, real time monitoring, and data management (Raj and Jayanthi 2018; Vidic et al. 2017) (Fig. 19.2).

**Bluetongue**: Bluetongue disease refers mainly the disease of ruminants including both domestic and wild animals, however Sheep are badly infected with disease. Cattle although frequently get infection than sheep but they lack symptoms most of the times. It is normally an insect-borne disease caused by bluetongue virus (BTV) and transmitted by different species of midges Culicoides. The infected animals
Botulism: Botulism is a food borne disease caused by Clostridium botulinum bacteria which produce highly potential neurotoxin commonly known as botulinum. It is a rapid onset fatal disease of cattle and avian species. Botulism typically represents by hindlimb weakness followed by collapse, paralysis, and death. Animal carcasses, poorly prepared silage and rotting organic material are the main sources of bacterial infection. Although the vaccine is available for this disease but still it is not completely eradicated. The disease outbreak can be seen in poultry and waterfowl (Mariano et al. 2019).

Brucellosis: Brucellosis is a bacterium causing the disease which mainly affects livestock including goats, sheep, cows, and some wild ruminants like deer, bison, and elk. It is caused by bacteria of genus Brucella. The disease mainly characterized by stillbirth or abortion in animals. The disease is spread through contaminated milk, birthing fluids, the infected placenta of animals, or direct contact with other animals or human beings. Canines can also infect with bacteria, but they are rarely spread infection to human beings. Complications associated with brucellosis consist of inflammation of the brain, infection of the heart’s inner lining, meningitis, and lesions on the bones and joints (Shoukat et al. 2017).

Ehrlichiosis: Ticks are the carrier of this disease which commonly developed in canine bitten by infected ticks. It is caused by intracellular obligate organisms that belong to genus Ehrlichia, Anaplasma, and Neorickettsia of Anaplasmataceae family. The parasite is primarily infecting the immune cells of canines and humans. Infected
animals are suffered from fever, Reticuloendothelial hyperplasia, lymphadenopathy, Splenomegaly, loss of stamina, stiffness, and edema of limbs (Mylonakis et al. 2019).

**Hendra virus Disease**: It is mainly a disease of fruit bats which can be infectious to horses also. Hendra virus infection has infrequently been infectious to humans who came into contact with an infected horse. Infected horses may possess a range of symptoms like fever, respiratory, and neurological disorders and show rapid onset illness. The host develops symptoms within 5–21 days after infection with Hendra virus. At initial stage, some common symptoms appear as fever, cough, headache, and tiredness whereas later, meningitis and coma have been seen in severe infection conditions. Hendra virus disease can be fatal sometimes (Field et al. 2011).

**Hydatid disease**: Hydatidosis, echinococcosis, or hydatid disease, caused by cyst consist of *Echinococcus granulosus* tapeworm (Dog Tapeworm) larval stage, is an extremely serious condition and sometimes may be fatal. The disease is mainly infecting dogs and other canines. Infected animals shed eggs in their faeces which further infect other host by swallowing these eggs or by direct contact with infected dogs. The cyst can be remained inside the liver and lungs for months to several years. The disease show signs of weight loss, weakness, and loss of appetite. The rupture of cyst may cause serious allergic reactions even death of animals. Although Hydatid infection is potentially severe but may be treatable. The disease occurs worldwide, commonly in grazing areas (Qingling et al. 2014).

**Listeriosis**: Animals, fishes, crustacean, birds, and even humans can be infected with Listeriosis; which is a serious infection and become fatal sometimes. *Listeria monocytogenes* is the causative agent of this food borne disease. It has the potential to transmit from one cell to another and can cross intestinal, placental, and blood brain barriers. The disease is characterized by encephalitis, meningitis, meningoencephalitis, stillbirth, abortion septicemia, perinatal infections. Listeriosis is a sporadic disease which spread through soil, water, milk, meat, seafood, and vegetables. There is no vaccine available for this disease so it can be prevented only through hygienic practices (Oevermann et al. 2010).

**Newcastle disease**: Newcastle disease virus (NDV) is a causative agent of Newcastle disease of domestic poultry and other species of birds. It is primarily represented by acute respiratory diseases, but diarrhoea, depression, or nervous manifestations can also be seen predominantly as a clinical form. Infected animals shed infection through respiratory discharge, eggs, and faeces. In poultry disease, may spread by ingesting water or food contaminated with virus. Movement of infected poultry birds, contaminated equipment, or litter plays an important role for spreading viruses. The signs of disease in an infected organism are appeared in 2–12 days of exposure of virus (Brown and Bevins 2017).

**Nipah virus disease**: Nipah virus or NiV belongs to genus henipavirus and paramyxovirus family causes a highly fatal disease Nipah. Natural host of nipah virus is fruit bat and currently, it affects pigs and humans very severely with high mortality rate. The virus is spread through bat urine, faeces, birthing fluids, and saliva. It is assumed that bat excreta initiate infection in pigs. The virus mainly affects the nervous system and respiratory system. The virus is highly contagious to pigs and associated with barking pig syndrome (BPS) and encephalitic syndrome
Nipah virus may also infect dogs naturally and causes a distemper-like syndrome which is a highly fatal condition (Ang et al. 2018).

### 19.2.2 Non-Communicable Diseases

**Ruminal tympany:** It is also known as bloat. The disease mainly found in ruminant animals and characterized by high amount of gas in rumen. It can be divided into two phase, primary frothy bloat, and secondary free gas bloat. In a natural process, the rumen is dedicated for fermentation of eaten food by gut microbes and the fermentation process produces excessive amount of gas which expelled out from rumen by burping continuously but sometimes gas becomes trapped inside the rumen. This condition is remarked as bloat or ruminal tympany. In primary bloat, produced gas trapped within fermenting material which causes a raised amount of foam and unable to remove by burping. The disease is characterized by distension of abdomen on left side, distress, and difficulty in breathing. This disease can be fatal if gas accumulation process continues which also distended right side of abdomen. After visualization of such symptoms, the cattle death may occur within 3–4 h. In the secondary bloat, oesophagus becomes blocked so accumulated gas cannot be pass through it (Priyanka and Dey 2018).

**Nutritional deficiencies in animals:** In the case of animals, this is very difficult to find out the nutritional deficiencies. Most of the animals suffer from malnutrition. There is a lack of signs related to most of the nutritional deficiencies because signs are common and not specific such as loss of appetite, reduction in growth, and thriftiness. Multiple types of nutritional deficiencies may be caused in many animals due to starvation. Deficiency of some essential amino acids or suboptimal feed intake may result into protein deficiencies which causes weight loss and fatter carcasses in pigs. In lactating animals for example cows, protein deficiency directly affects milk production. Some fatty acids like linoleic acid are found very essential in the diet and utilized in production of another essential form i.e. longer chain fatty acids. The lack of linoleic acid in the diet leads to scaly dermatitis, necrosis in skin, unthrifty appearance, and hair loss in growing pigs. Deficiency of minerals like calcium and phosphorous may outcome as a disease known as rickets in pigs, dogs, and others. The disease is characterized by deformity, lameness, and bending of bones specifically long bones. Consequences of severe conditions are fracture and paralysis at posterior parts, generally in old ones. Salt deficiency also affects the growth of animals.

Iodine deficiency may result into hairless and week pig’s new-born. New-born pigs may show enlarged thyroids and histological abnormalities. Enlarged thyroid can also be seen in many animals and known as Goitre. Iodized salt may get rid of this disease.

Iron and copper deficiencies efficiently develop anaemia in animals which is caused by a reduction in haemoglobin synthesis. Anaemia may be recognized by low RBC and haemoglobin count, enlarged heart, edema, and thumps. Deficiency of zinc, selenium, and vitamin E also have an adverse effect on growing or younger ones.
Vitamins are very essential for the development and metabolic processes in humans as well as in animals. In livestock and pets, if they provided with some supplemented commercially available diets then chances are very low to face the vitamin deficiency challenges because these are fortified with vitamins. Vitamin A deficiency affects eyes, epithelial tissues of important organ systems like the nervous, urinary, digestive, respiratory, and reproductive. Vitamin K deficiency is related with lengthened blood clotting and sometimes animals may die due to haemorrhage. Riboflavin deficiency in pigs may result into impaired reproduction. Vitamin B deficiency also affects severely to neonatal pigs in terms of voice failure, hyperirritability, and incoordination like symptoms. Biotin deficiency also characterized by excessive hair loss, dermatitis, inflammation of mouth, and mucous membrane (İnnis 2000; Vieyra-Reyes et al. 2017; Shukla et al. 2016).

19.3 Development of Nano-Biosensing Devices for Detection of Animal Diseases

Nano biosensing devices exploit a biorecognition element which can be DNA/RNA, antigen/antibodies, enzymes, aptamers, and other polymers, etc. There are several studies done to develop a nano-biosensing device by using various biomarkers. Here, some types of biosensors description are given that are developed to detect several serious diseases (Table 19.2).

19.3.1 DNA Sensors

DNA based sensors are developed for the detection of several biomarkers depend upon the specific nucleic acid sequences. Various forms of nanomaterial are used for signal amplification which generated through the hybridization of two complementary DNA. Anthrax disease can be detected through a label free nanopore real time sensing device, in which a single-stranded DNA (ssDNA) was used as a molecular probe for anthrax lethal factor (Wang et al. 2014). A unique nanostructure based geno-sensor was fabricated to detect Brucella-specific probe. A gold nanoribbon surrounded by gold nano blooms were further deposited on polycrystalline gold surface by sonoelectrodeposition method. In this approach, methylene blue was used as redox marker to detect complementary sequence, sequences with one-, two-, and three bases mismatches (Rahi et al. 2015). Another DNA biosensor also studied for Brucella species detection in animals which consists of a specific oligonucleotide probe taken from S711 gene region and gold nanoparticle. This probe hybridized with complementary DNA biomarker present in a clinical sample. The device was capable to detect unamplified Brucella genomic DNA up to 7 pg µL⁻¹. The DNA biosensor
Table 19.2 List of different types of fabricated Nano-biosensors in past few years for some common animal diseases

| Nano-biosensor       | Disease                  | Nanomaterial                      | Detection limit       | Reference                |
|----------------------|--------------------------|-----------------------------------|-----------------------|--------------------------|
| DNA biosensor        | Brucellosis              | Gold (nanoribbons/nanoblooms)     | 1.71 zmol dm$^{-3}$   | Rahi et al. 2015         |
|                      |                          | Gold                              | 7 pg µL$^{-1}$        | Sattarahmady et al. 2016 |
| ehrlichiosis         |                          | QCM based                         | 4.1x10$^9$ molecules µL$^{-1}$ | Bunroddith et al. 2018 |
| Newcastle Disease    |                          | Magnetic nanoparticles (MNPs)     | 75 fM                 | Tian et al. 2016         |
| Aptasensor           | Avian influenza          | Gold                              | 0.25 HAU              | Karash et al. 2016       |
| Anthrax              |                          | Multiwalled carbon nanotubes      | 20 ng m L$^{-1}$     | Karimi and Dabbagh. 2019 |
| bovine viral diarrhea|                          | Gold                              | 800 copies mL$^{-1}$ | Park et al. 2014         |
| Imunosensor          | Bluetongue               | Gold                              | 10 – 2 fg mL$^{-1}$  | Yin et al. 2012          |
|                      | Hydatoid                 | Silicon                           | 300 fg mL$^{-1}$     | Lv et al. 2017           |
|                      | Enzootic bovine leukemia | Magnetic gold nanoparticles        | 0.95 mg mL$^{-1}$    | Baniukevic et al. 2013   |

exhibited high sensitivity and selectivity to amplified clinical samples (Sattarahmady et al. 2016). In a study, gold nanorods are functionalized with specific ssDNA probe of ‘cadF gene’ to detect campylobacter species. In this study about 283 stool samples were analysed and showed 44 positive cases, that indicated sensitivity of device, rapid in comparison to PCR, culture, and real time PCR (Shams et al. 2019). Another study demonstrates the utilization of quartz crystal microbalance (QCM) in combination with PCR assay for successful detection of *Ehrlichia canis*. The QCM based DNA nano-biosensor device was reusable, simple and do not need any critical equipment. The basic principle of this device was DNA-DNA hybridization without any cross hybridization. The limit of detection of QCM was calculated as low as 4.1 x 10$^9$ molecules/µl of 289 bp *E. canis* PCR product that represented to 22 copy numbers/µl of *E. canis* (Bunroddith et al. 2018). Newcastle disease virus RNA detection was carried out by Tian and co-workers by combination of two highly efficient techniques that are loop-mediated isothermal amplification (LAMP) and opto magnetic nanoparticle-based readout system. The detection limit was 10 aM of target sequence in just 30 min (Tian et al. 2016).
19.3.2 **Aptasensors**

Aptasensors are fabricated by employing aptamers. Aptamers are naturally occurring or synthesized short random oligonucleotides or peptides sequences. Generally, they are developed through SELEX method. In the animal disease detection aptasensors were also utilized for rapid and accurate detection of disease biomarkers. An electrochemical graphene field-effect transistor based aptasensor has been developed for detection of anthrax toxin (Kim et al. 2013). The avian influenza detection can be possible through aptamer-based nano-biosensor devices. Several aptasensors work has been carried out for detection of avian influenza virus. For example, an impedance aptasensor was developed for the detection of highly pathogenic avian influenza (H5N1). To enhance impedance signal, a gold nanoparticle-based amplifier was designed and functionalized with H5N1-aptamer and thiocyanuric acid. The device exhibited a robust, specific, and rapid detection method for the H5N1 virus with the detection limit of 0.25 haemagglutination unit (HAU) (Karash et al. 2016). Aptasensors were also used for detection of Anthrax disease in animals. Recently, a nano-biosensor device which was based on multi-walled carbon nanotubes and fluorescence aptasensors was fabricated. In this study, researchers detected ‘recombinant protective antigen domain 4 (rPAD4)’ of *Bacillus anthracis* which plays an important role in the development of disease. The aptamers were labelled with gel green fluorescent dye and immobilized on carbon nanotubes to give amplified signals after hybridization of complementary sequences. The device had the potential to be used for diagnostic tests for anthrax in a fast, accurate, sensitive, and cost-effective manners (Karimi and Dabbagh 2019). Another frequently occurred disease in animals is bovine viral diarrhoea that could be also detected by aptasensors. In 2013 a biosensor based on two different aptamers was fabricated for successful screening of binding to bovine viral diarrhoea virus type 1 (BVDV type 1) in a clinical sample. The aptamer had a high affinity and specificity to this virus biomarker. In this study, the work was based upon basic principle of aptamer-aptamer sandwich type sensing platform in which one aptamer immobilized with gold nanoparticle and other hybridized with viral DNA BVDV type 1. The device was capable to detect 800 copies/ml (Park et al. 2014).

19.3.3 **Immunosensors**

Immunosensors are basically worked on the principle of antigen and antibody reaction. Several types of biosensors have been developed to detect animal diseases in minimum time and cost-effective way. Immunosensors utilized different type of transducer surface such as electrochemical, and optical (colorimetric, surface plasmon resonance (SPR), fluorescent, chemiluminescence), etc. Bluetongue virus associated biomarker VP7outer-core protein was detected by a nanobiosensor fabricated by exploitation of gold nanoparticle probe-based assay and bio-barcode assay
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In this device anti-VP7 monoclonal antibodies and ssDNA are immobilized on magnetic microparticle probes. The developed biosensor exhibited the detection limit of $10^{-2}\text{fg mL}^{-1}$ (Yin et al. 2012). Electrochemical immunosensor consists of single gold nanowire that has been developed in 2015 for the detection of bovine viral diarrhoea virus. In this device researchers immobilized captured biomarker of virus on gold nanowire covalently by electrodeposition method. Immunosensing device was applied for detection of serum antibodies in the serum of infected animals. Team specified their device as a very sensitive with very low detection limit so could be applied for on-farm diagnosis for animal health monitoring (Montrose et al. 2015). BVDV monitoring could make possible through another microfluidic immunosensor by Heinze and co-workers in 2009. In this study they demonstrated a microfluidic based platform which consist of anti-BVDV monoclonal antibodies immobilized on carboxylated polystyrene microparticles. The performance of device had been compared with real time PCR where they found the very low detection limit in microfluidic device (Heinze et al. 2009). Enzootic bovine leucosis is a blood borne disease which affect mainly cattle and caused by BLV or bovine leukosis virus. The virus resides in white blood cells and asymptomatic most of the time. SPR based immunosensor was fabricated recently in 2019 for detection of BLV in blood serum of sick animals (Klestova et al. 2019).

An optical immunosensor for the detection of BLV has been developed by exploiting the UV and visible photoluminescence property of zinc oxide nanoparticles. The device was suitable for field use. The device showed high sensitivity and a wide range of leucosis antibody detection i.e. 0.001 mg mL$^{-1}$ to 1 mg mL$^{-1}$ (Ruban et al. 2017). Another surface-enhanced Raman scattering (SERS) based immunosensor has been also developed for the detection of this disease in 2013. In this study magnetic gold nanoparticles (MNP-Au) functionalized with fragmented antibodies specific for gp51 biomarker were used. They were resulted out the limit of detection as 0.95 $\mu$g mL$^{-1}$ and limit of quantification as 3.14 $\mu$g mL$^{-1}$ for gp51 (Baniukevic et al. 2013). A method for the diagnosis of foot and mouth disease was also developed with the help of an electrochemical immunosensor. A non-structural protein i.e. 3ABC of associated disease was detected through specific antibodies by utilization of a screen-printed electrode (Longinotti et al. 2010). Hydatid disease is associated with Echinococcus granulosis. Several studies have been carried out for the development of immunosensor to detect the associated biomarker. In a study, researcher developed silicon microcavities based nanosensor to perform antigen antibody interaction on it. An associated protein named protein kinase P38 was targeted for detection of hydatid diseases (Lv et al. 2017). Quantum dots based immuno biosensor also demonstrated in a 2017 study. In this device they immobilized Egp38 antigen on silicon pores which further functionalized with anti-p38 labelled CdSe/ZnS QDs. This was a fluorescence-based detection. They achieved detection limit 300 fg mL$^{-1}$ for Egp38 antigen (Li et al. 2017). Very recently, an immunosensor has been developed for this disease using square wave voltammetry technique. Cysteamine/phenylene isothiocyanate linkers have been coated on gold electrodes followed by immobilization of either purified ‘rabbit polyclonal antibody’ or ‘recombinant antigen B’ (AgB) to detect hydatid antigen. Detection limits for
echinococcus antigen and antibody were 0.4 pg mL$^{-1}$ and 0.3 pg mL$^{-1}$, respectively. The device is low of cost, sensitive and can be used as a point of care device (Eissa et al. 2020). Newcastle disease is also a fatal disease which affect several animals worldwide. A very simple electrochemical immunosensor was developed recently for detection of NDV. In this device chicken egg yolk antibodies (IgY) was utilized as a biorecognition element and were specific for NDV antigen. The sensor had exhibited a sensitivity range of $10^6$ to $10^2$ EID$_{50}$ mL$^{-1}$ (Thinh et al. 2018). Listeriosis is also a very harmful disease and can be detected through immunosensors. A 2013 work reported a Screen-printed carbon electrode modified with gold nanoparticle exhibited great sensitivity for detection of Listeria species. *Listeria monocytogenes* presence was monitored through conjugating secondary enzyme-labelled antibodies (Davis et al. 2013). The biosensor found to be effective in detection of other enteric bacterial species such as *E. coli* and *Salmonella Typhimurium*. Another 2017 study revealed an immunosensor fabricated with a pair of monoclonal antibodies. These pair of mAbs used to recognize P60 protein associated with Listeria species (Wang et al. 2017).

### 19.3.4 Miscellaneous

CRISPR-Cas assay with a fluorescence-based point-of-care (POC) system has been developed for the detection of African swine fever virus detection. The LOD was found as 1 pM in 2 h (He et al. 2020). Recently, a metal oxide semiconductor (MOS) based sensor was developed for detection of *Campylobacter jejuni* in a milk sample. This microbial agent is responsible for several gastrointestinal related diseases in humans. A MOS sensor has the ability to differentiate between contaminated and control samples (Núñez-Carmona et al. 2020). Another advancement in nanobiosensors can be represented by wearable biosensors. For continuous real time monitoring of herd of animals and livestock; wearable biosensors show a great significance in the health management of animals. They provide physiological information through non-invasive, dynamic measurement of biomarkers in biofluids like saliva, sweat, tears, and interstitial fluids (Neethirajan 2017).

### 19.4 Future Aspects

Nano-biosensing devices are known for their high sensitivity, simplicity, and selectivity to detect animals or human diseases. They are able to provide rapid results with low cost in comparison to conventional methods (Malik et al. 2013). Animals are extremely susceptible to infection because of unhygienic living environment therefore suffer with number of communicable diseases and their direct contact with human beings make the situation more problematic. Animal communicable diseases cause significant economic loss in various ways like loss in food production system,
and increased veterinary costs (Kivaria 2006; Ott et al. 1999; Dufour 1999; Neethirajan 2019). We consider that nano-biosensors have capability to advance conventional technologies for detection of disease-causing microorganisms and can improve the surveillance system to prevent any disease outbreak. Wearable devices can play an important role in future to manage animal diseases. Real time field monitoring, data networking, sampling methods, and mobile analysis will provide remarkable support through highly sensitive and selective nano-biosensors. The data through device will help in disease control and prevention of outbreak in poultry, livestock as well as wild animals.

19.5 Conclusion

Prevention of communicable diseases and non-communicable diseases is very essential for the health management of animals. Human beings are also affected with animal disease directly or indirectly and have various common diseases. The first step required for prevention of any disease is accurate diagnosis. It is important to develop some reliable, cost effective, and less time-consuming methods. Fast diagnosis is must in some disease for example anthrax which causes death within 2 days. Sometimes some diseases are remained asymptomatic like bovine leucosis, so they also need accurate detection in very low concentration. Nanotechnology exhibit several new opportunities to fabricate new devices for the successful determination of diseases. With the help of biomarkers, these nano-biosensors have given promising results in the diagnosis of animal diseases. Communicable and non-communicable diseases affecting animals at a different level can now detect at an early stage, monitored, and controlled with the help of nano-biosensor.

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