

# Chapter 13

## Role of Sensors, Devices and Technology for Detection of COVID-19 Virus



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### 13.1 Introduction

Many people in Hubei Province of China with symptoms like cough, fever, and shortness of breaths were first admitted into local hospitals in December 2019 [1, 2]. Initial screening by doctors using CT (computed tomography) scan suggested that patients have symptoms like pneumonia. But RT-PCR (real-time polymerase chain reaction) results suggested that the disease was not related to pneumonia. It has different origins. Later in January month it was discovered that the virus has similarity to SARS-CoV, Middle East respiratory syndrome coronavirus (MERS-CoV) and bat coronavirus of RaTG13 with ~80%, 50% and 96% similarity, respectively [3]. This virus was named SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) and the resultant pandemic is known as COVID-19. The world is caught off guard by the SARS-CoV-2 which has infected a total of over 27.5 million people and caused ~900,000 deaths worldwide (WHO, 2020) as of 9 September 2020 [4]. After two localized outbreaks, viz. SARS coronavirus (SARS-CoV) in 2002 and

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293

Middle East Respiratory syndrome coronavirus (MERS-CoV) in 2012, SARS-CoV-2 is the third severe pandemic of this century caused by coronavirus. Immunocompromised and those on active therapy have higher vulnerability to COVID-19 [5, 6]. Mainly the lungs, heart, kidneys, genitals and liver are affected due to COVID-19 [7]. Acute symptoms like acute kidney injury, abnormal hepatic function, cardiac injury and acute respiratory distress syndrome (ARDS) have been found in patients having acute COVID-19 symptoms [8–11]. Most people who are 60+ years or having health problems like heart and lung disease, diabetics or those who have poor immune systems are easily affected and vulnerable to COVID-19 [12]. Initially, most of the infected individuals were showing some disease symptoms for the virus infection, but presently many cases have arisen without any symptoms, thereby emphasizing its asymptomatic nature. These asymptomatic individuals further spread the virus in their community. Mostly human beings are spreading the virus knowingly or unknowingly through their communities. This virus quickly spread throughout the world and halted daily activity. The rapid transmissivity guided by asymptomatic infectivity and quick spreading of this virus demand rapid detection tools along with urgent strategies of interventions [13].

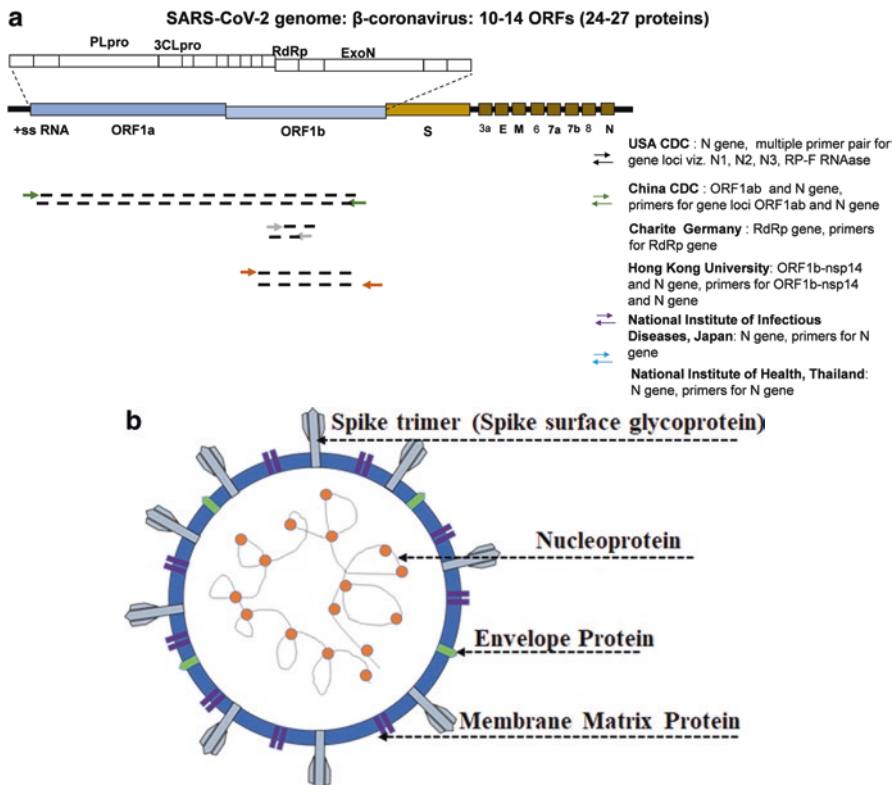
As of now no medicines are available to cure it. Therefore, there are enormous challenges for us to solve the problem globally with the help of government, citizens and common people. To solve this problem, we have to use the available techniques, precaution and safety. To understand the spectrum of techniques which can be employed for rapid and robust detection of the pathogen, we have to understand its biological properties. The existing knowledge of the biological characteristics of the virus can be exploited for evolving the existing diagnostic tools. The key biological attributes central to the virus can be briefly presented as its genomic organisation, replication timespan and mutation rate which are important for sensitivity of nucleic acid-based diagnostic technique and the features of viral entry and disease pathogenesis. Therefore, in this chapter we have discussed the biological property of COVID-19, followed by transmission of the disease to human being. Finally we have discussed the available techniques, sensors, devices, future techniques and technologies that can be used to detect the virus rapidly.

## **13.2 Biological Characteristics of COVID-19**

The biological characteristics of SARS-CoV-2 are described briefly as follows:

### **13.2.1 Genome**

SARS-CoV-2, a beta-coronavirus, has a single-stranded positive-sense ribonucleic acid (RNA) genome. The specialty of a positive-sense RNA genome is the ability to be directly used for translating the nucleic acid molecule to generate multiple copies



**Fig. 13.1** (a) Genomic organization of SARS-CoV-2 virus and utilization of various genes by different infectious disease organizations across the world. The genome encodes for 2 large open reading frames (ORF1a and ORF1b) and 8–12 other genes translating to 24–27 proteins. The colour-coded arrows define the directionality of amplification in RT-PCR technique used as a COVID-19 diagnostic tool followed by the information of genes and primer pairs utilized by the organization to detect SARS-CoV-2 in the patient sample using RT-PCR. (b) Structural organization of SARS-CoV-2 virus

of protein molecules. This RNA genome has ten genes which are utilized to synthesize proteins. Usually one gene codes for one protein, but in this unique design, one gene is involved in coding different proteins. Such a unique design is possible due to one long gene *orf1ab* which leads to the formation of a polyprotein that is cleaved into 16 proteins by proteases (Fig. 13.1a). The genome has nucleotide identity of about 50%–96% nucleotide identity with other viruses of the coronavirus family [14]. Apart from proteases, RNA polymerase (RNA-dependent RNA polymerase which generates a RNA molecule from another template RNA molecule) and a proofreading exonuclease essential for error-proof replication, the genome predominantly encodes for four structural proteins, namely, (I) spike surface glycoprotein, (II) small envelope protein, (III) two membrane-bound matrix proteins and (IV) nucleoprotein or nucleocapsid (Fig. 13.1b) [15].

### ***13.2.2 Replication Timespan and Mutation Rates***

In comparative analysis with other coronavirus family of viruses, SARS-CoV-2 virion is estimated to enter the nasal epithelial cell within 10 minutes of adherence, multiplies to generate intracellular virions in approximately 10 hours and bursts open from the infected cells with a burst size of 1000 virions [16]. The mutation rate defined as the number of substitutions per nucleotide site per replication cycle is a key parameter governing viral evolution. Having an error correction mechanism, it is estimated that SARS-CoV-2 accumulates  $10^6$  mutations per replication cycle which implies about 1000 mutations getting fixated per year in the viral genome. Overall, replication timespan of the virus is considered as 10 hours with a burst size of 1000 virions. These estimations are crucial in designing diagnostic tools, mathematically modelling viral spread and strategies of intervention against the virus [14].

### ***13.2.3 Viral Entry and Pathogenesis***

Using colocalization fluorescence experiments, Zhou et al. [2] demonstrated the interaction of angiotensin-converting enzyme 2 (ACE2) receptor with SARS-CoV-2. The viral entry requires binding of spike protein (S) to receptor ACE2 present almost ubiquitously in all types of host cell [17, 18]. Patients, who become critical post-infection, develop acute respiratory distress syndrome (ARDS) [19]. ARDS is marked by collapse of lung function due to maladaptive immune response. One of the leading causes of such immune response is activation of lung-resident immune cells activating complement system driving the release of pro-inflammatory cytokines, thus accounting for the damage of vascular endothelial cells of blood vessels supplying lung alveoli [20].

## **13.3 Transmission and Risk Factors**

It was reported that initially consumption of wild animals/seafoods in Hubei Province is the source of COVID-19 [21]. Later it was transmitted from human to human in a market and became widespread [22, 23]. Due to the attributes of the infection, some people are showing symptoms, whereas others are asymptomatic. These asymptomatic and symptomatic individuals touching uninfected people or coughing in crowded areas are the reasons for fast spread in heavily populated areas [24–26]. It was reported that aerosols (droplets) having dimension less than 5  $\mu\text{m}$  can live for at least 3 hours. Researchers also showed that COVID-19 can be alive on metal or plastic surfaces or on the clothes also [27]. If the proper environment is found, then COVID-19 can be alive for a few days even in wastewater also. From China, COVID-19 spread into Asian countries like South Korea, Japan and Thailand

in January 2020 [28]. By the end of January, the USA has the first case of coronavirus. In Europe the first COVID-19 patients were found in Italy (Milan region). Similarly in India, the first case was reported in Kerala State. These persons had a flight history from China [29, 30]. Sudden increase of patients was found in India when the “Shramik special” train was introduced in India at the end of May. Many migrant labourers are travelling on these trains to reach their native places. Suddenly an increase of positive cases was found in India. In the present situation, there are many positive reported cases per day (>30,000) in Brazil, the USA and India. These trends prove that transmission of this virus is due to human interaction, touching and gathering in small occluded places.

### 13.4 Methods to Collect the Samples

Before diagnosis, sample collection is the first step, and it is as per the demand of the diagnosis test. The predominantly used diagnostic tool for rapid detection of infection with high sensitivity involves employing reverse transcriptase polymerase chain reaction (RT-PCR). The sample used to extract viral RNA is obtained from the upper respiratory tract samples like nasopharyngeal and oropharyngeal swabs or washes and aspirates (interim guidelines by Centers for Disease Control and Prevention). Serological tests used to probe antibodies generated in response to viral proteins involve harvesting blood plasma from patients after a minimum of 5 days post-infection [31].

### 13.5 Diagnostic Tools

Initially the symptoms of the patients were fever, shortness of breath and coughing. These symptoms are similar to pneumonia, influenza or normal cold. So, doctors have difficulties in determining the exact cause of the disease. Later nucleic acids tests were performed to confirm the virus. Due to its new biological structure and properties, RT-PCR was first used to diagnose the virus followed by CT scan of the chest. There are also different techniques available which can be used to determine COVID-19. They are discussed below.

#### 13.5.1 RT-PCR

RT-PCR is the routine diagnostic tool employed to detect RNA virus infections [32]. RT-PCR forms the primary method to detect SARS-CoV-2 and diagnose COVID-19. RT-PCR, in brief, involves exponential amplification of a template RNA to cDNA (complementary DNA) using gene-specific primers (short DNA

probes) by using RNA-dependent DNA polymerase called reverse transcriptase. For strain specificity and sensitivity in detection of viral genome in patient samples, primer design should be furnished with utmost precision [33]. The process flow of generating RT-PCR-based diagnostic kit comprises two steps: (a) sequence alignment and primer design for viral strain-specific gene and (b) assay optimization for amplification, sample preparation and testing. The target genes used by various existing diagnostic kits have been displayed in diagrammatic representation of viral genome for better visualization of RT-PCR diagnostic tool (Fig. 13.1a). Positive controls for setting up reaction standards are generated by using in vitro transcription kits for transcribing the template viral gene of interest already inserted in a plasmid [34]. Since RNA has relatively low stability and ribonuclease (RNase) from various sources is a robust and abundant enzyme omnipresent on any lab bench setup, isolating viral RNA from patient samples emerges as the biggest bottleneck. Use of standard RNA isolation kits, therefore, is a prerequisite for using this diagnostic tool. To alleviate this requirement, efforts are ongoing to generate an agile RNA preparation method for COVID-19 detection [35].

### 13.5.2 Chest CT Scan

Chest computed tomography (CT) scan is an alternative and confirmation technique for the detection of COVID-19. A group of doctors led by Dr. T. Ai in the department of radiology at Tongji Medical College in Wuhan, China, had conducted chest CT and RT-PCR for 1014 patients between 6 January and 6 February 2020 [36]. They have used RT-PCR as a reference and performed the chest CT for confirmation of the virus. Similarly dynamic conversion of RT-PCR results of a patient, i.e. positive to negative or negative to positive results of RT-PCR, are analysed with serial chest CT scan results for more than 4 days. They revealed that chest CT scan is a better diagnostic tool for COVID-19 with higher sensitivity. Positive results of 88% was found when chest CT scan was conducted compared to 59% positive RT-PCR. Among the negative RT-PCR results, chest CT scan showed 75% positive results. Chest CT scan showed 97% sensitivity, 25% specificity and 68% accuracy for the detection of COVID-19.

In Rome, Italy, tests were conducted for chest CT scan along with RT-PCR between 4 March 2020 and 19 March 2020 [37]. A total of 158 cases were studied. After taking swab for RT-PCR studies from the patients, they went for chest CT image acquisition. Images were captured while the patients were in supine position without any contrast medium injection. Patients having both positive RT-PCR and chest CT scan ground glass opacities, bilateral pneumonia and sub-segmental vessel enlargement (>3 mm) were confirmed for 100%, 91% and 89%, respectively, compared to RT-PCR cases. Their results are also similar to the results published by Chinese researchers. Sensitivity, specificity and accuracy from the study were found to be 97%, 25% and 68%, respectively. Though chest CT scan shows high accuracy to predict the infected individuals, it has several limitations. First of all, the chest CT

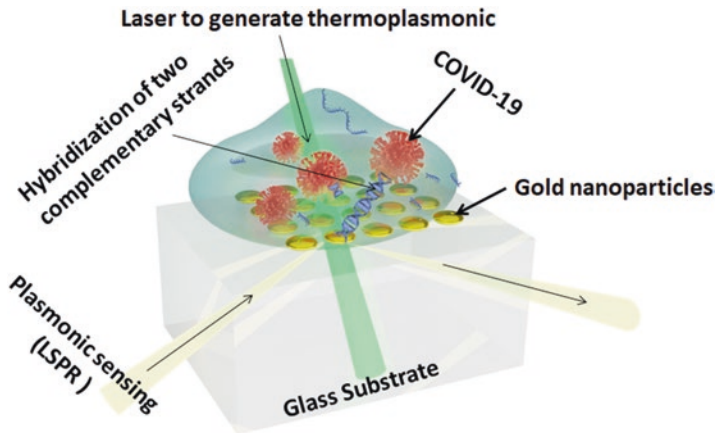
scan is a bulky system. It needs specialized technicians to operate, and finally to conclude the results, we need specialists in those areas. These are the main disadvantages for chest CT scan.

### ***13.5.3 Optical Plasmonic-Based Detection***

Optical methods can be used to determine COVID-19. There are several techniques in optical-based detections among which SERS (surface-enhanced Raman spectroscopy) and localized surface plasmon resonance (LSPR) methods are the most reliable and trusted ones. SERS is an optical technique used to determine the biological (single molecule) and chemical samples. A report has been published on single-molecule SERS (SM-SERS) where bovine serum albumin (BSA) was the protein sample and Traut's reagent (TR) was chosen as a protein linker [38]. The binding between BSA and TR on the gold surface changes the spectral response of SERS, which detects the presence of targeted virus protein. As we discussed earlier COVID-19 consists of a protein; therefore, SM SERS method with suitable plasmonic materials can be used in the future to detect COVID-19.

Localized surface plasmon resonance (LSPR) is another promising alternative detection technique for sensing analytes for biosensing application. LSPR is a collective oscillation of free surface electrons of materials (generally metal or highly doped semiconductors) in the presence of light. Combining thermoplasmonics (localized heating in nanostructure) and LSPR effect, G. Qiu et al. have published a work on SARS-CoV-2 detection [39]. Thermoplasmonic effects are used to generate heat for hybridization methods of complementary strands of DNA like the methods used for RT-PCR techniques, and these hybridization methods can be detected simultaneously using LSPR method. According to G. Qiu et al.'s device design, AuNI nanostructures was able to generate thermoplasmonic heat (532 nm wavelength as laser source), and then the hybridization of nucleic acid of SARS-CoV-2 virus was transduced using LSPR. LSPR was generated at the interface between glass and the liquid environment using a wide-spectrum LED. The response of the LSPR was retrieved using the windowed Fourier transform phase extraction method. By using the 532 nm-centred wavelength excitation laser with 32 mW power, they were able to generate  $\sim 41.08$  °C.

For real-time sensing, they used artificially synthesized DNA sequences of SARS-CoV-2. They functionalized the surface of sensors by forming Au-S bond between the synthesized thiol cDNA of RdRp-COVID and AuNIs. When they injected the analytes with different molar concentrations (0.1 pM–50  $\mu$ M), the RdRp-COVID sequence was hybridized with the surface-functionalized thiol cDNA of RdRp-COVID in the presence of heating. Thus the refractive index near the AuNI surface changed; therefore, there is a change of LSPR response. From the change of LSPR response, they have detected the presence of SARS-CoV-2. According to their studies without the presence of thermoplasmonic can show false-positive response which is not reliable. By using thermoplasmonics, they were able to sense



**Fig. 13.2** Schematic illustration of the device. Two complementary strands of RNA are hybridized on the gold surface in the presence of green lasers. LSPR responses were recorded from the bottom of the device using a white light

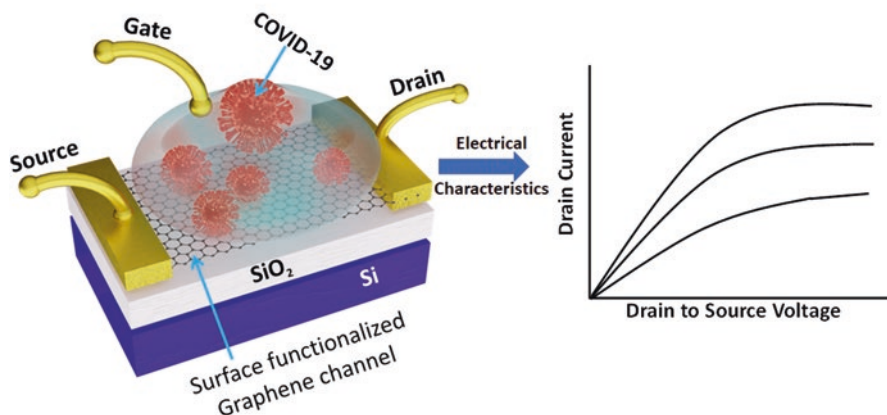
$0.22 \pm 0.08$  pM concentrated RdRp-COVID sequence which is very promising for real-time application. Figure 13.2 depicts the working principle of thermoplasmonic effect to detect COVID-19.

#### 13.5.4 FET-Based Biosensor

FET (field effect transistor)-based biosensors are used in many cases to detect the biological samples [40]. Fast detection with less quantity of samples and high sensitivity makes it popular biosensors and point-of-care applications. Mainly oxide materials, 2D materials are used for FET-based biosensor applications. FET-based biosensors can be an alternative to detect COVID-19 viruses. Recently one journal paper and one patent were published/filed for detecting the COVID-19 virus using graphene and diamond nanocarbon as a sensing layer. Graphene was earlier used to detect RNA [41]. G. Seo et al. have used graphene as a sensing layer of FET for detection of COVID-19 [42]. They have discussed thoroughly how to prepare the sample and detect the virus. In their study, specific antibodies against COVID-19 spike proteins were used to bind it, and the concentrations of 1 fg/mL in phosphate-buffered saline and 100 fg/mL clinical transport medium were detected.

Among all the proteins, spike protein has distinct characteristics like it is predominantly a transmembrane and highly immunogenic protein of the virus with highly specific amino acid sequence. These features were used in their study to bind this protein with antibodies. Antibody-coated COVID-19 samples were placed on the FET through 1-pyrenebutyric acid N-hydroxysuccinimide ester (PBASE) as a medium. This medium acts as an interface coupling to be a probe linker for gate terminal. Measurement was performed at constant gate voltage, and by measuring





**Fig. 13.3** Schematic of FET-based biosensor with electrical characteristic representation

the change of slope due to presence of antibody, they have detected the virus. They have found the limit of detection (LOD) of graphene-based FET sensor to 1 fg/ml of target SARS-CoV-2 with antigen protein.

Another group in China (X. Zhang et al.) has also used graphene-based FET to develop a coronavirus immunosensor. In their study they have shown that their device can capture the spike protein S1 in COVID-19 within 2 minutes with a detection limit of 0.2 pM [43]. Figure 13.3 shows the schematic diagram of FET-based biosensors and their electrical characteristic representation. Instead of graphene, any other oxide materials and 2D transition metal dichalcogenides can be also used as a channel material (sensing). AKHAN Semiconductor, a prominent diamond semiconductor technology, has applied for a patent in US Patent and Trademarks Office (USPTO) to detect COVID-19 using Miraj Diamond nanocarbon materials technology for biosensing field-effect transistors (bio-FET) [44].

### 13.5.5 Electrochemical-Based Sensors

Electrochemical-based approach can be useful to determine COVID-19. Many researchers have used electrochemical techniques to determine protein [45]. SARS-Cov-2 has some protein structures. If it is able to bind with sensing materials, then there is a change of current. By measuring the changing of current, COVID-19 can be determined. Mostly metal oxides, nanowires, CNTs and graphene are used for electrochemical detection of proteins. Due to high surface-to-volume ratio, nanostructures are preferred in determining the proteins and other biosensor applications. A.T. EzhilViliana et al. have fabricated the sensing layer on polycarbonate substrate where gold wire acts as a working electrode and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride/N-hydroxysuccinimide-activated 3-mercaptopropionic acid (MPA) was used as a self-assembled monolayer

agent and bovine serum albumin (BSA) acted as a blocking agent before immobilizing the C-reactive protein (CRP) [46]. They have measured trace amount of CRP, a biomarker for real-time monitoring of cardiovascular disease and inflammation, using electrochemical techniques. A highly selective electrochemical platform was developed for detection of protein kinase activity in normal human serum [47]. S.K. Arya et al. have used electrochemical ELISA method to detect bladder cancer protein markers, nuclear mitotic apparatus protein 1 (NUMA1) and complement factor H-related 1 (CFHR1) in urine [48]. Similarly screen-printed gold electrode with modified rGO and CNTs was used as electrochemical ELISA-like immunosensor [49]. These sensors were used to detect two miRNAs, viz. miR-141 (a prostate biomarker) and miR-29b-1 (a lung cancer biomarker).

### ***13.5.6 Enzyme-Based Detection***

Onset of any infection is characterized by protective response generated by the immune system in the form of antibodies against a specific protein or a short peptide sequence of protein called antigen from the infectious agent [50]. Enzyme-based assays rely on strong and specific antigen-antibody interaction. Enzyme-linked immunosorbent assay (ELISA) has been effectively developed for a reliable diagnosis of COVID-19. Based on the recombinant nucleocapsid protein of SARS-CoV-2, antibodies against the coronavirus were detected in patients with confirmed or even suspected COVID-19 at about 40 days post-onset of symptoms. This serodiagnostic ability of the test was investigated for sensitivity, specificity, consistency rate, positive predictive value (PPV) and negative predictive value (NPV) [51].

### ***13.5.7 Micro-PCR***

In order to reduce the processing time per patient sample for this test, loop-mediated isothermal amplification (LAMP) enables nucleic acid amplification in short time by utilization of 4–6 specially primers and a DNA polymerase with chain displacement activity under constant temperature. Combined with reverse transcription, RT-LAMP allows rapid and direct detection of RNA. Named as iLACO (*isothermal LAMP-based method for COVID-19*), such coupling of RT-LAMP along with pH-driven, colorimetric detection technique has been recently developed [52].

### ***13.5.8 Paper-Based COVID-19 Detection***

Due to rise of asymptomatic individuals, there is a challenge to rapidly detect the virus and keep them quarantined for preventing the further spreading of the virus in the community. Recent research shows that COVID-19 can be alive in wastewater

for several days and viruses can be isolated from the faeces and urine of infected people. It is a problem for the locality where asymptomatic people live. Therefore there is a challenge to determine the virus in those areas. Recently researchers have shown the ability of paper-based sensors to detect different pathogens like malaria. Paper-based sensors are inexpensive, use-and-throw and rapid detection techniques. Paper-based sensors are easy to fabricate in large scales. Due to its small size, lots of sensors can be easily transported, thus allowing easy diagnoses in large residential areas. Recently K. Mao group has shown that paper-based sensors and devices can be used to detect COVID-19 in wastewater [53]. Recently B.S. Batule et al. have developed paper-based RNA detection from mosquito-borne disease [54]. They have selectively detected RNAs of Zika from the serum samples.

### 13.6 Use of Technology: About Technology/Electronics Tools

Existing methods like RT-PCR, chest CT scan and enzyme-linked immunosorbent assay (ELISA) can be used to detect the virus. But these processes are time-consuming. So there is a gap between detection of infected people and spreading the virus in the locality as human beings are primarily a source for spreading COVID-19 in masses. But the spreading of viruses is done by human beings. It is easy to find the COVID-19-affected person. By quarantining him/her, we can stop the spread of the virus. But the problem is the asymptomatic person. If he/she is not tested for the virus, there is a high chance that the affected asymptomatic person can spread the virus in large areas. In this scenario existing technology like artificial intelligence (AI), machine learning (ML), Internet of Things (IoT), computer vision, big data analysis and image processing can be used to stop the spreading of the virus. Deep learning can be developed as an automatic, accurate, cost-effective, time-efficient and easily performed system for screening COVID-19. Many institutes such as the Allen Institute and leading research groups are collaborating and providing weekly updates of open research dataset regarding COVID-19 [55]. These data become scholar articles which help to conduct further research projects and improvisation. In this pandemic situation, it is mandatory to integrate and analyse the COVID-19 patients' data at the large scale using advanced machine learning algorithms, understanding pattern of spread, improvement in diagnostic accuracy and speed and identifying the sensitive cases based on genetics and physiology of the person.

Since the worldwide COVID-19 outbreak, advanced machine learning methods are already being used in CRISPR-based detection assay, taxonomic classification of genomes, survival prediction of severe patients and searching for potential drugs to treat COVID-19 [56–58]. Certainly, any experimental hypothesis must be tested further for improvement with fine experimental designs and tools to make the system more reliable.

Machine learning, a subset of artificial intelligence, is presently used by researchers and technologists to combat COVID-19 pandemic. Many researchers' ongoing efforts have developed few diagnostic and testing approaches through machine

learning algorithms. High-sensitivity and fast CRISPR-based system for screening of SARS-CoV-2 virus has started using machine learning. Using past patterns of distinct respiratory images of COVID-19 patients, a neural network classifier was developed for large-scale screening. Moreover, time-efficient automated monitoring system of COVID-19 patients uses deep learning analysis of thoracic CT data [57, 59, 60]. Hosting, modelling and sharing of integrated computational data whether it is scientific, clinical or biomedical are critical to accelerate the operationalization of AI protocol to respond to COVID-19 pandemic worldwide.

Artificial intelligence and machine learning not only play an important role in rapid and accurate testing for diagnosis but also make a protected protocol to stop spread by eliminating contacts with infected people which might help the hospital arrangement and patients to operate COVID-19 pandemic. Google DeepMind has developed a deep learning system which recently released protein structures of COVID-19. This will become valuable information in making vaccine cocktails against it in a short span [56, 61].

To get reliable results on predictions, past records could be exchanged and shared to a framework. Figures 13.4 and 13.5 show the application of AI, machine learning, big data analysis and smartphones to tackle COVID-19. Such processes help to grow transfer learning and framework dataset to construct large datasets using multiple smartphone onboard sensors.

Nowadays, smartphones are not simple instruments but embedded with many sensors and computational capabilities. Therefore, smartphones are able to sense several parameters or visual data simultaneously about daily activities. Capability to capture, collect and store large volume data can be useful to make artificial intelligence systems either suspect or affirm infected cases of COVID-19 [62]. More importantly, if smartphone cameras are able to capture CT scan images of infected patients then comparative analysis with the recorded data to diagnose or detect the level of lung inflammation. Research suggests some well-known symptoms of

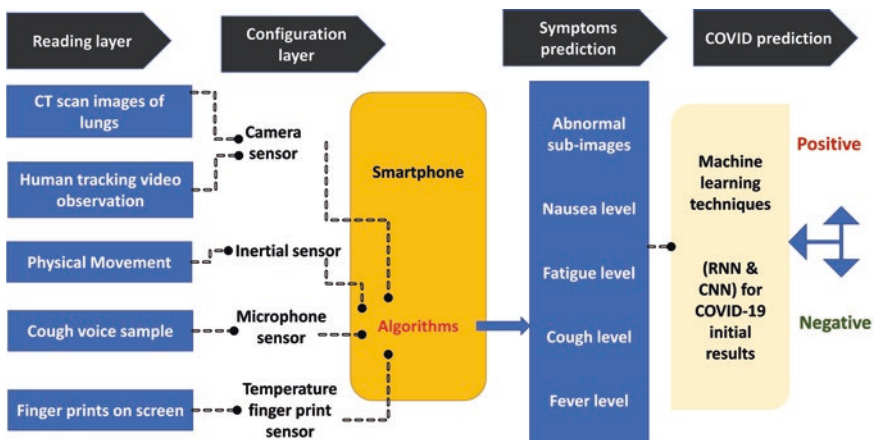
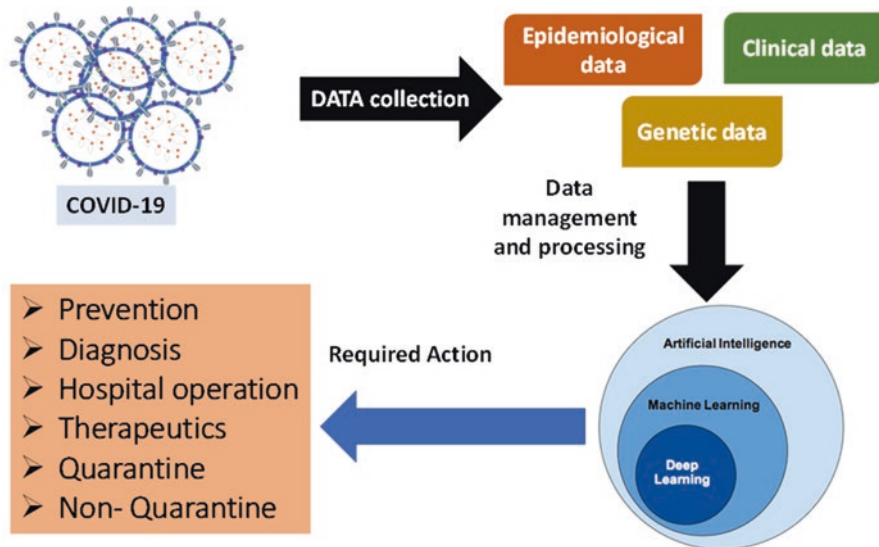


Fig. 13.4 Application of artificial intelligence and machine learning in the fight against COVID-19



**Fig. 13.5** Cloud computing and big data analysis for COVID-19 detection

infected cases such as headache, dry cough, fever, fatigue and interruption in breathing. These symptoms will become important parameters to differentiate COVID-19 from other infections like flu, cold or hay fever.

An important task is to make a framework using each level of every symptom monitored by onboard embedded sensors in smartphones. These main sensors are cameras, microphone, temperature sensor, inertial sensors etc. Existing COVID-19 symptoms would be used to read, detect, monitor and confirm infection by smart sensors of phones. Machine learning algorithms are separately applied to these sensors, most importantly detecting the level of symptoms, for example, camera-captured images or activity videos, to measure human fatigue in different circumstances. Temperature fingerprint sensor is to detect fever level through the touchscreen. Apart from this onboard inertial camera (accelerometer sensor) can also be optimised to measure fatigue level. Camera and inertial sensors in smartphone can be used to measure and monitor the neck posture and level of human headache. Similarly nausea prediction can be accomplished through video-observation using smartphones. In addition, using microphone chipset in comprehensive studies has been done to indicate the type of cough [63–67].

Smartphone-based apps were implemented in the USA and the UK. A total of 2,450,569 UK and 168,293 US citizens used the app to report the symptoms for COVID-19 between 24 March and 21 April 2020. Among all, 18,401 individuals have undergone COVID-19 tests, and 65.03% individuals tested positive when they have reported losing smell, whereas 21.71% tested positive who do not have symptoms like losing of smell. Then a mathematical model was implemented, and using all the app data, it was predicted that 140,312 individuals will have COVID-19 [68]. Singaporean government has introduced “Trace Together app” on 20 March 2020 to

find COVID-19-infected people nearby [69, 70]. Similarly the Government of India also introduced “Aarogya Setu” App to find the individuals who have SARS-Cov-2 symptoms by contact tracking on 22 April 2020 [71]. If any individual is affected with COVID-19, then any person, who has contact history with the affected person, can be easily recognized by using these apps, and so medical check-up and testing will be arranged for them. Many other countries have also introduced similar types of app. A. Imran et al. have developed an app “AICOVID-19” which uses artificial intelligence to predict COVID-19 by analysing the cough sample. Cloud-based AI engine was used to diagnose or predict the affected person by analysing the cough samples within 2 minutes. This AI engine can differentiate the COVID-19-infected person and other non-affected COVID-19 coughs with 90% accuracy [72]. Therefore, such mobile apps based on AI are excellent alternate ways to find the individual who needs COVID-19 testing immediately. Big data analysis plays an important role in analysing the pandemic like SARS-Cov-2. The National Health Command Center (NHCC) of Taiwan uses big data to stop and control the spreading of viruses. The NHCC has used immigration and customs database with the health insurance database for making big data analysis. After the declaration of COVID-19 by the WHO, the NHCC used these databases along with new technology like QR code scanning, travel history and health symptoms to identify the persons with travel history to infected areas. Then they were quarantined at home and were monitored through their phone. Using big data analysis along with other modern technologies, Taiwan has stopped spreading the virus and prevented the epidemic in their country [73].

### **13.7 Plasma Therapy and Vaccine for Treatment of COVID-19**

At present no particular vaccines are available to cure this disease. Many virologists, pharmaceutical companies and research institutes are now trying to develop the drugs or vaccine for COVID-19. But it is too early. It will take time to develop the final version of drugs as it requires many trials. Presently alternative ways to cure the patients were found by using plasma therapy. Here plasma is collected from the patients who have recovered from COVID-19, and then these plasmas are used as vaccines and applied to other infected patients who have symptoms like COVID-19. Favourable results were found using plasma therapy [74, 75] (Table 13.1).

### **13.8 Technology Challenges**

There is a challenge for any government, research institutes and hospitals and the human race when a pandemic condition like COVID-19 breaks out. Due to the enormous population, it is very tough for the organization to control and prevent the

**Table 13.1** Emerging techniques for SARS-CoV-2 diagnostics

Platform used	Type of detection	Working principle	Type of clinical sample	Biomarker	Ref.
CRISPR	CIA	CRISPR-/Cas12-based lateral flow biosensor	Serum	Nucleic acid	[76]
Electro-chemical	ELISA	Binding of biomolecules with electrochemical signal collection	Urine	Protein	[48]
LAMP	LAMP	Isothermal DNA synthesis using self-recurring strand displacement reactions; positive detection leads to increased sample turbidity	Throat swabs	Nucleic acid	[77]
FET-based sensor	Electrical	Graphene layer is used as a channel of FET and characterized drain voltage and current	Throat swabs	Spike protein	[42, 43]
Paper based	RT-LAMP	Two-step advanced paper systems for simultaneous extraction, amplification and detection of viral RNAs	Serum	Nucleic acid	[54]
Antibody test	ELISA	Antibody response with COVID-19 and evaluation of serodiagnostic value	Nasopharyngeal and/or oropharyngeal swabs	Protein	[51]
Smartphone app	App	App is used for checking the cough and others	Cough, sound	NA	[66–68]
RT-lamp	LAMP	Reverse transcriptase LAMP reaction for RNA targets	Nasopharyngeal aspirates	Nucleic acid	[78]
RT-PCR	Real-time fluorescence	Detection of the white blood cell	Throat swabs	Nucleic acid	[79]
Artificial intelligence	Machine learning recorded data	Detection of many parameters such as CT scan, X-ray, posture, fatigue level, fever level etc. and compare with past positive data	–	–	[62, 72]
Thermo-plasmonic	Optical	Localized heating at plasmonic resonance starts in situ hybridization	–	Nucleic acid	[39]

pandemic. Therefore, the need for advancements in the medical field gained more attention. People are also very cautious about their daily routine and health conditions. In order to check COVID-19 symptoms like cough, fever, fatigue etc., there are several android app-based solutions proposed by several information technology (IT) researchers. In order to satisfy the needs of the people in the medical field, a cost-efficient and effective healthcare system that can monitor continuously the person is needed. In case of an emergency situation, the patient's condition is not notified to anyone where he cannot receive any help. In this type of scenario, this may even lead to death. So, in order to reduce such a situation, there is a need for systems

that monitor the patient's condition 24/7 and notifies when there is a sudden change in the patient's condition. There are many researchers working in the area of health-care monitoring systems, where most of the time they do not have storage of any continuous monitoring data that will help for future predictions; that is one of the challenges of using technology for COVID-19.

Real-time patient prediction can be a technological solution using the Internet of Things (IoT) and machine learning (ML) that can continuously monitor the patient/user and calculate or measure his/her vital sign information and make predictions using the user's data stored in the cloud. After successful ML algorithm implementation, it can be used for prediction of COVID-19 symptoms; also, people can have real data of affected patients.

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