Multi-Functioning Sensor for Detection of COVID 19

¹N. Mukund Balaji, ¹B. Tech Student, Acharya Institute of Technology, Bangalore-560107, India ²Suneetha T.B ²Head of Dept. of Biotechnology, Acharya Institute of Technology, Bangalore-560107, India

Abstract: The recent outbreak of the SARS-CoV-19 virus or commonly known as novel corona-virus disease has spread worldwide and has already affected higher than 200 countries. A rapid and quick identification of the existence of the COVID-19 virus in contaminated surfaces, water, food and in a patient's specimen is a prerequisite to competently intervene in its widespread as well as counteract such epidemics, bacterial or viral outbreaks along with bioterrorism. The widely used instrument for diagnosis of SARS-CoV-19 is (RT-PCR) i.e. Reverse transcriptase polymerase chain reaction. However, it has shown some drawbacks like long processing time and has also testified innumerable false-negative or false-positive cases, particularly in the primary stages of the corona virus outbreak. In this paper, we propose a multifunctional sensor which conducts numerous measurements of various parameters required for detection of COVID-19 virus. The most commonly observed symptoms for COVID-19 is fever, reduction of WBC count. With these parameters in mind a multi-functioning sensor is designed with two sensors i.e. a temperature sensor for the detection of fever by monitoring body temperature and an optical sensor which provides an oblique illumination with LEDS which helps in analyzing the WBC concentration in the blood capillaries. A particular parameter is independently measured by each sensor and a combination of all the independent values is obtained and analyzed. This information is processed to provide a calculated electrical output which can be visualized to detect COVID-19. This diagnostic tool makes the system compact and decreases the cost of several sensors during the isolation and treatment of infected patients. The study done here gains insight into a multifunctional sensor and its applications in nucleic acid tests as well as diagnosis of viral diseases like SARS, MERS and COVID-19.

Keywords- SARS-CoV-19, Multi-functioning sensor, Diagnostic tool, Fever, WBC count, Nucleic acid tests

1. INTRODUCTION

Coronavirus hailing from the family of Corona-viridae are non-segmented RNA virus that are positive-sense enveloped. [1,2] The ultra-structural morphology of COVID-19 virus is shown in Fig. 1. The picture was obtained from the image library of the Centers for Disease Control and Prevention (CDC).

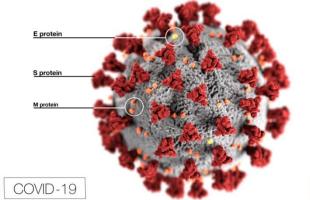




Fig.1.The ultra-structural morphology of COVID-19

This figure represents S-spike, M-membrane and E-envelop that is located on the outer surface of virus. The virus proves to be fatal due to its potential transfer ability of crossing the species barrier from animals to humans.

Since December 2019, a progression of patients with obscure reason pneumonia had been accounted for in Wuhan, Hubei area of China. [5] WHO (World health organization) on March 11, 2020 declared coronavirus disease as a public health emergency and a pandemic globally. [4] The utmost infected individuals were identified as males who had adverse health conditions like hypertension, cardiovascular diseases and diabetes. Fever, cough, shortness of breath and fatigue are the most commonly observed symptoms in this COVID-19 disease. The transmission of the virus is observed to take place through direct contact with the infected individual or in close quarters with them. The isolation of the virus on January 7, 2020 lead to the initiation in development

of diagnostic tools that are highly accurate, reliable, compact and highly sensitive. Therefore, it is vital to precisely diagnose the patients alleged with SARS-CoV-19 infection for the opportunity to isolate the virus and the treatment of the patients. The widely used test for diagnosing SARS-CoV-19 currently is the (RT-PCR) i.e. reverse transcription quantitative—polymerase chain reaction assay which involves amplification of viral RNA from the sample collected from the diagnosed patient. As reported in several articles, the retrieval of a specimen from lower respiratory tract has caused discomfort and at certain cases bleeding in the patients. It also puts the health care professionals at risk of transmission of the COVID-19 virus. However, this RT-PCR technique has certain drawbacks like the lack of real time monitoring, long processing time along with trained staffs for operating advanced laboratory equipment. Therefore, scientists and doctors all over the world are engaged in developing easier and cheaper real time diagnostic tools for detection of COVID-19 virus.

Recently, biosensors have gained unimaginable attention in the medical field especially in diagnosis of various viral and bacterial diseases. Biosensors can be well utilized in areas like drug detection, food quality management and diagnostic of diseases. In this work, we propose a multifunctional sensor which conducts numerous measurements of various parameters required for detection of COVID-19 virus. A particular parameter is independently measured by each sensor and a combination of all the independent values is obtained and analyzed. A signal processing algorithm is required to combine the obtained independent values to provide a resultant measurement. This system is called a Multisensory system. Multisensory data fusion is the mechanism of obtaining an overview of the resultant measurement by combining all the independent sensor measurements. [15]

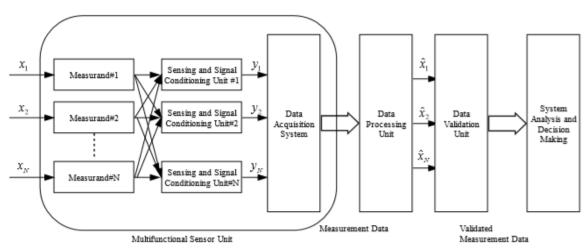


Fig 2: Signal/data processing of a multifunctioning sensor

The most commonly observed symptoms for COVID-19 is fever and increase in WBC count (85.71%). [16, 17, 18] With these two parameters in mind a multi-functioning sensor is designed with two sensors i.e. a temperature sensor (*LM35 series*) for the detection of fever by monitoring body temperature, an optical sensor which provides an oblique illumination with LEDS which helps in analyzing the increase in WBC concentration in the blood capillaries. The LM35 series sensors have been considered here for the body temperature measurement. Its temperature measurement range entails from 55 °C - 150 °C making it suitable for detecting a fever. [20] A portable device for measurement of WBC by placing the patient's fingertip on it without the need for a blood test has been developed by a team of international researchers. The project is called Leuko and it has developed an optical sensor which provides an oblique illumination with LEDS which helps in analyzing the WBC concentration in the blood capillaries. [19] The widespread of the SAR-CoV-19 has been exponential and has already 90 times higher laboratory confirmed cases than the total confirmed cases of MERS and SARS. [21] Therefore a well-integrated multi-functioning sensor can be used as an ideal candidate for detecting COVID-19 and such viruses. Multi-functioning sensors can play an effective role in detection of virus in food quality management, drug detection and diagnosis of viral diseases due to their specificity, accuracy, rapidity and compactness of the equipment. Due to the continuously increasing number of affected individuals all over the world, there is undoubted need for faster and more accurate diagnostic tools for identification of the coronavirus which can immensely contribute to the intervention and control of the worldwide pandemic.

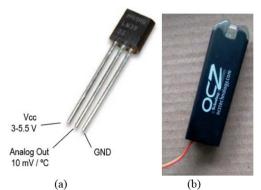


Fig 3: (a) Regular LM35 sensor (b) Encapsulated LM35 sensor

2. METHODOLOGY

2.1. DIAGNOSIS (COVID-19)

In the city of Wuhan of China, a large portion of people were widely diagnosed with pneumonia from an unknown causative agent and was reported in December 2019. The causative agent was then identified as SARS-CoV-19. It has been posed as a worldwide threat due to its rapid transmission from human to human through air droplets. More information about transmission is available on the reference mentioned adjacent. [17, 18]. Therefore, it is vital to precisely and rapidly diagnose patients suspected with COVID-19 infection to carry out necessary actions for treatment and their isolation. Some of the commonly observed characteristics in the affected individuals are: Weakness, diarrhea, chest tightness, fever, vomiting, cough etc. which can be used for clinical manifestation. Of all the clinical characteristics, the presence of cough and fever were the most frequently observed symptoms.[16] Coronavirus disease is also diagnosed with the supplementary information obtained from the laboratory results. [17, 18] In a test done by a hospital on 14 confirmed COVID-19 cases, 12 people were reported to have a sharp increase in the white-cell count (85.71%) and a significant decrease of the lymphocyte and monocyte count was also identified. [16] Thus, the clinical laboratory results prove vital for a doctor's consideration during the detection of the novel coronavirus infection.

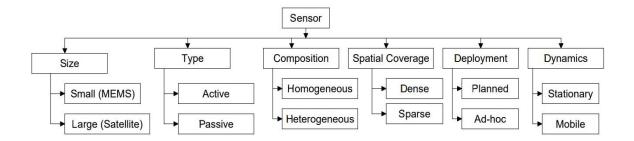
2.2. MECHANISM OF ACTION (COVID-19)

SARS-COVID-19 are positive stranded RNA viruses with a protective nucleocapsid. To interpret or intervene in the pathogenetic mechanism of the virus, it is imperative to understand its viral structure and its genome. The entry of SARS-CoV-19 into a human body is observed to take place through respiratory droplets that are less than >5-10 μm in diameter from sneezing and sneezing. From the inner respiratory tract, it travels through the trachea and reaches the lungs instantly. It then progressively makes its way into the blood vessels through the alveolar sacs. The blood vessels have an inner thin flat layer of cells called endothelium. This endothelium layer has surface receptors and enzymes, and in this case the surface enzyme is ACE-2. The spike protein of the SARS-CoV-19 attaches itself to the ACE-2 enzyme, which leads to the inflammation of the endothelium cells in the blood vessels. Angiotensin (peptide hormone that causes vasoconstriction) is converted into Angiotensin-1 by the enzyme Renin, the angiotensin-1 is further converted into angiotensin-2 with the help of enzyme ACE. Now with the assistance of ACE-2 enzyme, the peptide hormone Angiotensin-2 is converted into Angiotensin-1, 7 which is a vasodilator and reduces the inflammation. However, when the virus binds to the enzyme ACE-2 acting as a competitive inhibitor, it can no longer convert angiotensin-2 into angiotensin-1, 7. This leads to an increased level of angiotensin-2 in the blood vessel which causes vasoconstriction, increased blood pressure, increased vascular permeability, pulmonary edema and causes oxidative stress in the endothelium. Just below the endothelium, Von Willebrand's factor is present and this Von Williebrand's factor which acts as a prothrombin is released into the lumen of the blood vessel upon the inflammation of the endothelium cells coupled with increase in oxidative stress. This leads to form intra-arterial thrombosis. An infected person on an approximate of day 21 has been observed to have abnormally increased secretion of Von Williebrand's factor in the blood vessels.

To summarize, when the virus binds the endothelium, it takes out ACE-2 by competitive inhibition, now ACE-2 cannot prevent angiotensin-2 which is now reining unrestrained, therefore causing excess oxidative stress and release of increased levels of NADPH oxidase leading to more inflammation of the endothelium cells. NADPH oxidase is coupled with increased levels of Von Williebrand's factor to form intra-arterial thrombosis (Leading to myocardial infarction). The final common agent in this process taking most of the patients to the intensive care is a process termed as oxidative stress. The people with worst oxidative stress are the people with diabetes, obesity and cardio-vascular diseases and these are exactly the same kind of people who have the highest risk of mortality in COVID-19.

2.3. MULTI-FUNCTIONING SENSOR FOR THE DIAGNOSIS OF COVID-19

2.3.1. INTRODUCTION OF A SENSOR



The flowchart provided above depicts the different attributes of a sensor. A system which actively responds to physical stimulus, ultimately providing an electrical output is called a sensor. The selection of a particular sensor depends directly on the application it is being used. [15] The various available types of sensors in the market are listed below:

- Biosensor
- Chemical sensor etc.

The characteristics of a sensor can further be divided into two categories namely, (a) static and (b) dynamic. More information about sensors, their types and their signal processing strategy is available in the provided reference adjacent. [15]

2.3.2. DESIGN OF A SENSOR

There are two important stages in the designing of a multi-sensor which are:

- Design of sensor unit [23]
- Development of algorithm for signal reconstruction [24] [25]

2.3.3. FUNCTIONALITY OF MULTI- SENSOR

In this paper, we are proposing an idea of utilizing a multi-functioning sensor which has the ability to detect COVID-19 virus by real time analysis of the individuals. The multi-functioning sensor entails a temperature sensor for fever detection and an optical sensor which has the ability to quantify the WBC count in the patient. The *LM35 series* is used as a temperature sensor in the design of this multi-functioning sensor. These LM35 series are precision integrated-circuit temperature devices with an output voltage linearly proportional to the Centigrade temperature. [20] The LM35 device can provide typical accuracies of ± 0.75 °C change in temperature for a full -55 °C to 150 °C temperature range measurement. Self-heating is very low as it draws only 60 μ A of power from the supply. [26] The threshold temperature for fever detection can be set at 38 °C for all individuals and the electrical output for the measured reading should be transferred for further data acquisition and processing.

For the quantitative analysis of WBC, we use a device developed by a team of international researchers, this project is called Leuko. The patient is required to place his/her fingertip on the device, following which the optical sensor undergoes optical scanning with the help of oblique illumination with LEDs and captures images of the capillaries under the outer skin with cellular resolution. The obtained images are analyzed by the automatic algorithms that is capable of detecting of WBC and therefore provides the concentration/count of the WBC in the patient's blood. This compact device allows the patients to carry out such tests at home reducing the need to go to a hospital/diagnostic center. The number of white blood cells in the blood at normal conditions is 4500-10000 WBC per micro-liter, this can be used as a threshold count in the sensor for detection of abnormal increase in WBC count during the infection of COVID-19 disease. [19] Multiple sensors and their signal conditioning elements are connected to a data processing system. The data acquisition system in the multi-sensor is supplied with the measured data through electrical impulse from both the temperature sensor and optical sensor for further processing. Data processing unit carries out the various data processing operations like signal reconstruction on the obtained data. Reliability of the data from the sensor is a paramount important entity [27], [28]. Once the data is processed, it is then visualized to gain the desired outcome, in this case whether a patient is positive or negative of being infected with COVID-19 with the parameters that is considered. Therefore, a well-integrated multi-functioning sensor can be used as an ideal candidate for detecting COVID-19 and such viruses.

3. RESULT AND DISCUSSIONS

3.1. TO ENSURE RELIABILITY IN A MULTI-FUNCTIONING SENSOR

A sensor called SEVA i.e. self-validating has been developed which has the capacity to self-diagnosis the multi-sensor to provide the measurement as well as the diagnostic values. The figure shown below portraits the functionality of the SEVA sensor and the multiple outputs is listed below. To ensure reliability in a multi-sensor, we use this sensor analysis approach as the manual approach is prone to errors in the article. [29], [30] and time consuming. In [31], the authors have

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introduced a failure detection and recovery (FDIR). The reliability software analysis and its failure detection in the system is detailed

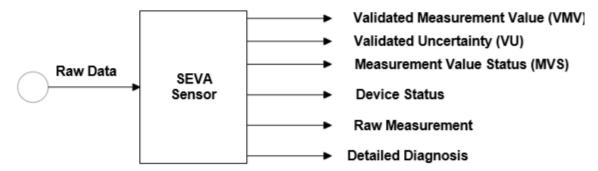


Fig 4: Self- validating sensor

3.2. LIMITATIONS OF A MULTI-FUNCTIONING SENSOR

Pressure, humidity, temperature and vibration are environmental variables which have a direct effect on dynamic and static performance of the sensor. A sensor's accuracy and its usual range is confined to the linear region of the sensor's features. [15]

3.3. SOLUTION FOR THE LIMITATIONS

One of the many methods to linearize sensor output is linearization based on Artificial Neural Network. It is the most frequently used approach which provides superior results compared to others.

3.4. ADVANTAGES OF MULTI-FUNCTIONING SENSOR

Various advantages are observed in a multifunctional sensor system are listed below,

- Convenient processing
- Lower power consumption
- Compactness

3.5. DISADVANTAGES OF MULTI-FUNCTIONING SENSOR

The Multi-functioning sensor has some inherent disadvantages i.e.

The integration of several sensing unit is a risk of failure because if one integration fault occurs there can be a shattering incident as all the systems rely on the multi-sensor.

4. CONCLUSION

In this paper, we propose a multifunctional sensor which conducts multiple measurements of various parameters required for detection of COVID-19 virus. Here, an overall study of the virus activity is done and a multi-sensor has been specifically designed for the diagnosis of viruses like SARS-CoV-19 by combining an efficient temperature sensor such as the LM35 series and an optical sensor which has the ability to quantitatively analyze WBC has been developed by the project LEUKO. These devices entail qualities quoted as rapidity, sensitivity and specificity. The advantages, disadvantages, limitations and its reliability of such a multi-functioning sensor has been studied and mentioned here thoroughly. The total confirmed cases have already been observed to rise above 90 times of that of MERS and SARS. Therefore, the proposed well integrated multi-functioning sensor proves to be an easy to implement and reliable diagnostic tool to drastically improve the rapidity and accuracy in the detection of SAR-CoV-19 as well as other viral diseases and dismisses the burden on PCR-based tests.

REFERENCES

- [1] Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395(10223):497–506
- Fehr AR, Perlman S, Coronaviruses: an overview of their replication and pathogenesis. In: Maier HJ, Bickerton E, Britton P, eds. Coronaviruses: Methods and Protocols. Vol. 1282. New York, NY: Springer; 2015:1-23
- Kim Y-I, Kim S-G, Kim S-M, et al. Infection and rapid transmission of SARS-CoV-2 in ferrets. Cell Host Microbe 2020; (e-pub ahead of print). doi: 10.1016/j.chom.2020.03.023
- WHO Director-General's opening remarks at the media briefing on COVID-19-11 March 2020 n.d. https://www.who.int/dg/speeches/detail/whodirector-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020.(accessed March 22, 2020).
- Coronavirus Update (Live): 629,450 Cases and 28,963 Deaths from COVID-19 Virus Outbreak Worldometer https://www.worldometers.info/coronavirus/.(accessed March 28, 2020).
- To KK, Tsang OT, Chik-Yan Yip C, et al. Consistent detection of 2019 novel coronavirus in saliva. Clin Infect Dis 2020;4-6:ciaa149

ISSN: 2278-0181

Vol. 9 Issue 07, July-2020

- Wu Y, Ho W, Huang Y, et al. SARS-CoV-2 is an appropriate name for the new coronavirus. Lancet 2020;395(10228):949-950
- Khurshid Z, Asiri FYI, Al Wadaani H. Human saliva: non-invasive fluid for detecting novel coronavirus (2019-nCoV) Int J Environ Res Public Health 2020;17(7):22-25
- Azzi L, Carcano G, Gianfagna F, et al. Saliva is a reliable tool to detect SARS-CoV-2. J Infect 2020; (April): S0163-4453(20)30213-9
- [10] Xu R, Cui B, Duan X, Zhang P, Zhou X, Yuan Q. Saliva: potential diagnostic value and transmission of 2019-nCoV. Int J Oral Sci 2020;12(1):11
- [11] Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020;395(10223):507-513
- [12] Patel R, Babady E, Theel ES, et al. Report from the American Society for Microbiology COVID-19 International Summit, 23 March 2020: value of diagnostic testing for SARS-CoV-2/COVID-19. MBio 2020;11(2):e00722-20
- [13] Report of the WHO-China Joint Mission on Coronavirus Disease. 2019 (COVID-19). Available at: https://www.who.int/ docs/defaultsource/coronaviruse/who-china-joint-missionon-covid-19-final-report.pdf. Accessed May 8, 2020
- [14] To KK, Tsang OT, Leung WS, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. Lancet Infect Dis 2020;20(5):565-574.
- [15] Recent Advances in Multifunctional Sensing Technology on a Perspective of Multi-Sensor System: A Review by Bansari Deb Majumder, Joyanta Kumar Rov. Subhransu Padhee
- [16] Multiple parameters required for diagnosis of COVID-19 in clinical practice- Pinggui Lei, Bing Fan, Jujiang Mao and Pingxian Wang Published online 2020 Mar 19. doi: 10.1016/j.jinf.2020.03.016
- [17] Shi H., Han X., Jiang N., Cao Y., Alwalid O., Gu J. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, china: a descriptive study. Lancet Infect Dis. 2020 doi: 10.1016/S1473-3099(20)30086-4. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [18] Guan W.J., Ni Z.Y., Hu Y., Liang W.H., Ou C.Q., He J.X. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020 doi: 10.1056/NEJMoa2002032. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [19] Optical sensor-driven device can count white blood cells through the skin: A portable optical device for placing on the fingertip can count white blood cells without a blood test. - BioOptics World Editors
- Multi-Sensor System for Remote Environmental (Air and Water) Quality Monitoring- Mitar Simić, Student Member, IEEE, Goran M. Stojanović, Member, IEEE, Libu Manjakkal and Krzystof Zaraska
- [21] Mahase, E. Coronavirus: COVID-19 Has Killed More People Than SARS and MERS Combined, Despite Lower Case Fatality Rate. Br. Med. J. 2020, M641.
- [22] C.-Y. Chong and S. P. Kumar, "Sensor networks: evolution, opportunities, and challenges," Proceedings of the IEEE, vol. 91, no. 8, pp. 1247-1256, 2003.
- [23] J. Sun and K. Shida, "Multi-layered sensing approach for environment perception with one multi-functional sensor," IEEJ Transactions on Sensors and Micromachines, vol. 120, no. 4, pp. 162-168, 2000.
- [24] R.Z.Morawski, "Unified approach to measure and reconstruction," IEEE Transactions on Instrumentation and measurement, vol. 43, no. 2, pp. 226-231,
- X. Liu, J. Sun, and D. Liu, "Nonlinear multifunctional sensor signal reconstruction based on total least squares," in Journal of Physics: Conference Series, vol. 48, no. 1. IOP Publishing, 2006, p. 281
- [26] P. W. Alexander, L. T. D. Benedetto, T. Dimitrakopoulos, D. B. Hibbert, J. C. Ngila, M. Sequeira and D. Shiels, "Field-portable flow-injection analysers for monitoring
- [27] Z. Shen and Q. Wang, "Data validation and validated uncertainty estimation of multifunctional self-validating sensors," IEEE Transactions on Instrumentation and Measurement, vol. 62, no. 7, pp. 2082-2092, 2013.
- [28] J.-l. Yang, Y.-s. Chen, L.-l. Zhang, and Z. Sun, "Fault detection, isolation, and diagnosis of self-validating multifunctional sensors," Review of Scientific Instruments, vol. 87, no. 6, p. 065004, 2016.
- [29] M. Henry and D. Clarke, "The self-validating sensor: rationale, definitions and examples," Control Engineering Practice, vol. 1, no. 4, pp. 585-610,
- M. Henry, "Recent developments in self-validating (seva) sensors," Sensor Review, vol. 21, no. 1, pp. 16–22, 2001.
- [31] Z. Shen and Q. Wang, "Failure detection, isolation, and recovery of multifunctional self-validating sensor," IEEE Transactions on Instrumentation and Measurement, vol. 61, no. 12, pp. 3351-3362, 2012.