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Catheter like in vivo fiber optic probe for rapid diagnosis of SARS-CoV-2

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ABSTRACT

With the persistent rise of COVID-19 cases, it is imperative to have rapid assessment of infection with minimal logistics. Although different diagnostic techniques for SRAS-CoV-2 are available, there are limitations in terms of turn-around time, sensitivity, and specificity issues. In this direction, this work reports the effective exploitation of fiber optic biosensor especially for in vivo identification of SARS-CoV-2. The proposed catheter like probe is envisioned to alleviate the need for sample storage as well as other allied complicacies. The scheme for qualitative as well as quantitative assessment is elaborately presented here for this portable probe. The proposed probe equipped with rapid diagnosis is believed to have immense potential through adaptive measures.

1. Introduction

SARS COV-2 has taken a large toll in the global arena. It seems that the whole world is reeling under the powerful grip of this deadly virus. The virus has severe impacts on global economy. Even the developed nations have registered highest fatalities incurred by the virus. Although the fatalities have dropped marginally, still the picture is gruesome. As per reports, there are varieties of symptoms (COVID-19, 2020; https://www.cdc.gov/coronavirus/2019-ncov/lab/guidelines-clinical-specimens.html; https://www.mohfw.gov.in/pdf/5Sample%20collection-packaging%202019-nCoV.pdf; Biswas, 2021; https://www.belfasttelegraph.co.uk/news/health/coronavirus/coronavirus-two-northern-ireland-firms-are-selling-covid-19-tests-around-the-world-but-no-orders-from-nhs-39057806.html), which can help us to identify that the person is infected, or not. However, since the outbreak from Wuhan, China; all premier health agencies as well as govt. organizations are keeping a close watch/track on it (https://www.belfasttelegraph.co.uk/news/health/coronavirus/coronavirus-two-northern-ireland-firms-are-selling-covid-19-tests-around-the-world-but-no-orders-from-nhs-39057806.html; Details, 2019; HHS Supports Development of First High-Throughput COVID-19 Diagnostic Test, https://www.hhs.gov/about/news/2020/03/09/hhs-supports-development-of-first-high-throughput-covid-19-diagnostic-test.html). Earlier the symptoms are simply restricted to high persistent fever; shortness of breath; fatigue etc. Now, it has permeated into other sectors. Loss of smell or taste is now granted as another symptom of this virus. Apart from this, even roughness of skin or rashes has been regarded as precautionary symptoms of Covid-19. The gruesome picture is further aggravated by the arrival of new Corona Strains, as declared by United Kingdom this year following which lock down has been imposed in major cities across the world. Notwithstanding these signs, the danger lies with the asymptomatic one. As per reports, these asymptomatic patients act as super-spreader (Biswas, 2021;https://www.belfasttelegraph.co.uk/news/health/coronavirus/coronavirus-two-northern-ireland-firms-are-selling-covid-19-tests-around-the-world-but-no-orders-from-nhs-39057806.html; Details, 2019; HHS Supports Development of First High-Throughput COVID-19 Diagnostic Test, https://www.hhs.gov/about/news/2020/03/09/hhs-supports-development-of-first-high-throughput-covid-19-diagnostic-test.html). They unknowingly infect the persons who are exposed to them. As a result, there is high risk of community spread/transmission. Once this happens, the whole locality as well as region is at risk. If we look at the available diagnostic schemes, SARS-CoV-2 can be identified through several ways. Starting from RT-PCR, it can be sensed through several techniques (Zehnbauer and Diagnostics in the Time of Coronavirus Disease, 2019; Nag et al., 2020; Matsuda et al., 2021; Soleimani et al., 2021; Holzner et al., 2021; Scohy et al., 2020; Li et al., 2020; Whitman et al., 2020). It is worthy to mention that there may be asymptomatic/symptomatic/pre symptomatic cases. Along with that, another important parameter/factor is the viral load. The existing procedures, although robust in their domain, cannot act as standalone units for diagnosis of SARS-CoV-2. So far, the existing detection mechanisms are concerned, molecular diagnosis is always preferred to others as it can provide accurate diagnosis. Meanwhile, rapid antigen and rapid antibody test are emerging as potential candidates towards quick identification of SARS-CoV-2. Within a short span of time, diagnosis results can be achievable; thus, enabling mass
tracing. However, in most cases, RT-PCR is considered as one of the best schemes as it has 95% accuracy. It is also regarded as the gold standard. The time taken during conduction of the test is a real concern. With daily spike in Covid-19 cases, the search for an effective and rapid point-of-care is extremely imperative. Barring aside the developed nations, the developing nations are under huge pressure to combat this Covid-19.

So far, there are reports of firms as well as drug companies that come up with rapid test. However, they are not adequate. The absence of a rapid standalone test could be easily felt when there are thousands of new cases daily. Driven by these challenges, this brief article attempts to propose for an innovative arrangement which could give the results within a very short span of time. The current work proposes a novel fiber optic sensor with provisions for in vivo sensing of infection via either nasopharyngeal or oropharyngeal swabs. The proposed scheme is envisioned to take care of the sensitivity as well as specificity issue which is considered as an impairing issue in the existing rapid tests. The qualitative as well as quantitative schemes has been nicely dwelt upon to enable this proposed probe a versatile one.

2. Sars cov 2

The 2019 Novel Coronavirus (2019-nCoV or SARS-CoV-2) bears similar sequence to the first SARS-CoV virus and bat coronaviruses. To be precise, belonging to the coronavirus family, it is a positive-sense single-stranded RNA (+ssRNA) (Biswas, 2021;https://www.belfasttelegraph.co.uk/news/health/coronavirus/coronavirus-two-northern-ireland-firms-are-selling-covid-19-tests-around-the-world-but-no-orders-from-nhs-39057806.html; Details, 2019;HHS Supports Development of First High-Throughput COVID-19 Diagnostic Test, https://www.hhs.gov/about/news/2020/03/09/hhs-supports-development-of-first-high-throughput-covid-19-diagnostic-test.html; Zehnbauer and Diagnostics in the Time of Coronavirus Disease, 2019; Nag et al., 2020). The main transmission of COVID-19 is ascribed to the respiratory droplets. The virus COVID-19 is found to be a total nightmare as it has taken a large toll. Many companies are gearing together to come up with it. Few developments are being made in the labs to formulate probe, which can detect the virus rapidly. In most of the cases, the testing is invasive in nature. Even after symptoms, the patients in some cases appear to be negative.

Different diagnostic techniques are available to diagnose COVID-19 (Nag et al., 2020; Matsuda et al., 2021; Soleimani et al., 2021; Holzner et al., 2021; Scohy et al., 2020; Li et al., 2020; Whitman et al., 2020; Cassaniti et al., 2020; Wan et al., 2021; Murugan et al., 2020). Further, the requirement of careful storage of samples/swabs along with trained personal remains another hurdle. Similarly, most of the testing schemes are not recyclable which limits their use. With a view to getting a fair insight into the available techniques, a comparative treatment in tabulated form has been provided via listing of the important parameters linked to tests [see Table 1].

It is quite evident that rapid antigen test as well as rapid antibody test work efficiently when the viral load is high. In low viral loads, both the tests lose their sensitivity. However, through an optimized threshold value of viral load in conformity with WHO guidelines, the covid cases can be tested in mass scale with these techniques, although RT-PCR is always regarded as the gold standard.

| Tests                  | Patient type     | Viral Load | Response time | Sensitivity | Specificity | Ref.               |
|------------------------|------------------|------------|---------------|-------------|-------------|-------------------|
| Rapid Antigen Test     | Symptomatic/asymptomatic | Low        | NS*           | 96.7%       | 100%        | (Matsuda et al., 2021) |
| BioSpeedica COVID19 Speed-Antigen Test | Symptomatic/pre symptomatic/asymptomatic | High | NS           | 65.5%       | 100%        | (Soleimani et al., 2021) |
| AgPOCT (Boehr)         | Symptomatic/asymptomatic | High       | NS           | 68.9%       | 99.6%       | (Holzner et al., 2021) |
| Cortes COVID-19 Ag Respi-Strip | NS                  | High       | 30 Mins      | 100%        | 100%        | (Scohy et al., 2020) |
| Rapid Antibody Test    | IgM/IgG           | NS         | High         | 20 mins     | 81.8–100    | 84.3–100         | (Li et al., 2020) |
|                        | IgM/IgG           | NS         | NS           | 63.3        | 100         | (Whitman et al., 2020) |
|                        | IgG/IgM           | NS         | NS           | 88.66       | 90.6        | (Cassaniti et al., 2020) |

* denotes “Not specified”.

Fig. 1. Schematic of intensity modulated U-shaped probe.
For example, if attained intensity calibration procedure. threshold for positive cases identifications; thereby approximating the combined profiles corresponding to positive (SARS-CoV-2 infected) and samples without any infection from SARS-CoV-2. Accordingly, the assist the coupled localized surface plasmon resonance; it is preferable to of suitable functionalities corresponding to analyte. The exposed region have noble metal nanoparticles, which is further immobilized with suitable bio receptors/bio linkers. As for this proposed catheter like probe, antibodies/protein could be taken as bio receptors/bio linkers for SARS-CoV-2 (Boruah et al., 2020). The as assembled catheter like probe when encounters the analyte, i.e., the virus, there occurs intensity variation which eventually leads to modulated light intensity. The intensity variation becomes more prominent when there is impregnation of suitable functionalities corresponding to analyte. The exposed region is then subjected to impregnation of suitable functionalities. In order to assist the coupled localized surface plasmon resonance; it is preferable to have noble metal nanoparticles, which is further immobilized with suitable bio receptors/bio linkers. As for this proposed catheter like probe, antibodies/protein could be taken as bio receptors/bio linkers for SARS-CoV-2 (Boruah et al., 2020). The as assembled catheter like probe when encounters the analyte, i.e., the virus, there occurs intensity modulation, as depicted in Fig. 1.

The signal interrogation can be executed via two routes—namely intensity based, or wavelength/frequency based. However, if we look at the expediency of the schemes, the intensity-based interrogation method can be deemed to be the best fit as it will require minimal logistics; albeit the detector should be of high precision. Once the proposed setup is tested in a controlled environment such as positive samples (infected with SARS-CoV-2); the time resolved intensity profile could be deciphered [see Fig. 1]. Similarly, the same set up can also be checked for samples without any infection from SARS-CoV-2. Accordingly, the combined profiles corresponding to positive (SARS-CoV-2 infected) and negative (SARS-CoV-2 not infected) can be correlated in order to set a threshold for positive cases identifications; thereby approximating the calibration procedure.

For example, if attained intensity $I > \text{Threshold Intensity } I_0$; it implies $+ve$ (1)

$\text{Attained intensity } I < \text{Threshold Intensity } I_0$; it implies $-ve$ ............(2)

The proposed U-shaped technique has excellent sensitivity from parts per trillion (ppt) to parts per billion (ppb) levels as published reports (Sahajpal et al., 2020; Funari et al., 2020; Boruah et al., 2020; Boruah and Biswas, 2018; Boruah and Biswas, 2021). As validated by (Funari et al., 2020; Boruah et al., 2020; Boruah and Biswas, 2018; Boruah and Biswas, 2021), the U-shaped probes possesses a rapid response time of 15 s to 60 s at maximum. Likewise, recyclability and repeatability are the two other features possessed by this U-shaped fiber as evidenced in these literatures.

Once we are sure enough of getting similar results in case of nasopharyngeal/oropharyngeal swab, we can deploy our proposed setup for real time detection.

As shown in Fig. 2 (a) and (b), the schematics are illustrated. The first figure (a) implies probing of nasopharyngeal swab whereas (b) implies oropharyngeal swab.

As illustrated in Fig. 2, the U-shaped probe upon interaction with nasopharyngeal/oropharyngeal swab triggers modulated intensities. If the attained intensity abides by equation (1), then the swab examined person can be declared to be infected with SARS-CoV-2. Otherwise, as per equation (2), the swab belonging to the examined person is negative. Accordingly, the device can be customized with two indicators implying $+ve/-ve$ detection based on intensity profile. Moreover, depending on the modulated response along with calibration from gold standard, the viral load can also be incorporated in the proposed scheme. The handheld unit as depicted in Fig. 2 a and b comprises of a display for qualitative/quantitative test results along with optical and electrical interconnects, namely suitable detector as receiver and suitable optical source as transmitter. In addition, wireless feature can also be arranged inside this. We propose the dimension of this scheme to be of 50 mm $\times$ 20 mm $\times$ 10 mm through optimal miniaturization. Depending on the receptor for functionalizing the probes, the two schemes are very viable/adoptable. The positivity of the cases is confirmed based on the modulated responses that is obtained with respect to the swabs. Before implementing it to direct sample analysis, the optimization of bio-receptor with different species of viruses belonging to the family of SARS-CoV-2 will be carried out. Accordingly, the modulated response engaging the particular bioelectrode conducotive to specifically corona virus will be noted and accordingly, the proposed scheme will be calibrated. Provided there is modulated response above the threshold value,
the diagnosis will be done. This will, as such, enable us to avoid the case of false positive results. This way, the sensitivity of the probe can be managed at its optimum level.

The proposed scheme will render a qualitative analysis as illustrated in Fig. 3. In other words, the confirmation of a patient whether he/she is positive or negative can be discerned out. With a little bit of upgradation/tweaking during calibration prior to real time test; there is every possibility of estimating or assessing the trace of SARS-CoV-2. This will help in identifying the level of infection in the patient’s body. Alternatively, different traces of SARS-CoV-2 spiked samples can be analyzed through the prototype, which will result in modulated intensity levels. Taking note of these magnitudes of modulated intensities, it is feasible to deploy the prototype for quantitative estimation/assessment too, as depicted in Fig. 3. This can be adapted in both the schemes. Apart from this, the scheme being portable and miniature in size can be easily combined with wireless facility through customized apps via SMARTPHONE. As such, the test results can be easily tucked in cloud storage so that subsequent e-health care can be administered. Although the proposed scheme could be a viable technique for rapid assessment of covid cases, however, testing of the probe via real data analysis could have been more conclusive. It is assured that adoption of the proposed scheme for sensing real samples is on the pipeline and will be executed in future.

4. Conclusion

In summary, a novel catheter like in vivo sensing of SARS-CoV-2 is proposed here. This specialized fiber optic probe with synergistic integration of optimized photonics with further assistance of suitable biomarkers for SARS-CoV-2 can yield rapid diagnosis via insertion into the nasal/oral tract. Based on intensity modulation, the sensing scheme emerges to be very cost effective with minimal logistics. This unique adaptation is very simple to use without requiring any trained personal. The miniaturized version can be easily executable for self-analysis; thus, alleviating hassles as well as discomfits faced by patients going for established/registered clinics/lab/hospitals. Rendering not only qualitative assessments, the prototype can be also tuned to undergo quantitative assessment via controlled standardization against intensity magnitudes against spiked SARS-CoV-2 infection. In addition, the proposed probe, once suitably optimized and calibrated with gold standard, can be reusable which can thereby lessen the turn-around time. We believe that the proposed scheme has immense potential in the effective assessment of viral infection in the current scenario of the pandemic.

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6. Availability of data and material

There is no associated data.

7. Authors’ contributions

Author RB has done everything.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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