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Label-free electrochemical aptasensor for rapid detection of SARS-CoV-2 spike glycoprotein based on the composite of Cu(OH)$_2$ nanorods arrays as a high-performance surface substrate

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**ABSTRACT**

The development of advanced electrode materials and the combination of aptamer with them have improved dramatically the performance of aptasensors. Herein, a new architecture based on copper hydroxide nanorods (Cu(OH)$_2$ NRs) are directly grown on the surface of screen printed carbon electrode (SPCE) using a two-step in situ, very simple and fast strategy and was used as a high-performance substrate for immobilization of aptamer strings, as well as an electrochemical probe to development a label-free electrochemical aptasensor for SARS-CoV-2 spike glycoprotein measurement. The Cu(OH)$_2$ NRs was characterized using X-ray Diffraction (XRD) and electron microscopy (FESEM). In the presence of SARS-CoV-2 spike glycoprotein, a decrease in Cu(OH)$_2$-NRs-associated peak current was observed that can be owing to the target-aptamer complexes formation and thus blocking the electron transfer of Cu(OH)$_2$ NRs on the surface of electrode. This strategy exhibited wide dynamic range in of 0.1 fg mL$^{-1}$ to 1.2 µg mL$^{-1}$ and with a high sensitivity of 1974.43 µA mM$^{-1}$ cm$^{-2}$ and low detection limit of 0.03 ± 0.01 fg mL$^{-1}$. of SARS-CoV-2 spike glycoprotein deprived of any cross-reactivity in the presence of possible interference species. In addition, the good reproducibility, repeatability, high stability and excellent feasibility in real samples of saliva and viral transport medium (VTM) were found from the provided aptasensor. Also, the aptasensor efficiency was evaluated by real samples of sick and healthy individuals and compared with the standard polymerase chain reaction (PCR) method and acceptable results were observed.

1. Introduction

Sensitive and selective designation of pathogens in complex actual samples is very significant. In global diseases for example coronavirus disease 2019 (COVID-19) pandemic, a selective, accurate, inexpensive, rapid and portable test is needed to diagnostic test at home and preventing the spread of the disease.

Recently, electrochemical sensors and biosensors have attracted a lot of attention due to their ability to detect selectively and sensivity a wide range of targets and in medical diagnosis and biomedical research, food control, environmental monitoring, forensics, drug discovery and etc. are of great importance [1–15]. Among the various biomolecules used to preparation of biosensing layers, aptamers have received much attention from researchers in recent years. Aptamers, as synthetic antibodies, are one of the most promising molecular probes that are synthesized and selected in vitro through the ligand evolution and also the exponential enrichment (SELEX) process and they can be used to detect a wide range of targets, from small molecules to intact cells [16–19]. Among the advantages of aptamers, which make them a noteworthy choice for the development of biosensors, are three-dimensional unique binding sites against their targets, low cost, easy modification, fast production, less immunogenicity, long-term stability, reversible denaturation and pH/temperature stability [20–27]. Different types of aptamer sensors (aptasensor) have been developed based on various transducers, including: electrochemical methods, surface plasmon resonance, colorimetric approach, fluorescence spectroscopy, optical transducers, etc. [28–32]. Among these techniques, electrochemical methods have received many attentions due to their innate high sensitivity, fast response times, real-time monitoring, simplicity, cost effectiveness, small sample amount requirement, low detection limits, amenability to miniaturization, etc. [33–36].

In recent years, with remarkable achievements in nanotechnology
and nanoscience and taking advantage of the attractive advantages of electrochemical methods and integration with bio-diagnostic elements as a receiver have received much attention for the production of sensitive and efficient biosensors. The use of nanostructures has been shown to have a significant effect on the performance of aptasensors. Proper nanomaterial design not only provides a good substrate for anchoring aptamer strings, but also dramatically increases the sensitivity and performance of aptasensors by creating a larger, more biocompatible surface \[37–44\]. For this purpose, various nanoparticles have been used to develop aptasensors, for example: quantum dots, metal nanoparticles, carbon-based nanostructures, conducting polymers metal organic frameworks, and so on \[45–49\]. Among these, nanoparticles based on transition metals are of great interest due to their mesoporosity, natural abundance, environmental friendliness, high electrocatalytic activity and high electrical conductivity \[10,24,50,51\].

Copper nanoparticles have been widely used owing to their distinctive properties including: availability, easy synthesis, cost-effective, low toxicity and biocompatibility \[41,44,52,53\]. Among the various methods of synthesizing copper nanoparticles, the in-situ growth method is an attractive method because nanoparticles can be synthesized directly on the surface of electrode without the need for adhesives and organic solvents, which is fast and facile synthesis procedure and has the ability to morphological controllability and thickness. Also, in comparison with traditional methods of electrode modification, such as drop or film casting, this method prevents the aggregation of nanoparticles and is uniformly placed on the electrode surface, leading to increased stability, conductivity and their active surface \[54–55\]. Cu(OH)\(_2\) NRs, in addition to providing an extremely large surface area for aptamer strings further loading, also act as a suitable electroactive substrate owing to the large amount of copper placed on the electrode surface and the creation of an excellent cathodic current in the phosphate buffer, therefore, it can be a unique choice as a platform for the preparation of label free and ultrasensitive electrochemical aptasensors. Cu(OH)\(_2\) NRs have shown significant performance in a variety of applications including electrocatalysis, and energy storage because of their good electrocatalytic performance and high surface area but as far as we know, they have not yet been used to improve the performance of electrochemical biosensors \[54–58\].

In this study, a new architecture is designed to increase the efficiency of label free and ultrasensitive electrochemical aptasensor based on Cu(OH)\(_2\) NRs to SARS-CoV-2 spike glycoprotein measurement. Cu(OH)\(_2\) NRs are directly synthesized on the SPCE surface using a two-step in situ, very simple and fast method. The provided aptasensor showed satisfactory results in the diagnosis of SARS-CoV-2 spike glycoprotein including a wide dynamic range, low detection limit, selectivity and possibility of application in real samples. Also, compared to the PCR test of real samples of sick and healthy individuals, the results were very promising.

2. Experimental section

2.1. Materials

SARS-CoV-2 spike glycoprotein was purchased from cusabio Company (https://www.cusabio.com). The sequence of specific aptamer for SARS-CoV-2 spike glycoprotein \[59\] that was purchased from Bioneer Company (South Korea) is indicated below: 5′-NH\(_2\)-TGCTCTTTCCGCTTCTTCGCGGTCATTGTGCATCCTGACTGACCC-TAAGGTGGCACATCGGCGCCGTAAGTGCCGTGTGTGCGAA-3′.

Analytical grade of sodium hydroxide (NaOH \(>99\%\)), ammonium proxidisulfate ((NH\(_4\))\(_2\)S\(_2\)O\(_8\) \(>98\%\)), copper sulfate (CuSO\(_4\) \(>99\%\)), ammonium sulfate ((NH\(_4\))\(_2\)SO\(_4\) \(>99.5\%\)) and all other reagents were bought from Merck or Sigma-Aldrich and they were used without additional purification. Furthermore, 0.1 M disodium hydrogen phosphate (Na\(_2\)HPO\(_4\) \(>99\%\)) and monosodium dihydrogen phosphate (NaH\(_2\)PO\(_4\) \(>99\%\)) were used to preparing the phosphate-buffered solutions (PBS). The all experiments were performed at room temperature.

Scheme 1. Schematic illustration of the steps of the aptasensor preparation.
2.2. Instruments and electrodes

In order to investigate surface morphology, a MIRA3 TESCAN-LMU field-emission scanning electron microscope (FESEM) was applied which was then equipped with an EDS probe. The electrochemical investigations were recorded using a μ-Autolab type III/FRA2 (Eco Chemie B.V., Utrecht, The Netherlands) instrument equipped with NOVA software. The SPCE (bought from Dropsens (Spain)) was applied as a three-electrodes planar based on a graphite working electrode, silver pseudo-reference electrode and a carbon counter electrode. In order to measure the pH, the Metrohm pH meter (model 780 pH/mV meters) was applied.

2.3. Cu@SPCE fabrication

The Cu@SPCE and Cu(OH)$_2$ NRs@SPCE were prepared following the previous literature reports [55]. Before modification of SPCE, its surface was cleaned by electrochemical method. For this purpose, 10 μL of NaOH solution (0.1 M) was dropped onto the surface of SPCE and a sweeping potential was applied during 10 consecutive cycles and finally, the electrode was dried under N$_2$ gas. Then, 10 μL of the 0.5 M of (NH$_4$)$_2$SO$_4$ solution containing 0.02 M of CuSO$_4$ was dropped on the surface of electrode and a constant potential of −0.6 V during 600 s was applied in order to the electro-deposition of Cu clusters with suitable thickness and brilliant rose gold-colored onto SPCE surface (Cu@SPCE).

2.4. Cu(OH)$_2$ NRs@SPCE fabrication

In order to in situ growth the Cu(OH)$_2$ NRs on the surface of SPCE a drop of an alkaline oxidant solution containing 3.0 mL of DI water, 0.7 mL of (NH$_4$)$_2$S$_2$O$_8$ (1 M) and 1.4 mL of NaOH (10 M) it was placed on the electrode at room temperature. After 2 min, the Cu metal film turned into a uniform blue-colored Cu(OH)$_2$ NRs@SPCE [60]. Then, Cu(OH)$_2$ NRs@SPCE was washed with DI water and dried under N$_2$ gas. Cu(OH)$_2$ NRs@SPCE was used in order to develop of label free and ultrasensitive electrochemical aptasensor.

2.5. Preparation of the aptasensor

In this step, a drop of 5′-NH$_2$-aptamer solution (3 μM) was dropped on the Cu(OH)$_2$ NRs@SPCE surface for 1 h to immobilize the aptamer strings. Next, aiming at block the available non-bonded active surface, and avoid nonspecific adsorption, the BSA solution (10 μL of 1%) was incubated on the aptamer/Cu(OH)$_2$ NRs@SPCE surface for 30 min. Also, if not used of BSA, many non-specific sites cause non-specific adsorption, and results obtained from the measurements will not be accurate, because in real samples, other components of the real samples may cause interference in the signal peak due to blockage of other proteins, presence of ions, etc. The resulting electrode was named BSA/aptamer/Cu(OH)$_2$ NRs@SPCE in this step. After each step, DI water were used to wash the electrode surface to remove the unbonded molecules and dried under N$_2$ gas.

3. Results and discussion

3.1. Investigation of the Cu(OH)$_2$ NRs@SPCE characterization

The electrode modification method by Cu(OH)$_2$ NRs is shown in Scheme 1. The following mechanism that proposed by Zhang et al., can be explained the fabrication of.

Cu(OH)$_2$ NRs [60]:

$$Cu + 4NaOH + (NH_4)_2S_2O_8 \rightarrow Cu(OH)_2 + 2Na_2SO_4 + 2NH_3↑ + 2H_2O$$

In alkaline solution, the surface of metallic copper was quickly converted and oxidized to Cu$^{2+}$ using (NH$_4$)$_2$S$_2$O$_8$ after only a few

![Fig. 1. The FESEM images of Cu@SPCE (a-c), EDX spectrum (d) and EDS mapping of Cu@SPCE (e-g).](image-url)
minutes. Then, due to the highly alkaline condition, square planar coordination of Cu$^{2+}$ to OH$^{-1}$ groups was occurred, giving rise to stoichiometric chains alone. Then, these chains were connected through the bridging OH$^{-1}$ groups along the z-axis, which formed a nanowires structures [60].

In order to monitoring the structure and morphology of rod-like structures of Cu(OH)$_2$ NRs/SPCE, the FESEM images were used. Initially, the morphology of metallic copper that deposited on the surface of SPCE was investigated. As shown in Fig. 1 a–c, the well-ordered and vertically Cu clusters arrays, which are made from the accumulation small particles of its, were uniformly deposited on the SPCE surface which provides surface availability for the formation of Cu(OH)$_2$ NRs structures. Next, the Cu clusters were converted to Cu(OH)$_2$ NRs via chemical oxidation technique and the surface morphology of the blue film formed on the electrode surface was investigated using FESEM images. The FESEM images in Fig. 2a–c display the morphology changes of Cu clusters during the process of chemical conversion to Cu(OH)$_2$ NRs by diameter of 100 nm, which grown in different directions and uniformly cover the surface of the electrode.

The EDX results were examined to evaluate elemental composition of the modified SPCE at each stage. Fig. 1d shows the EDX spectrum of Cu@SPCE, which shows the attendance of Cu in Cu@SPCE, C that originated from SPCE. Moreover, in the Cu(OH)$_2$ NRs @SPCE EDX spectrum, in addition to the elements Cu and C, O was observed, which
confirms the successful change of Cu to Cu(OH)$_2$ NRS (Fig. 2d). Furthermore, the EDS mapping displaying the well and uniform distribution of Cu clusters on the Cu@SPCE (Fig. 1e-g) and Cu and O for Cu(OH)$_2$ NRS@SPCE (Fig. 2e-h) (C originated from SPCE). These results were consistent with the literature [55,56].

In order to evaluate the crystal structure of the as-prepared Cu(OH)$_2$ NRS, the XRD technique was applied (Fig. 3). The Cu(OH)$_2$ NRS shows diffraction peaks at 16.7, 23.8, 34.0, 38.2, 39.8, 53.2, 56.2, 63.4, 71.1$^\circ$ that are well matched with the (0 2 0), (0 2 1), (0 0 2), (0 2 2), (1 3 0), (1 5 0), (1 5 1), (0 6 2), (0 8 0) planes of the standard crystallographic spectrum of Orthorhombic Cu(OH)$_2$ (JCPDS no. 013-0420) structure with standard lattice constants of $a = 2.949$ Å, $b = 10.590$, $c = 5.256$ Å (Fig. 3), confirming the successful preparation of pure Cu(OH)$_2$ NRS.

The FT-IR spectroscopy was further applied to study the structure of Cu(OH)$_2$ NRS and also the interaction of aptamer with Cu(OH)$_2$ NRS. Fig. 4a shows the FTIR spectrum of aptamer with two sharp peaks at 3462 and 1639 cm$^{-1}$, which can be related to the N–H/O–H and C–O/N–H vibrations modes in the aptamer strings, respectively. The FT-IR spectrum of the synthesized Cu(OH)$_2$ NRS shows two strong peaks at 3569 and 3315 cm$^{-1}$ related to the O–H stretching vibration mode in Cu–O–H structure which supports the formation of hydroxyl groups at Cu(OH)$_2$ NRS, and the peaks at 940, 691, and 520 cm$^{-1}$ can be related to the Cu–O stretching and Cu–O–H bending vibrations modes (Fig. 4b) [55,61]. Moreover, the band around 1374–1628 cm$^{-1}$ shows the stretching mode of the absorbed water in the Cu(OH)$_2$ NRS. The FTIR spectra of aptamer/Cu(OH)$_2$ NRS shows some differences compared to the Cu(OH)$_2$ NRS (Fig. 4c). Change in the position and the intensity of O–H/N–H group in 3443 cm$^{-1}$ and the appearance of C–O group in 1641 cm$^{-1}$ can be indicated a successful attachment of the aptamer onto the Cu(OH)$_2$ NRS.

### 3.2. Electrochemical study of the proposed aptasensor stepwise preparation

The step-by-step fabrication process of aptasensor was characterized by square wave voltammetry (SWV) in BPS (0.1 M) with pH 7.4 (Fig. 5A). First, for the bare SPCE no obvious peak was observed (curve a, $I_{pc} = 0$). After Cu(OH)$_2$ NRS was embellished on SPCE surface (curve b, $I_{pc} = 152.87$), an cathodic peak current of Cu(OH)$_2$ NRS at 0.17 V was clearly appeared that this cathodic peak is suspected to be due to the electroreduction of Cu(OH)$_2$ to Cu$_2$O [62,63]. In the next step, as expected, after the immobilization of the aptamer strings as non-electroactive substance, the peak current reduced significantly (curve c, $I_{pc} = 101.32$), because the aptamer strings hindered electron transfer due to steric/conformational restrictions. After this step, similarly, cathodic peak current was further reduced with BSA assembled on the surface of modified electrode (curve d, $I_{pc} = –83.33$), indicating blockage of possible residual active site at the surface of modified electrode. Interestingly, after the embellishment of
800 pg mL\(^{-1}\) of the SARS-CoV-2 spike glycoprotein, cathodic peak current reduced obviously (curve e, \(I_{\Delta} = -34.66\)), shows that aptamer strings have captured the target molecules and the formation of SARS-CoV-2 spike glycoprotein-aptamer complex, induced conformational changes of the bound aptamers and increase steric/conformational restrictions that increased the space barrier and retard the electrolyte solution to reach the SPCE surface. These observations showed that the aptasensor preparation was successful. Further, the electrochemical behaviors each step of electrode modification were investigated using electrochemical impedance spectroscopy (EIS) responses, as a sensitive electrochemical technique [7], in PBS with pH = 7.4 containing K\(_2\)Fe(CN)\(_6\)/K\(_4\)Fe(CN)\(_6\) (5 mM) in a 1 to 1 ratio at a potential of 0.23 V. Fig. 5B displays the Nyquist plots that the observed semicircle portion at high frequencies is associated the electron-transfer resistance (\(R_{ct}\)) and the linear part at low frequencies is associated the finite propagation process. First, a quite small resistance to electron-transfer was observed for the bare SPCE (\(R_{ct}\)) and when incubating with 800 pg mL\(^{-1}\) of the SARS-CoV-2 spike glycoprotein, \(R_{ct}\) increased obviously (\(R_{ct} = 24.9\) k\(\Omega\), curve “c”), representing a successful connection of SARS-CoV-2 spike glycoprotein to aptamer strings. Thereby, the EIS signals which were consistent with SWV response confirm the correctness of the aptasensor development. Besides, inset Fig. 5B showed a Randles equivalent circuit was well-fitted with the obtained plot and the symbols in the equivalent circuit include the solution resistance (\(R_s\)), the Warburg impedance element (\(Z_{w}r\)), the resistance of the charge-transfer (\(R_{ct}\)). A comparison between experimental impedance data with the data obtained by nonlinear fitting using the Randles equivalent circuit for the aptasensor showed this data fits well in this circuit equivalent. The most important parameter in this study is \(R_{ct}\), which indicates the resistance to charge transfer between the redox probe and the surface of electrode. Therefore, to estimate the \(R_{ct}\), all EIS experimental data were fitted in equivalent circuits. The circuit fitting data with fitting percentage are shown in Fig. S1.

3.3 Optimization study of the experiment

Some parameters need to be optimized to achieve the best sensing performance of aptasensor. Optimal aptasensor preparation conditions were evaluated by SWV response in PBS with pH = 7.4. A neutral medium is obligatory to avoid the being demolished of aptamer strings as biological molecules, so all experiments are carried out in PBS at pH 7.4. The concentration and time required for immobilization of aptamers were optimized as important factors in preparation of aptasensors. Therefore, the aptamer concentration on the surface of electrode could directly affect the target capture efficiency. As displayed in the Fig. S2A and B, the most adsorption of aptamer strings on the surface of the modified electrode was 3 \(\mu\)M and the incubation time was selected as 1 h. If there is not enough time to immobilize the BSA molecules, many non-specific sites cause non-specific adsorption, so, we optimized the incubation time of BSA as significant parameter and 30 min was chosen as the optimum incubation time (Fig. S2C). Furthermore, to get the
highest aptasensor response of in the minimum time, the optimum time for aptamer incubation was assessed with SARS-CoV-2 glycoprotein molecules, and, hence, the maximum answer was obtained in 15 min (Fig. S2D).

Moreover, Besides, it is worth mentioning that EIS was applied to monitor each electrode signal for further confirmation. As shown in the inset in Fig. S2, signal growth stopped after reaching the optimal values consistent with SWV.

3.4. SWV performance of the aptasensor for SARS-CoV-2 glycoprotein molecules determination

The SWV experiment was applied to evaluate aptasensor performance based on Cu(OH)$_2$ NRs in PBS (pH = 7.4) ranging from 0.1 to –0.5 V with the optimum conditions (Fig. 3C). By incubating different concentrations of SARS-CoV-2 spike glycoprotein on the provided aptasensor surface, the amount of Cu(OH)$_2$ NRs-associated SWV peak current decreased in proportion to the SARS-CoV-2 spike glycoprotein concentration that is due to the inhibition of Cu(OH)$_2$ NRs electron transfer by the SARS-CoV-2 spike glycoprotein-aptamer complex formation at the aptasensor surface. The calibration curve was plotted using signal (ΔI) versus SARS-CoV-2 spike glycoprotein concentration on a logarithmic scale in the range from 0.1 fg mL$^{-1}$ to 1.2 μg mL$^{-1}$ (Fig. 3D). The regression equation was $ΔI (\mu A) = –5.5284 \log C$ (fg mL$^{-1}$) – 17.319 ($R^2 = 0.9979$) and the detection limit is 0.03 ± 0.01 fg mL$^{-1}$ (S/N = 3). The sensitivity was also 1974.43 μA mM$^{-1}$ cm$^{-2}$. The provided aptasensor performance was compared with some previous reports. Table S1 showed a better detection limit and dynamic range than other reports of the provided electrobiosensor.

The good sensitivity of the provided aptasensor based on label-free approach may be attributed to use of unique Cu(OH)$_2$ NRs with high surface area and biocompatible environment structure, which provides a great surface area aimed at more loading of aptamer strings that increase the electrochemical signal as well as improves the sensitivity of the detection.

3.5. Selectivity, reproducibility, repeatability, and stability of the aptasensor

Selectivity plays a key part in the evaluation of aptasensor. Interference tests were performed to assure that the provided aptasensor could test precisely, and its selectivity was investigated by SWV, under the same conditions, by comparing the amount of ΔIpc after incubation of 500 fg mL$^{-1}$ of target and other interactions including influenza A H1N1, influenza A H3N2, SARS-CoV and MERS-CoV. As Fig. 6 shown, a large SWV response was generated by SARS-CoV-2 spike glycoprotein incubation while no significant response was observed in the attendance of off-target species. According to the obtained results, the provided aptasensor has excellent selectivity, that can be attributed to the selectivity and affinity of aptamer strings for SARS-CoV-2 spike glycoprotein and blocking of active sites remaining by BSA and avoiding unspecific adsorption.

The robustness and accuracy of the provided aptasensor, as a significant factor, was examined by SWV with five different electrodes (reproducibility, Fig. S3A) and five successive examinations for the same electrode (repeatability, Fig. S3B). The reproducibility of the provided aptasensor was assessed via five independent electrodes provided with the same experimental situation. Similar SWV responses were observed for aptasensors to measure 5 fg mL$^{-1}$ SARS-CoV-2 spike glycoprotein with 4.1% RSD, indicating very good aptasensor reproducibility (Fig. S3B), as well as, for five recurrent measurements of 500 fg mL$^{-1}$ of SARS-CoV-2 spike glycoprotein, an RSD = 1.6% value was obtained, signifying that the provided aptasensor has suitable repeatability.

Additional interesting feature of this provided aptasensor was its high working stability. The aptasensor stability was measured after the incubated with SARS-CoV-2 spike glycoprotein (500 fg mL$^{-1}$), and storage at 4°C for 10 days. The results obtained showed that in the SWV response compared to the initial measurement only a decrease of about 2.5% was observed, that designates the excellent stability of the provided aptasensor (Fig. S3C).
4. Conclusions

Sensor based on direct growth Cu(OH)₂ NRs by providing a high active surface can not only act as a biocompatible scaffold to anchor aptamer strands and load them further, but also as an electrochemical probe. This strategy exhibited wide dynamic range in of 0.1 fg mL⁻¹ to 1.2 μg mL⁻¹ and with a high sensitivity of 1974.43 μA mM⁻¹ cm⁻² and low detection limit of 0.03 ± 0.01 fg mL⁻¹ of SARS-CoV-2 spike glycoprotein and led to the development of one of the most sensitive electrochemical aptasensors capable of detecting SARS-CoV-2 spike glycoprotein with ultra-trace levels in saliva and VTM samples, as well as the provided aptasensor was usable in clinical trials to detect the SARS-CoV-2 virus in real samples of sick and healthy individuals. The provided aptasensor showed advantages such as excellent selectivity, wide dynamic range, low cost, good stability, good accuracy and precision and superior sensitivity. Though the provided strategy attentive on SARS-CoV-2 detection, it could possibly and widely be used with other analytes to create sensitive and stable biosensors as a significant tool for diagnosis of other pathogens.

5. Compliance with ethical standards

All experimental protocols were approved by the Experimentation Ethics Committee of Ilam University (Code: IR.ILAM.REC.1400.013). The clinical samples were provided from a local clinical laboratory. Informed consent was obtained from all participants included in the study.

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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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bioelechem.2022.108106.

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Table 1

Measurement of SARS-CoV-2 spike glycoprotein in actual samples with provided aptasensor (n = 3).

| Sample | Added Measured | Average | RSD (%) |
|--------|----------------|---------|---------|
| VTM    | 5 fg mL⁻¹      | 4.9 fg mL⁻¹ | 2.9 | 98 |
|        | 40 pg mL⁻¹     | 38.8 pg mL⁻¹ | 3.6 | 97 |
|        | 12 ng mL⁻¹     | 12.5 ng mL⁻¹ | 3.9 | 104 |
| Saliva | 5 fg mL⁻¹      | 5.1 fg mL⁻¹ | 2.7 | 102 |
|        | 40 pg mL⁻¹     | 41.8 pg mL⁻¹ | 3.3 | 104 |
|        | 12 ng mL⁻¹     | 11.8 ng mL⁻¹ | 3.8 | 98 |

Table 2

Detection of SARS-CoV-2 virus in clinical samples with provided aptasensor.

| Patients | PCR test | Aptasensor test | Patients | PCR test | Aptasensor test |
|----------|----------|----------------|----------|----------|----------------|
| #1       | +        | –              | #16      | +        | –              |
| #2       | +        | –              | #17      | +        | –              |
| #3       | +        | –              | #18      | +        | –              |
| #4       | +        | –              | #19      | +        | –              |
| #5       | +        | –              | #20      | +        | –              |
| #6       | +        | –              | #21      | +        | –              |
| #7       | +        | –              | #22      | +        | –              |
| #8       | +        | –              | #23      | +        | –              |
| #9       | +        | –              | #24      | +        | –              |
| #10      | +        | –              | #25      | +        | –              |
| #11      | +        | –              | #26      | +        | –              |
| #12      | +        | –              | #27      | +        | –              |
| #13      | +        | –              | #28      | +        | –              |
| #14      | +        | –              | #29      | +        | –              |
| #15      | +        | –              | #30      | +        | –              |
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