The review of affinity sensors for the diagnosis of COVID-19

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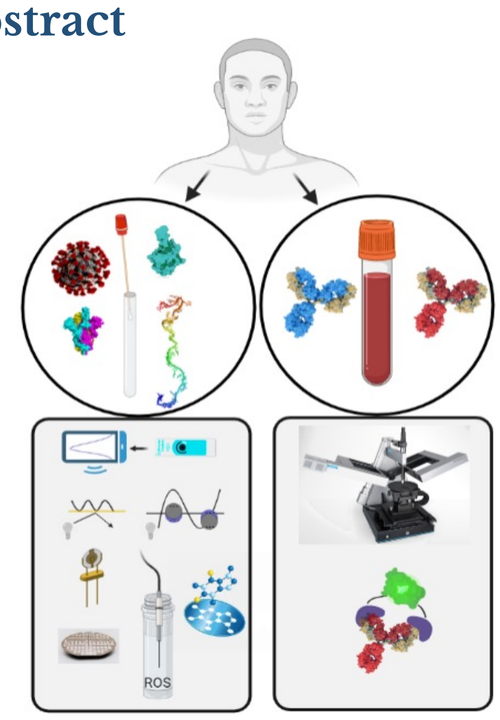
Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a spherical structure inside which is a helically symmetrical nucleocapsid containing positive-sense single-stranded RNA. SARS-CoV-2 genome expresses open reading frames encoding structural proteins, namely, spike (S), envelope (E), nucleocapsid (N), and membrane (M) protein (Figure 1). The entry of the SARS-CoV-2 into the host triggers the sequential chain stimulation of the different immune cells leading to the inducing of the humoral immune responses by expressing antigen-specific antibodies, mostly, immunoglobulins M (IgM) and G (IgG). Commonly, the S- and N-proteins act as antigens for specific binding to antibodies.

Reducing the dissemination rate by the implementation of fast and sensitive detection methods is the main tool against the spreading of SARS-CoV-2 causing the coronavirus disease 2019 (COVID-19). There are three general strategies currently used to detect SARS-CoV-2 and to diagnose COVID-19, namely, molecular tests based on the determination of viral RNA [1], antigen tests based on the determination of viral proteins, and antibody tests based on the determination of specific antibodies against the coronavirus (Figure 2). Besides the conventional approaches, affinity biosensors also showed efficacy in the determination of SARS-CoV-2 infection. Some of the sensors were reviewed in our paper (Table 1) [2].



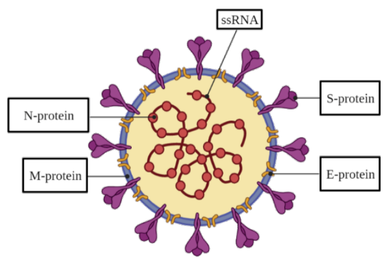


Figure 1. Schematic representation of SARS-CoV-2 structural proteins location.

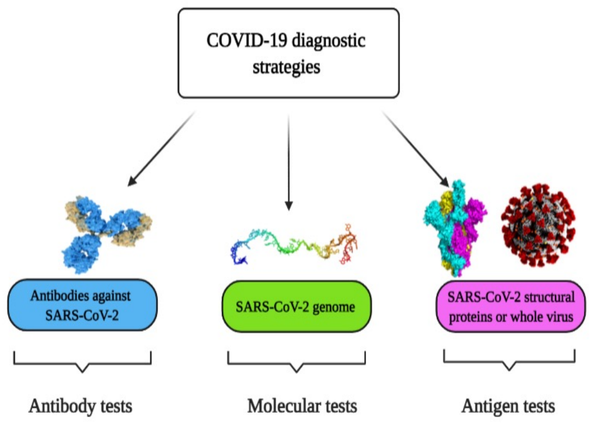


Figure 2. COVID-19 diagnostic strategies.

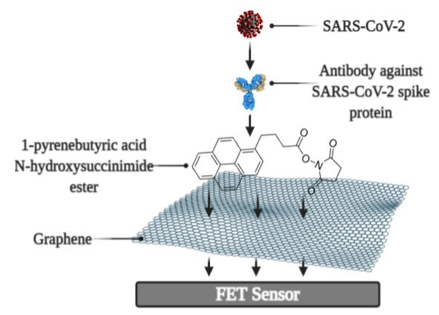


Figure 3. Schematic representation of field-effect transistor immunosensor.

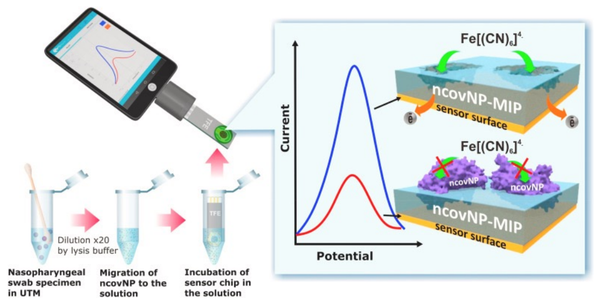


Figure 4. COVID-19 diagnostics principle by molecularly imprinted polymers based sensor [4].

Conclusion

As an analytical signal source for biosensing, nucleic acid hybridization, antigen-antibody interactions, monitoring surface alterations (Figure 3), and changes of reactive oxygen species levels [3] are employed (Table 1). Among the overviewed antigen-antibody affinity sensors, molecularly imprinted polymers based electrochemical sensor (Figure 4) with the lowest detection limit (15 fM) was shown as more stable in comparison to protein based sensors [4]. The spectroscopic ellipsometry and surface plasmon resonance based technique made it possible to draw important conclusions about the structure of the antigen-antibody complex, as well as to study the kinetics of its formation, which is valuable for the design of new immunosensors [5]. The review revealed that the biosensors with electrochemical based signal registration prevail in biosensing development due to their cheapness, simplicity, and mass production capability.

Table 1. Summary table of biosensors used for the diagnosis of COVID-19.

Biosensor	Biorecognition element	Signal source	Registration methods	Label need	Immobilization method	LOD/Sensitivity
Electrochemical based	Capture nucleic acid	RNA hybridization	Differential pulse voltammetry	Label nucleic acid	Au/Fe_3O_4 nanoparticles	200 copies/mL / 85.5%
Plasmonic based			Plasmonic photothermal + localised surface plasmon resonance	Label-free	Au nanoparticles	0.22 pM
Field-effect transistor based	Surface properties alterations	Antibody-antigen affinity	Field-effect transistor current response		1-pyrenebutyric acid N-hydroxysuccinimide ester	242 copies/mL
Quartz crystal microbalance based		S-protein binding	Change of quartz crystal microbalance resonance frequency		Self-assembled monolayer	-
Molecularly imprinted polymers based electrochemical	Molecularly imprinted polymers-modified electrode selective to N-protein	N-protein binding	Differential pulse voltammetry		Molecularly imprinted polymers	15 fM/-
Spectroscopic ellipsometry based	N-protein	Antibody-antigen affinity	Total internal reflection mode + surface plasmon resonance signals		Self-assembled monolayer	-
Optical based	S- or N-protein		Photoluminescence	Small BiT and large BiT fragments	-	-/89% (S-sensor) and 98% (N-sensor)
Reactive oxygen species detection	Multiwall carbon nanotube electrode	Reactive oxygen species level	Cyclic voltammetry	Label-free	-	Sputum sample vol. <500 µl / >97%

Acknowledgements

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