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Can Graphene-based Materials Play a Role in the Fight against COVID-19?

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THE newly emerged severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become a major global health problem today. SARS-CoV-2 virus can survive on various surfaces for periods ranging from a few hours to a few days. This increases the chances of COVID-19 spread to large populations. So, apart from an urgent requirement of medicines and vaccines, what is also required is the development and engineering of smart materials to combat SARS-CoV-2.

Graphene and related materials display outstanding electrical, mechanical, thermal, tribological, catalytic, energy storage, barrier, protective, sensing, and antimicrobial properties [Ferrari, A. C. *et al.*, Science and technology roadmap for graphene, related two-dimensional crystals and hybrid systems. *Nanoscale* (2015)]. So, can graphene-based materials play a crucial role in the fight against COVID-19?

While there is no research available to date that shows the application of graphene-based materials for combating SARS-CoV-2 virus and associated COVID-19, their outstanding physicochemical and antimicrobial properties suggest that these materials may play a crucial role on various fronts in the war against COVID-19. For instance, graphene-based materials could be used i) for the development of efficient diagnostic devices for SARS-CoV-2 detection, ii) as surface protective coatings to de-stabilize and minimize the survival time of this virus on diverse surfaces, iii) in the development of effective personal protective equipments (PPEs) and iv) in the development of 3D printed medical and engineering components, and so on.

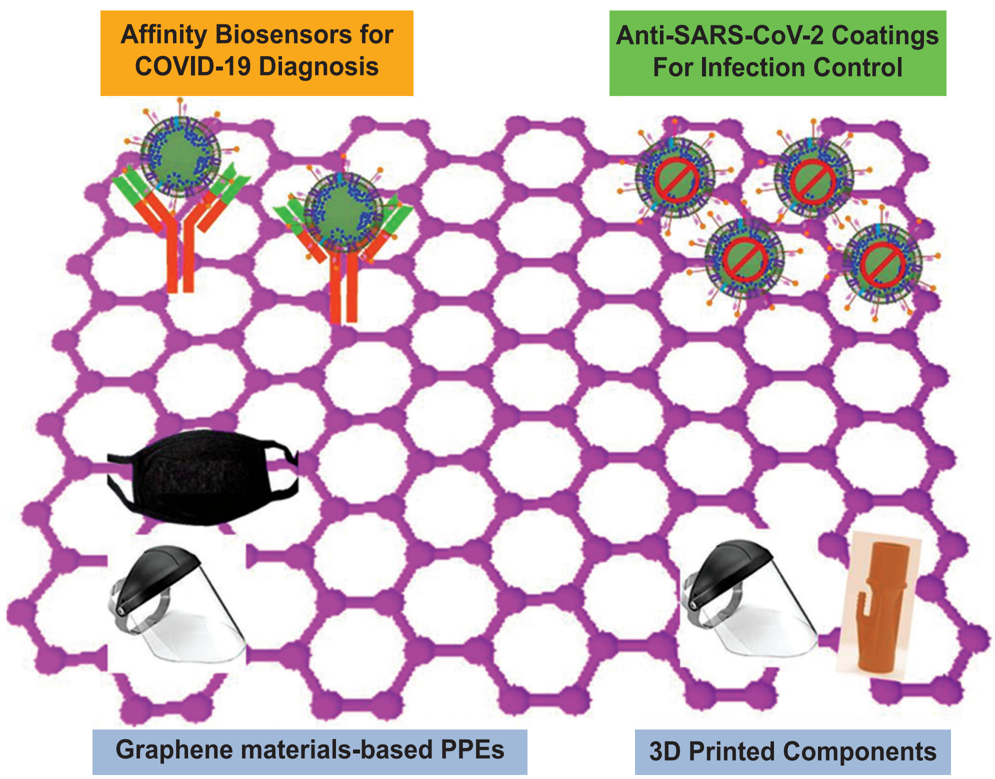


Figure 1: Schematic illustration of the application of graphene-based materials to combat COVID-19 disease

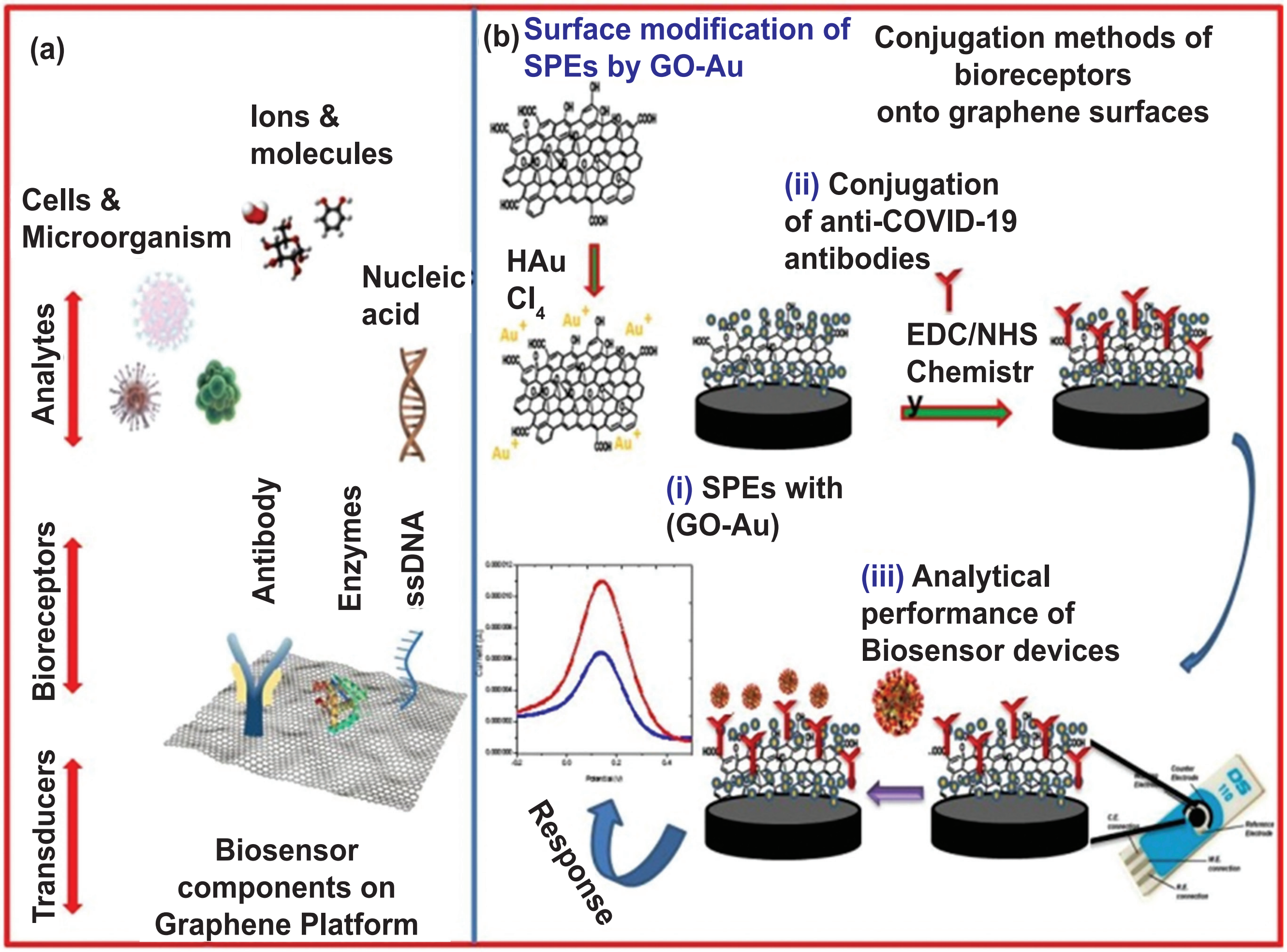


Figure 2: Schematic diagram showing a) the conjugation of different bio-receptors onto graphene platform and b) general methodology to develop graphene based electrochemical biosensor for SARS-CoV-2 detection.

Graphene and Related Materials

Graphene and related materials include Single-Layer Graphene (SLG), Bilayer Graphene (BLG), Multilayer Graphene (MLG), Graphene Oxide (GO) and their composites with metals, polymers and ceramics [Pasricha, R. *et al.* A facile and novel synthesis of Ag-graphene-based nanocomposites. *Small* (2009), and Ferrari, A.C. *et al.*, Science and technology roadmap for graphene, related two-dimensional crystals and hybrid systems. *Nanoscale* (2015)]. Graphene is a sp^2 bonded material that contains carbon atoms arranged in a hexagonal structure. SLG is a zero band gap material because the ϖ and ϖ* bands touch at the Dirac point. At Dirac point, the graphene electrons behave-like massless fermions that cause its high conductivity and mobility.

Graphene is one of the strongest materials ever tested; it displays high thermal conductivity and lubricity. Further, the stacking of two SLG layers in an AB configuration generates BLG while MLG contains a number of SLG stacked on top of one another. The electronic structure of graphene changes with increasing number of layers, changing its properties accordingly.

GO is an oxide graphene sheet that contains a number of functional moieties. Unlike graphene, GO possesses a band gap but its electrical conductivity, mobility and thermal conductivity are relatively inferior to graphene. Graphene, MLG and GO have also been widely explored as fillers to enhance the properties of polymers and metals in composite structures. Graphene and related materials have also shown potential in biomedical applications such as in biosensing, as antimicrobial materials, in tissue engineering, in drug delivery. Thus, graphene and related materials hold the possible potential to play a crucial role in the fight against COVID-19.

Biosensing Devices for COVID-19 Diagnosis

With the immense need to design new medicines and vaccines for COVID-19 treatment, the development of effective, accurate and standardized diagnostic methods for SARS-CoV-2 is extremely important. To “mobilize research on rapid point of care diagnostics for use at the community level” is one of the eight immediate research needs agreed and recommended by the World Health Organization (WHO) in February 2020.

Most of the diagnostic kits available for SARS-CoV-2 are based on polymerase chain reaction (PCR) such as RTPCR [Chan F.J., *et al.* Improved molecular diagnosis of COVID-19 by the novel, highly sensitive and specific COVID-19-RdRp/Hel

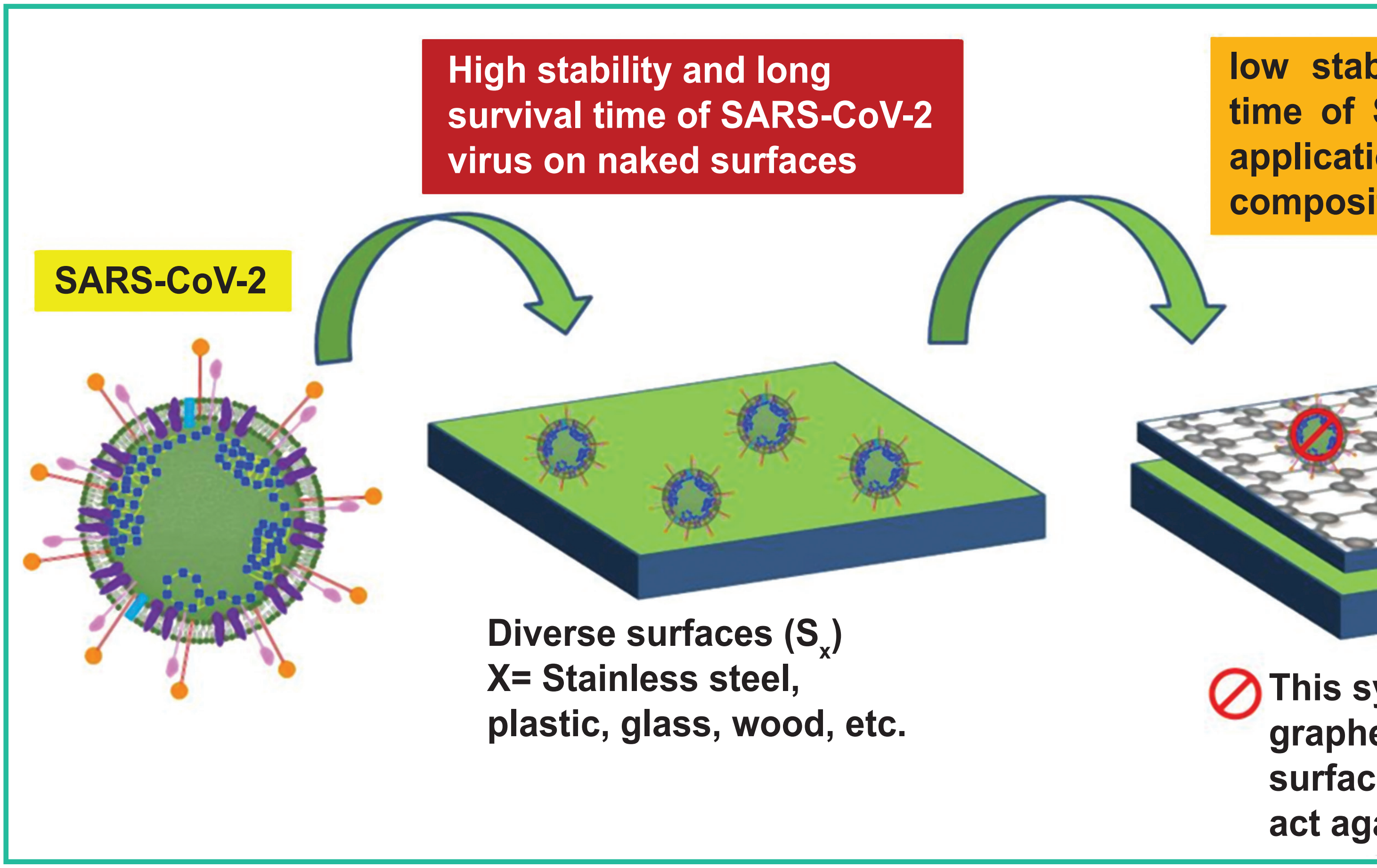


Figure 3: Schematic illustration of the interaction of SARS-CoV-2 virus on naked and coated surfaces. The SARS-CoV-2 virus has high stability and survival time,
An application of graphene-based materials as surface protective coatings may destabilize and minimize the survival time of SARS-CoV-2 virus which could ultimate

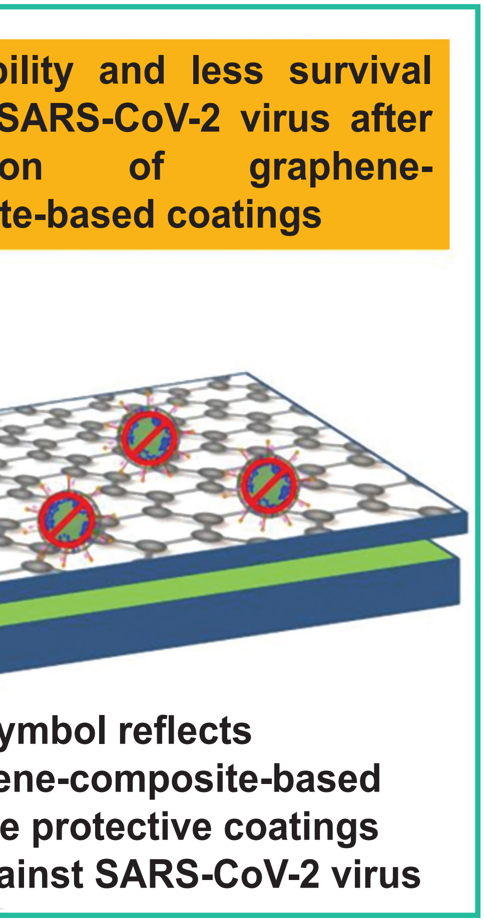
real-time reverse transcription-polymerase chain reaction assay validated in vitro and with clinical specimens. *J Clin. Microbiol.* (2020)]. The diagnosis involves qualitative and quantitative testing of the virus in the respiratory specimens including nasal and pharyngeal swabs, bronchoalveolar lavage fluid, sputum, or bronchial aspirates. Although this technique is sensitive and offers much specificity for a particular infection, it is time-consuming, requires expensive instruments and skilled personnel.

Considering the global demand for quick and cost-effective clinical diagnosis of COVID-19 disease, affinity-based biosensors can provide effective engineering solutions. Biosensors are attractive detection methods for molecules and small particles, such as virions, as they can produce rapid, sensitive, and specific signals [Pang J., *et al.*, Potential rapid diagnostics, vaccine and therapeutics for 2019 novel coronavirus (2019-nCoV): A systematic review. *J. Clin. Med.* 9, 623 (2020)]. A large number of studies have revealed that biosensor-based diagnosis of viral infection holds promise to provide low cost, high throughput, and faster way to detect the infection [Pang J. *et al.*, Potential rapid diagnostics, vaccine and therapeuticsfor2019 novel coronavirus (2019-nCoV): A systematic review. *J. Clin. Med.* 9, 623 (2020)].

In general, a biosensor consists of two elements: a bioreceptor and a transducer. The bioreceptor is a molecule that specifically recognises the targeted analyte e.g. enzyme, antibody, aptamer, DNA etc. The transducer is the part of the sensor that converts the biochemical signal generated during biomolecule-analyte interactions into a measurable signal. Graphene has been explored as a potential transducer material to design highly efficient, selective and sensitive biosensor devices due to its stable optical and electrochemical behaviour, high electrocatalytic activity, and excellent mechanical and thermal properties [Pumera M. Graphene in biosensing. *Mater. Today* 14, 308-315 (2011)].

Afsahi *et al.* developed a cost-effective and portable graphene-enabled biosensor to detect Zika virus with a highly specific immobilized monoclonal antibody. Field Effect Biosensing (FEB) with monoclonal antibodies covalently linked to graphene enables real-time, quantitative detection of Native Zika Viral (ZIKV) antigens [Afsahi, S. *et al.* Novel graphene-based biosensor for early detection of Zika virus infection. *Biosensors and Bioelectronics* 100, 85-88 (2018)].

Similarly, Liu *et al.* reported graphene-based electrochemical biosensor for pathogenic virus detection [Liu, F. *et al.* Graphene-based electrochemical biosensor for pathogenic virus detection. *Bio Chip J.* 5, 123-128 (2011)]. Thus, biosensors based on graphene-related materials could also be explored for early-stage quick diagnosis of COVID-19 disease. Figure 2b shows the general methodology that can



, from few days to few hours, on many surfaces.
ely contribute to control of the spread of COVID-19

be adopted to design graphene materials-based affinity electrochemical biosensors using anti-SARS-CoV-2 antibodies as bioreceptors.

Surface Protective Coatings

The novel coronavirus SARS-CoV-2 can easily settle on any surface. This is alarming for high contact surfaces, the surfaces that humans touch frequently, leading to enhanced chances of COVID-19spread. Recent research suggests that SARS-CoV-2 has variable survival time on different surfaces namely plastic (72h), stainless steel (48h), cardboard (24h) and copper (4h) (van Doremalen, N. *et al*. Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. *N. Eng. J. Med.* (2020). The components, products, and systems made up of these materials can harbour SARS-CoV-2 virus for longer duration (except copper), which will enhance the chances of virus spread. So, developing surface protective coatings with excellent anti-SARS-CoV-2 virus property (antimicrobial property) for diverse surfaces is important to control COVID-19 disease.

Graphene-based materials such as MLG, GO and functionalised MLG are known to have antimicrobial property, though the correlation between their antimicrobial and physicochemical properties is not fully understood. Graphene-based materials when explored as surface protective coatings may also play a critical role to minimize survival time of SARS-CoV-2 virus on diverse surfaces.

In particular, when used in combination with proven antimicrobial metals such as in form of SLG/MLG-copper composite, SLG/MLG-silver composite, GO-copper composite, GO-silver composite, and many other combinations, these materials can act as high-performance coatings to efficiently destabilize and minimize the survival time of SARS-CoV-2 virus on diverse surfaces. This would be extremely important for high contact surfaces i.e. surfaces of medical and surgical equipment, personal protective equipment, hospital doors and door handles, etc., to control the virus spread.

3D Printed Graphene-composites for Medical Components

As the coronavirus pandemic spread all over the globe the healthcare systems of even developed countries like USA, Italy, Spain, etc. are facing unprecedented challenges. In order to fulfil the requirement of medical equipments, professional additive manufacturing providers, makers and designers in the 3D printing community have already begun to respond to the global crisis by volunteering their respective skills to ease the pressure on supply chains and governments.

The current pandemic demonstrates the need for distributed manufacturing of essential items where local specialized requirements can be met by local resources. The3D printing of graphene-based materials could be very important in designing medical devices and PPEs. For instance, a hospital in Brescia, Italy with 250 coronavirus patients ran out of respiratory valves needed to connect the patients to the breathing machines. The original supplier was unable to meet the sudden high demand. The CEO of Isinnova, a Brescia-based engineering firm, used 3D printing to meet the hospital's demands and thus the patients' lives were saved (https://3dprintingindustry.com/news/3d-printing-community-responds-to-covid-19-and--resources-169143/) (https://3dprint.com/265022/3d-printing-for-covid-19-part-two-spare-valves-for-oxygen-masks/).

The shortage of COVID-19 testing kits and test swabs is also a very serious problem faced by all countries due to sample collection on a very large scale. In order to meet the requirement of test swabs, Formlabs (a 3D printer manufacturing company) recently launched a 3D printed test swab for hospitals (https://www.3dprintingmedia.network/3d-printed-nasal-swabs-covid-19/). In a single print, they can produce 300 test swabs at a time, enabling Formlabs to produce 75,000-150,000 swabs per day. This development will rapidly provide hospitals with access to large quantities of these essential COVID-19 test kit components.

Hospitals and cops are also facing shortage of N-95 face mask and face shield. Due to total lockdown, most of the manufacturing industries are closed. Therefore, several 3D printing firms have designed and made these face shields and masks at a very low cost. Owing to outstanding physical and antimicrobial properties 3D-printed graphene-based composites could be promising candidates for the development of components and devices required in treatment and protection of COVID-19 disease.

If further examined and assessed, graphene-based materials, due to their extraordinary and tunable properties, could make a huge impact in the fight against the COVID-19 pandemic.

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