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BIOSENSORS FOR PANDEMICS

Electrical probing of SARS-CoV-2 spike protein via a graphene field-effect transistor

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The outbreak of the new coronavirus COVID-19 in early 2020 is a major and global public health emergency. It has been realized that fast and specific detection of viruses have broad applications in the prevention and treatment of such infectious diseases and its clinical medicine. At present, polymerase chain reaction (PCR) and enzyme-linked immunosorbent assay (ELISA), are mainly used in clinical practice, but are time-consuming, require complex pretreatment of target molecules and costly.

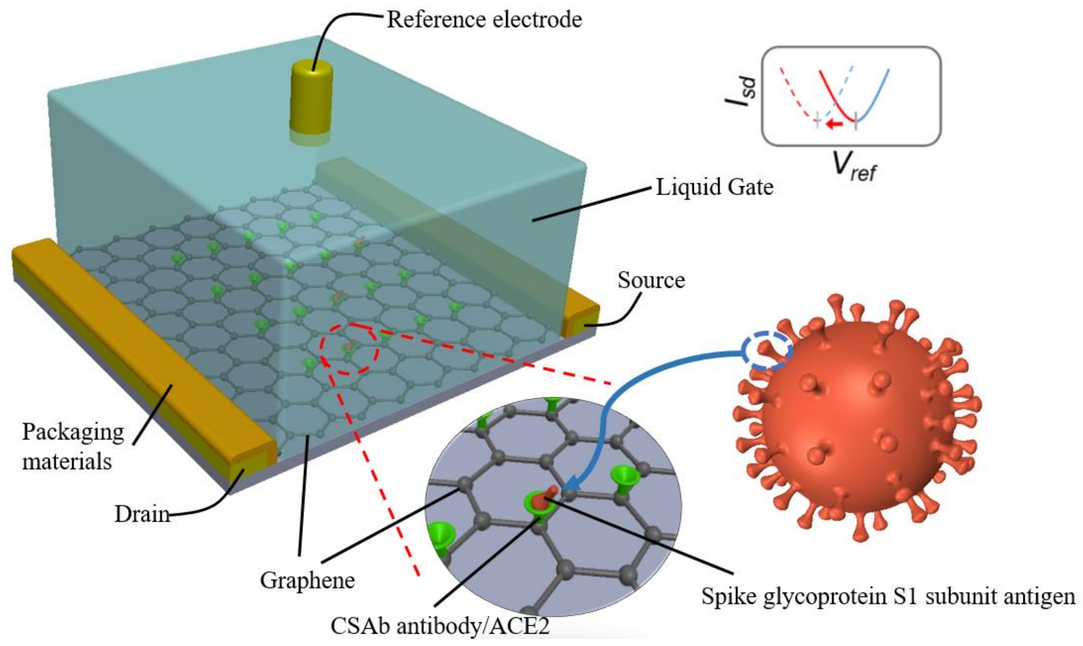

Figure 1: Schematic of a Gr-FET antibody/antigen biosensor

Here, we combined the unprecedented sensitive graphene field effect transistor (Gr-FET) with highly selective antibody/antigen interaction to develop immunosensors towards facile and fast detection of SARS-CoV-2 (and potentially SARS-CoV). Graphene is a two-dimensional material with excellent electronic properties and chemical stability. In Fig. 1, Gr-FET was constructed by utilizing graphene as the channel material and the reference electrode/buffer solution system as the liquid gate. The graphene surface is immobilized with SARS-CoV spike glycoprotein S1 subunit antibody (CSAb) or human angiotensin converting enzyme 2 (ACE2) through non-covalent functionalization[1]. During the test, the spike glycoprotein S1 antigen (including receptor binding threshold, RBD) of the SARS-CoV-2 binds to the CSAb and ACE2 on the graphene surface[2,3], inducing a change in the source-drain conductance of the Gr-FET via field effect as shown in Fig. 2 and Fig. 3, respectively.

At present, we are able to detect CSAb at a concentration of 0.2pM in the laboratory. If assuming a linear sensing response, we may deduce a limit of detection (LOD) as low as ~10fM at a signal-to-noise ratio of 1, which not only outperforms that of the state-of-the-art ELISA technology but also eliminates any complicated procedures for enzyme labeling and/or bulky/expensive optical instruments. Further results ensure that GFETs functionalized with SARS-CoV-2 antigen S1 can be used for efficient screening of neutralizing antibodies. Therefore, our developed Gr-FET-based antigen/antibody biosensors provide an alternative to resolve early diagnosis, as well as rational design of neutralizing antibody locking methods to resolve this ongoing public health crisis.

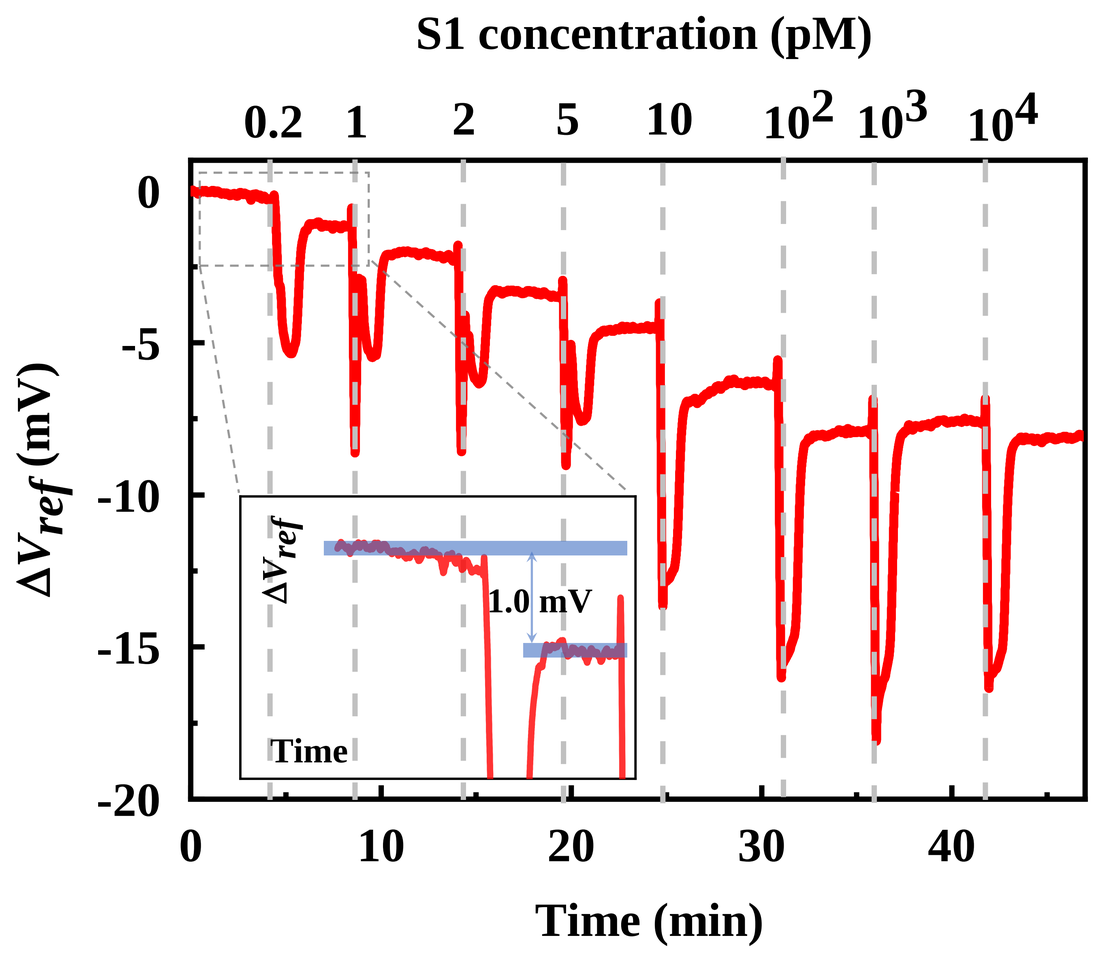

Figure 2: Detection of SARS-CoV-2 S1 with CSAb functionalized GFET biosensors. Shifts of the CSAb immobilized Gr-FET's ΔV_{ref} versus time upon the introduction of S1 solutions at various concentrations ranging from 0.2 pM to 10 nM.

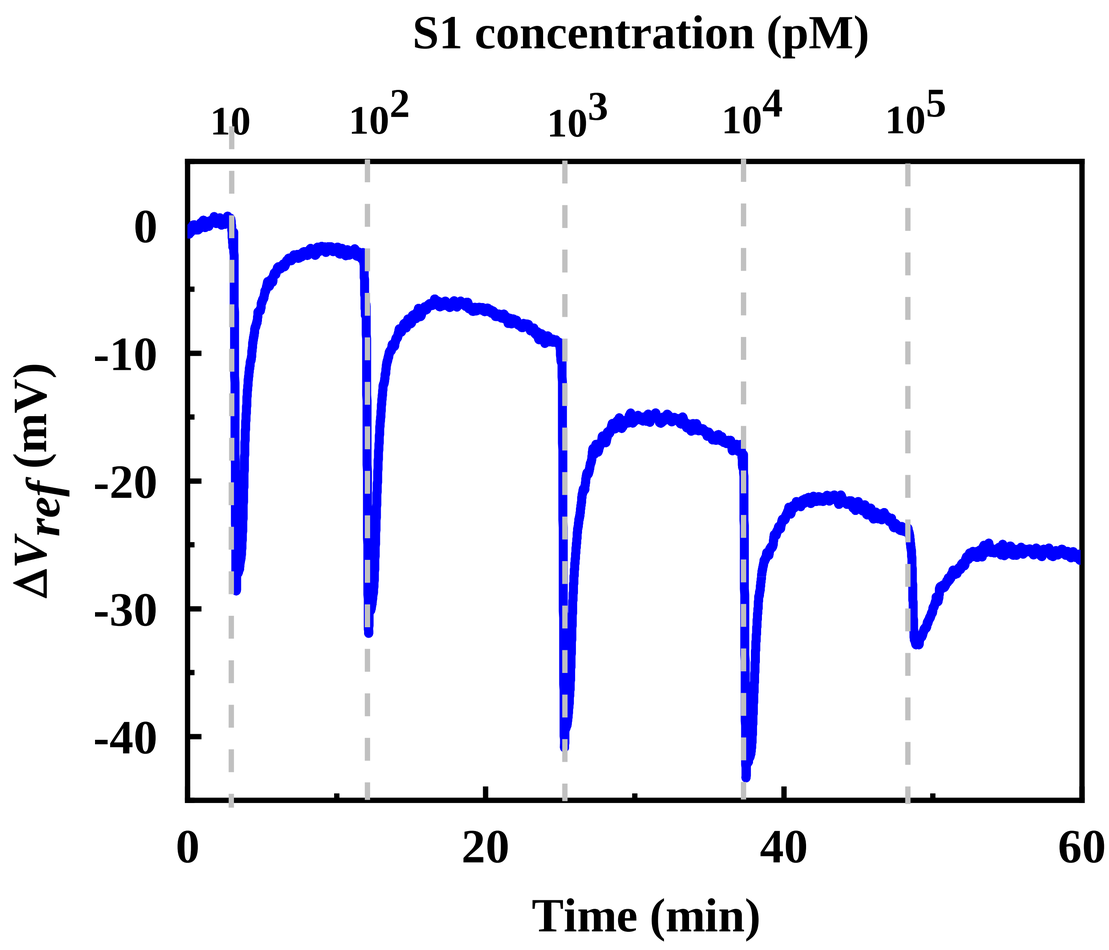

Figure 3: Detection of SARS-CoV-2 S1 with ACE2 functionalized Gr-FET biosensors. Shifts in ΔV_{ref} of the ACE2 immobilized Gr-FET versus time upon the introduction of S1 solutions at various concentrations ranging from 10 pM to 100 nM.

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