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Remote Floating-Gate Field-E ect Transistor with 2 Dimensional Reduced Graphene Oxide Sensing Layer for Reliable Detection of SARS-CoV 2 Spike Proteins

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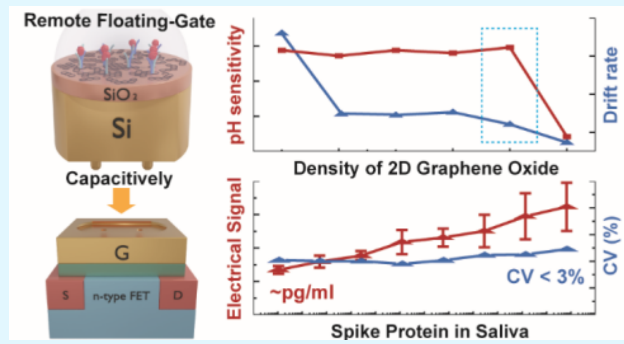
ABSTRACT: Despite intensive research of nanomaterials-based eld-effect transistors (FETs) as a rapid diagnostic tool, it remains to be seen for FET sensors to be used for clinical applications due to a lack of stability, reliability, reproducibility, and scalability for mass production. Herein, we propose a remote floating-gate (RFG) FET con guration to eliminate device-to-device variations of two-dimensional reduced graphene oxide (rGO) sensing surfaces and most of the instability at the solution interface. Also, critical mechanistic factors behind the electrochemical instability of rGO such as severe drift and hysteresis were identi ed through extensive studies on rGO solution interfaces varied by rGO thickness, coverage, and reduction temperature. rGO surfaces in our RFGFET structure displayed a Nernstian response of 54 mV/pH (from pH 2 to 11) with a 90 yield (9 samples out of total 10), coefficient of variation (CV) < 3 , and a low drift rate of 2 , all of which were calculated from the absolute measurement values. As proof-of-concept, we demonstrated highly reliable, reproducible, and label-free detection of spike proteins of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in a saliva-relevant media with concentrations ranging from 500 fg/mL to 5 g/mL, with an R^2 value of 0.984 and CV < 3 , and a guaranteed limit of detection at a few pg/mL. Taken together, this new platform may have an immense effect on positioning FET bioelectronics in a clinical setting for detecting SARS-CoV-2.



KEYWORDS: *SARS-CoV-2 biosensor graphene oxides RFGFET drift pH detection*

INTRODUCTION

The outbreak of coronavirus 2019 (COVID-19),[1] resulting from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has evolved into a global pandemic, causing more than 500 million infections and more than six million deaths (https://covid19.who.int/). The development of a reliable mechanism to track infectious diseases and their spread remains a challenge. Indeed, the early identi cation and diagnosis of potential pathogens is essential for preventing virus transmission.[2] The real-time reverse transcriptase polymerase chain reaction (RT-PCR) technique has been the gold standard for COVID-19 detection, but it can take hours to days to receive test results, as RT-PCR requires a large laboratory space, multistep sample preparation, and trained experts to perform the tests.[3] In contrast, several point-of-care (POC) testing tools based on lateral flow immunoassays (LFAs)[4] have been authorized by the U.S. Food and Drug Administration (FDA) for emergency use, which are still inadequate to precisely identify a particular phase of COVID-19 disease progression in patients.

Meanwhile, proof-of-concept eld-effect transistors (FETs) have been demonstrated for COVID-19 detection using nanostructured materials such as carbon nanotubes,[5] graphene,[6] reduced graphene oxide (rGO),[7] and transition metal dichalcogenide monolayers.[8] Those FET sensors eliminate the multiple laboratory steps that are typically required to amplify DNA sequence or immobilize the specialized reagents or enzymatic labels, as demanded by LFAs, conventional fluorescence, luminescence, and radioactive assays. A few reports on two-dimensional (2D) FETs have already shown excessively low limit of detection (LOD) for SARS-CoV-2 spike proteins (S proteins) down to 1 fg/mL,[6] while the LOD observed from the conventional LFAs is measured as 5 ug/mL

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