Fabrication of Ambipolar Nanoelectronic/Microfluidic-Integrated Biosensors for Cycle-Wise Real-time Biomolecule Quantification

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Field-effect transistor (FET)-based nanoelectronic biosensors made from emerging 2D layered semiconductors (*e.g.,* MoS_2 and WSe_2) have exhibited attractive characteristics, such as high biodetection sensitivity, low limit-of-detection (LOD), and good compatibility with planar nanofabrication processes, potentially enabling multiplexing sensor arrays.[1,2] However, such FET biosensors still suffer seriously from screening effects of analyte solutions, high noise levels from liquid solvents, and false signals related to nonspecific adsorption of untargeted molecules. These issues seriously limit the applicability of FET biosensors for rapid, precise, real-time quantification of targeted biomolecules in complex clinical solutions. To address these issues, additional device structures need to be fabricated and implemented for operating FET biosensors.

In this work, we fabricated WSe_2-based ambipolar FET biosensors, which are integrated with PDMS-based microfluidic channels. The ambipolar transport properties of such FET sensors enable high sensitivity and precision for biomolecule quantification. The integrated microfluidic channels enable a new approach for operating FET biosensors and realizing rapid, low-noise, highly specific, real-time biomolecule quantification. This new sensor measurement method is termed as Incubation-Flushing-Drying-Measurement (IFDM) cycle-wise quantification. The IFDM method can completely separate incubation and electrical measurement steps during a time-dependent binding-mediated quantification process, and therefore avoid all the issues mentioned above. Using our integrated sensors in combination with the IFDM method, we have successfully demonstrated the real-time detection of streptavidin with femtomolar-level LOD.

Specifically, Fig. 1a illustrates a WSe_2 FET sensor integrated with microfluidic structures. In this work, the WSe_2 FET biosensor was fabricated using our previously reported nanoprinting approach.[3] The as-fabricated WSe_2 FET was subsequently integrated with a PDMS-based microfluidic system consisting of microfluidic channels, inlet/outlet tubes, and a motorized syringe (Fig. 1b). This microfluidic system can deliver a series of timely sequenced reagent fluids (*i.e.,* analyte solution for incubation - pure buffer for flushing - air flow for drying and electrically measuring the sensor) to the FET. Fig. 2a shows a set of ambipolar transfer characteristics of a typical WSe_2 FET sensor, which were measured at a given analye concentration (*i.e.,* 30 fM Streptavidin) but various timely sequenced IFDM cycles (cycle step: 10 min). The corresponding time-dependent response curves acquired from the p- and n-branches of the characteristic curves are plotted in Figs. 2b and 2c, respectively. Our work demonstrated that our electronic/microfluidic-integrated biosensors in combination with the IFDM method can result in very low detection noise and also address the solution screening and the nonspecific adsorption issues mentioned above.

This work laid an important foundation for creating new integrated nanoelectronic biosensors that can enable rapid, low-noise, highly specific real-time biomolecule quantification.

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[2] H. Nam, B. Oh, P. Chen, M. Chen, S. Wi, W. Wan, K. Kurabayashi, and X. Liang, Scientific Reports, 5, 10546 (2015)
[3] H. Nam, S. Wi, H. Rokni, M. Chen, G. Priessnitz, W. Lu, and X. Liang, ACS Nano 7, 5870-5881 (2013)

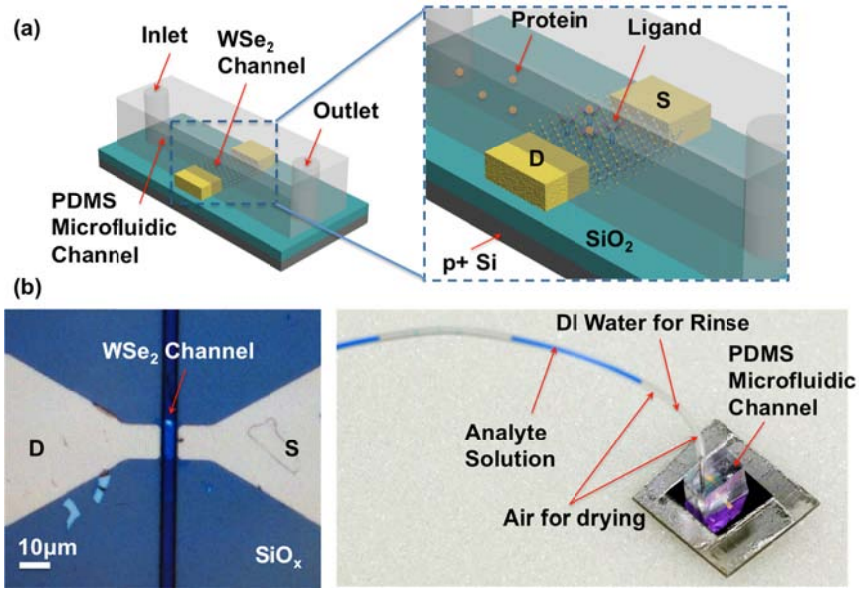

Figure 1: WSe_2 Transistor Biosensors: (a) Schematic figures of WSe_2 FET integrated with PDMS microfluidic channel and Biotin functionalization; (b) An exemplary WSe_2 transistor biosensor and the IFDM setup.

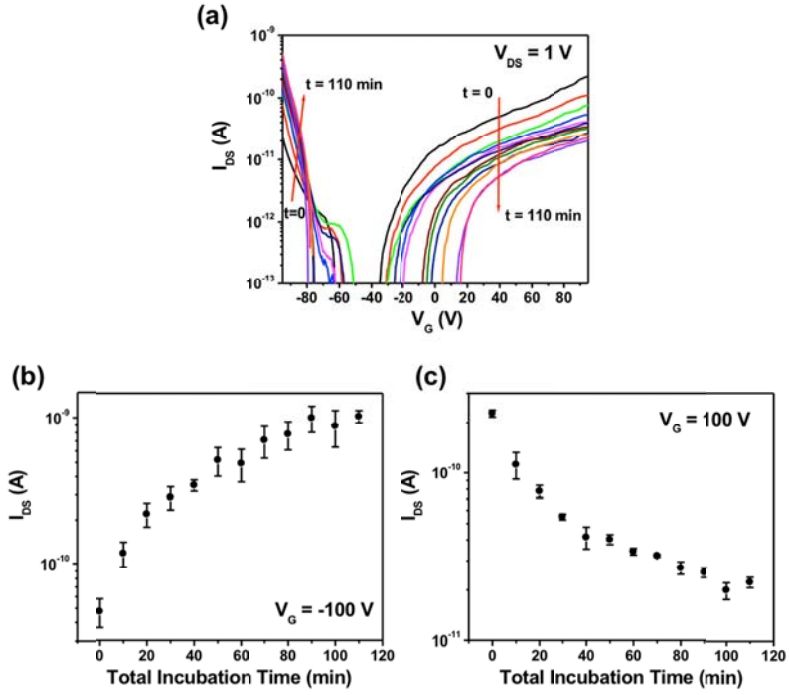

Figure 2: Sensor response characteristics of a WSe_2 FET biosensor for quantifying a 30 fM streptavidin solution: (a) Ambipolar transfer characteristics of the sensor measured at various IFDM cycles (cycle step: 10 min); (b) and (c) show the time-dependent response curves acquired from the p- and n-branches of the time-dependent transfer characteristics.