Towards a biosensing platform based on graphene field-effect transistors

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Miniaturized biosensing analytical devices are essential tools for the successful development of point-of-care testing, for so-called "intelligent factories" (Industry 4.0), and for automated environmental monitoring, due to the possibility of integration, automation, and connection between analytical devices. We propose the development of a miniaturized biosensing device based on liquid-gate graphene field-effect transistors (GFETs) comprising 3 modules: target extraction and purification, isothermal target amplification, and detection. The sensor readout consists of a home-made electronic platform, with the size of a credit card, to ensure portability (Fig. 1E). Here, we report on the detection module: the GFET sensor chip and a PDMS flow cell, fitting the sensor layout, are assembled and then inserted in the portable platform (Fig. 1C,D). This system, connected to a syringe pump and a multiposition valve, allows for automation, improving the precision over manually operated ones [1]. We focus on the detection of two molecular targets: a 30-nucleotides long single stranded DNA that is part of the genome of a Port wine grape variety, and an antigen that is a biomarker of the hemorrhagic transformation of ischemic stroke, matrix metallopeptidase 9 (MMP-9). For the target detection the GFET channel is functionalized with a molecular probe – a DNA sequence, complementary to the DNA target, or an anti-MMP-9 antibody, specific to MMP-9, respectively. Different linkers (PBSE, FSC and AO succinimidyl ester) in distinct solvents (ethanol, DMSO, and DMF) were tested and the highest surface coverage was obtained using PBSE in DMF, giving ~10^{13} molecules/cm^2 for DNA and ~10^{12} antibodies/cm^2 for anti-MMP-9 probe concentration. Each modification step was monitored by measuring 10 transfer curves and, from the last 3 curves, computing the average of the gate voltage values at which maximal channel resistance is observed (V_{Dirac}). The observed shifts in V_{Dirac} are consistent with a mechanism of local gating of graphene by charged molecules [3]. Target DNA was detected down to 1 aM, with a saturation attained at 100 fM and sensitivity to SNP, and MMP9 was detected in a range from 0.01 up to 10 ng/mL. These results show that graphene liquid-gate transistor sensors, with high sensitivity and low cost, are a promising technology for next generation lab-on-a-chip devices. Moreover our functionalization strategy can be easily transferred to a broad range of probes for the detection of biomarkers in many different fields.

References

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Figures

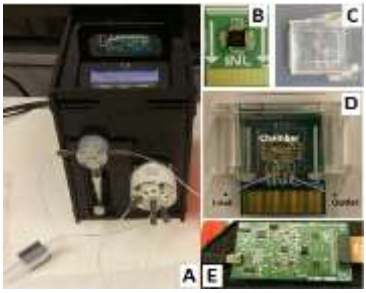

Figure 1: Detection module, A) Flow injection system; B) multi GFET chip; C) PDMS chamber; D) PDMS/GFET chip; E) platform readout.

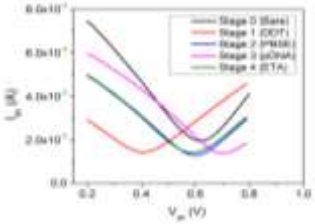

Figure 2: Transfer curves after each stage of GFET channel functionalization