

Biological matrix effects in graphene-based biosensors

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Biochips based on graphene transistors have shown great potential for detecting a wide variety of biomarkers [1], making the technology interesting for studying complex diseases, where simultaneous detection of a panel of biomarkers is required. However, some challenges are found to transit from a single biomarker detection system to a multiplex one [2]. The cross-reactivity between the different biomarkers and the biological matrix effects are the challenges approached and studied in this work. Cellular fibronectin (c-Fn) and matrix metalloproteinase-9 (MMP9) were chosen from a panel of six biomarkers associated with acute ischemic stroke that have been explored for patient stratification [3]. These two proteins were tested in saline solutions to calibrate the graphene transistor system and cross-reactivity (Figure 1 (a-b)). Results show a dynamic range from 10 pg/mL to 10 ng/mL for both biomarkers and no cross-reactivity for isolated exposure to a non-specific probe (antibody). Afterward, the biomarkers were spiked in human serum samples with different processing steps to assess the biological matrix's effect on the sensors' detection ability. Surface analysis was also performed to assess the effects of matrix elements adsorption in the detection system. The results show that it is possible to detect the biomarkers in human serum samples and explain how the biological matrix elements adsorption at the different graphene transistor surfaces (gate electrode and graphene sensing area) affects the sensor signal (Figure (c-d)).

References

- [1] Cabral, P. D. et al., *Materials*, 24 (2020) 5728
- [2] Wang, X. et al., *Electrochimica Acta*, 290 (2018) 356
- [3] Fernandes, E. et al., *Nanomedicine: Nanotechnology, Biology, and Medicine*, 30 (2020) 102287

Figures

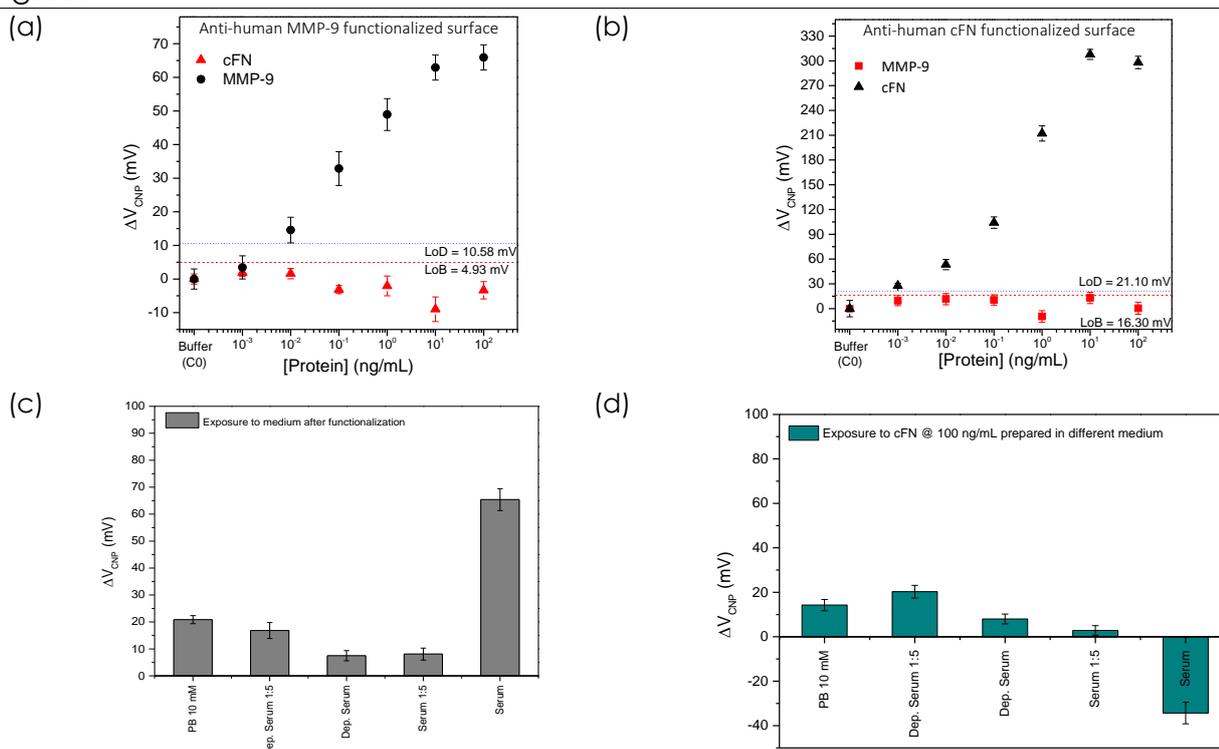


Figure 1: (a) Calibration curves in phosphate buffer for MMP9 and (b) c-Fn and corresponding cross-reactivity assay. (c) Effects of the biological matrix in the signal of functionalized graphene biochips and (d) effect after spike with 100 ng/mL of c-FN.