**Low-cost platform for determination of NTproBNP in saliva using graphene-based aptasensor**

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Abstract

Detection of trace concentrations of biomarkers can be essential if non-invasive analysis is employed, such as sampling of saliva, urine, or sweat. A significant early-stage heart failure biomarker N-terminal pro-B-type natriuretic peptide (NT-proBNP) can be found in saliva in concentrations of thousand times less than in blood plasma suggesting that non-invasive analysis require outstanding low detection limit. In this research, we propose a reduced graphene oxide-based FET device to develop a biosensor using specific anti-NT-proBNP aptamers for the detection of NT-proBNP in saliva. To address the need for low concentration detection in saliva, we included a correlation analysis of two FET parameters, Dirac point shift and transconductance variation to provide reliable biosensor performance. Namely, depending on the ionic strength of the solution, we found that correlation is significant (>0.8) for 0.01X PBS, while it is zero for 0.1X PBS. This can be associated to the long aptamer chain, consisted of 72 bases, that has significant effect on doping of rGO channel and such effect is screened by the ions of higher concentrations (> 16 mM). The analysis shows that chemical interaction between target and receptor is transformed into electrical signal, which is a result of either direct doping effect or charge mobility change. With such an approach, we observed a broad dynamic range of NT-proBNP concentrations in 0.01X PBS of 100 – 105 fg mL-1. Additionally, femtomolar detection of NT-proBNP is achieved in artificial saliva with limit of detection of 41 fg mL-1.