Hochschule Kaiserslautern
University of Applied Sciences

Applied Research Center
Integrated Miniaturised Systems

IMS

MUNASET - Multiparametric nanoelectronic biosensors for therapy response testing

Proteases recently emerged as a promising new class of biomarkers with a broad diagnostic, prognostic and therapeutic potential for different human diseases including neurological and psychiatric diseases, several types of cancer, and immune system disorders. However, there is a lack of tools for real-time activity analysis of disease-related protease biomarkers. To address this issue, we propose to develop a highly sensitive graphene-based biosensor platform for parallel detection of multiple proteases in serum. We will exploit a new label-free sensing mechanism based on charge removal due to cleavage of designer peptides by proteases. As a specific business case, we plan to address therapy response prediction along treatment of major depressive disorder (MDD). MDD is one of the most common and burdensome mental disorders worldwide. MDD is also among the most expensive brain diseases in Europe. While effective treatments exist, there is a high variability in treatment response. There are no serum-based tests to predict personalized therapy for MDD patients. The effective treatment is identified through trial and error, a great burden for patients and the health care system. A rapid, sensitive and easy-to-use test would allow faster and more precise treatment identification, improving therapy outcomes and reducing hospitalization times. Here, we plan to detect two protease biomarkers associated with MDD. The biosensors will be validated in clinical serum samples. Arrays of graphene biosensors will be integrated on silicon wafers with a multiplexed readout matrix to realize a miniaturized sensor system with multi-analyte detection capability, high dynamic range, high precision, low detection limit, and low material consumption. The resulting platform technology may enable various point-of-care diagnostic and therapy prediction tools. This will help secure industrial leadership of the EU over the entire value chain of novel graphene-based bio-analytical tools.

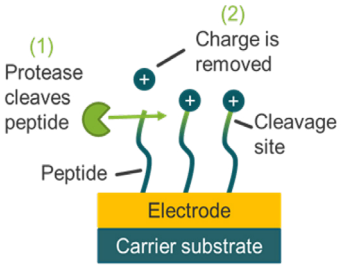

Figure 1: Concept of the protease biosensor: Synthetic peptides are designed to act as substrates for protease enzymes with high affinity and specificity. Proteases can cleave these peptides at a specific site (1). The charged group is then removed due to this enzyme-substrate interaction (2).

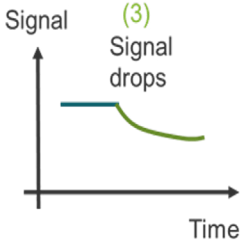

Figure 2: Sensor signal as a function of time has a stable baseline prior to protease action. The signal drops upon charge removal (3).

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