

Decoupling Optical and Electrical Transduction Mechanisms in Peptide-Functionalized Graphene Biosensors for Immune Cell Detection

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Summary:

We present a comparative graphene-enhanced peptide-based assay for the real-time detection of immune cell receptors. By directly comparing real-time optical (graphene-enhanced surface plasmon resonance, SPR) and electrical (graphene field-effect transistors, gFET) responses from identical peptide-functionalized graphene interfaces, this proof-of-concept study highlights the potential of graphene-based platforms for real-time sensing of living cells in point-of-care diagnostic applications.

Keywords: graphene biosensors, surface plasmon resonance, immune receptors, peptides,

Background, Motivation and Objectives

Graphene-based biosensors offer a highly sensitive and selective approach to detecting biological interactions. These sensors are generally based on the measurement of signal changes resulting from biomolecular events occurring at the interface between a transducer surface and functionalized biomolecular layers [1]. In recent years, peptide-functionalized surfaces have emerged as powerful tools for selective biosensing, as they can mimic biological recognition sites and enable controlled interaction with target receptors.

Among the various biological systems, immune cell receptors such as formyl peptide receptor 2 (FPR2) play a critical role in inflammation and disease progression. Specifically, peptides can selectively bind to these receptors, enabling targeted detection of immune cell activity. Consequently, peptide-based interfaces are regarded as promising candidates for real-time monitoring of receptor-ligand interactions.

However, challenges remain, including non-specific interactions that introduce false signals and differences in transduction mechanisms that complicate data interpretation and comparison. In this study, we present the development of a peptide-functionalized graphene-based sensing platform for the detection of HEK(FPR2) cells. The graphene surfaces were functionalized using PBA as a linker, followed by EDC/NHS activation to enable amine coupling of target and control peptides (see Fig. 1). The target peptide is designed to specifically bind FPR2 receptors, while the control peptide lacks affinity, enabling

selective validation [2]. This approach ensures stable peptide immobilization while maintaining sensitivity to cell-surface interactions. This strategy minimizes non-specific interactions while enabling selective binding of HEK(FPR2) cells. The peptide interface is applied to graphene-coated SPR sensor surfaces for optical measurements and to graphene field-effect transistor (gFET) devices for electrical measurements. The assay was initially developed and monitored in real time using state-of-the-art SPR technology. Subsequently, real-time analysis was performed using gFETs, considering their potential for translation into point-of-care diagnostics. Real-time optical and electrical responses from identical interfaces enable evaluation of binding behavior.

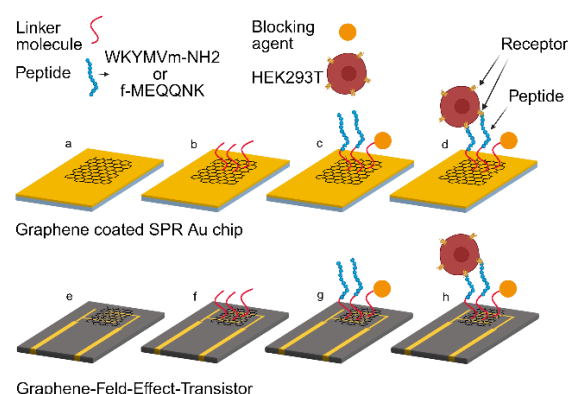


Fig. 1. Schematic illustration of the biosensing strategy of the proposed peptide-based cell detection assay using SPR and gFET.

Research novelty

A cross-platform validation strategy is introduced by directly comparing real-time SPR and gFET

responses from identical biointerfaces. This comparison was enabled by using CVD-grown monolayer graphene as the common sensing surface across both platforms, while enhancing SPR sensitivity.

The platform enables label-free, real-time detection of immune cell receptors directly on living cells, moving beyond conventional detection of soluble biomarkers. The results demonstrate correlated target-specific responses with minimal control interaction, confirming assay selectivity across both modalities.

Overall, this study establishes a framework for translating laboratory-grade SPR assays into scalable gFET-based sensing systems.

Results

SPR measurements show a clear increase in response upon exposure to HEK(FPR2) cells on the target peptide, while the control exhibits minimal signal, confirming selective binding. The signal increase reflects cell accumulation, and partial retention after washing indicates stable interaction.

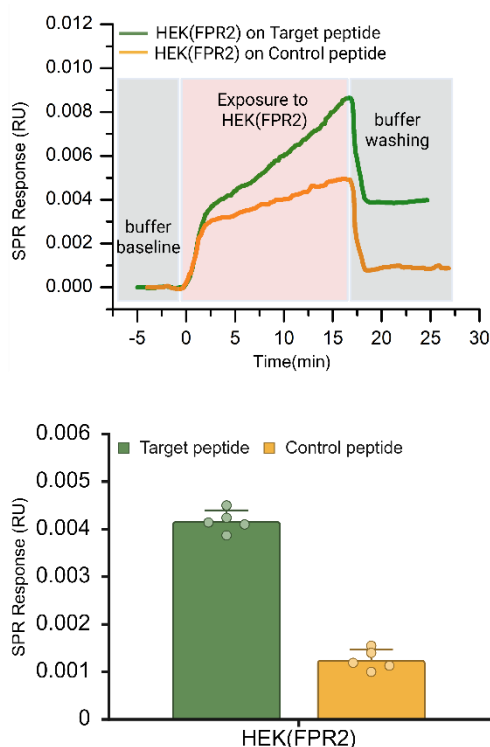


Fig. 2. SPR sensogram showing the peptide baseline, its exposure to HEK(FPR2) cells, followed by buffer washing. The target peptide exhibits a strong increase in response and remains above the baseline after washing, indicating stable binding. In contrast, the control shows minimal response and returns close to the baseline. The lower panel shows the mean response $\pm$ SD ($n = 5$). Adapted from [2].

Similarly, gFET measurements show a rapid increase in normalized current ($\Delta I_{ds}/I_{ds0}$) for the

target peptide, with negligible response for the control. The stable signal during exposure reflects changes in the local electrical environment. All measurements were performed at a concentration of 10,000 cells/ml under physiological buffer conditions.

Both platforms consistently show higher responses for the target peptide. These results demonstrate selective, real-time detection of HEK(FPR2) cells, with complementary optical (SPR) and electrical (gFET) readouts, supporting translation toward point-of-care sensing.

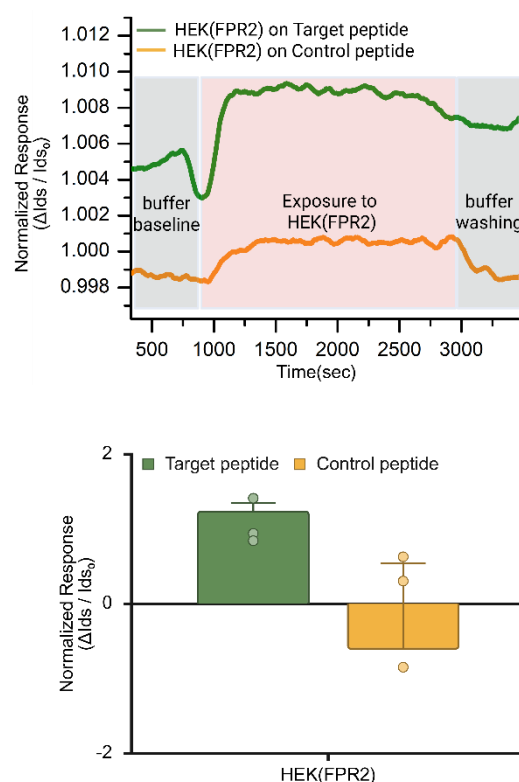


Fig. 3. gFET sensogram showing the baseline, its exposure to HEK(FPR2) cells, followed by buffer washing. The target peptide exhibits a strong increase in electrical response and remains above baseline after washing, while the control shows minimal change and returns close to baseline. The lower panel shows mean normalized response ($\Delta I_{ds}/I_{ds0} \pm$ SD, $n = 3$).

References

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