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著者(和文)	RUNGREUNGTHANAPOLTharatorn
Author(English)	Tharatorn Rungreungthanapol
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## 論文審査の要旨及び審査員

報告番号	甲第	号	学位申請者氏名	Tharatorn RUNGREUNGTHANAPOL		
論文審査 審査員		氏名	職名		氏名	職名
	主査	大河内 美奈	教授		早水 裕平	准教授
	審査員	芹澤 武	教授	審査員		
		多湖 輝興	教授			
田中 祐圭		准教授				

### 論文審査の要旨 (2000 字程度)

The title of this dissertation is “Development of a bioelectronic sensor for the detection of volatile organic compounds using olfactory receptor mimetic peptides” which consists of six chapters.

In Chapter 1, the overview of the study’s background focusing on volatile organic compounds (VOCs) and their detection, the conventional strategies for detecting VOCs, and their limitations were described. This chapter provides the objectives, significance, and structure of the dissertation. VOCs are used as non-invasive biomarkers for diverse detection applications however, limitations of the current VOCs detection techniques, involving sensor platforms and recognition probes, obstruct their applications. This research proposes a strategy to overcome these limitations by utilizing olfactory receptor (OR) mimetic peptide-modified graphene field effect transistors (GFET) for the development of sensitive and specific VOCs detection.

In Chapter 2, “Screening and characterization of limonene binding peptide from OR19a”, limonene, a characteristic VOC from citrus, was employed as a pilot target. Limonene binding peptide was screened from fruit fly’s OR19a, known for its precise limonene recognition ability, by a high-throughput screening technique utilizing peptide array and gas chromatography. The overall limonene binding capacity of the OR-derived peptides was evaluated, and peptides showing high binding specificity and sensitivity were selected. Then, nuclear magnetic resonance was used to analyze the limonene binding mechanism of the peptide, revealing the contribution of hydrophobic and electrostatic force interactions. These results indicated that the developed method could be used to search for short peptides that mimic the highly sensitive and specific VOC binding properties of ORs.

In Chapter 3, “Fabrication of limonene binding peptide-modified GFET and the detection of limonene”, the fabrication of LBP-modified GFET and its limonene detection were described. The peptide probe was bi-functionalized via linkage with graphene-binding peptide, enabling a simple one-step immobilization on GFET. The peptide functionalization was evaluated by the changes in electrical properties as the peptide self-assembly onto graphene and a peptide sensing layer was observed by atomic force microscopy. Next, limonene detection using the peptide-modified GFET sensor was demonstrated. The sensor showed a rapid response, high affinity, and high specificity with a dissociation constant of 13 pM for limonene. Furthermore, this chapter reported the detection of limonene from citrus, demonstrating the practical application of the sensor. The stability and repeatability were assessed through multiple detections with identical sensors.

In Chapter 4, “Implementation of the developed OR-mimetic peptide screening and utilization with GFET strategy for the detection of skatole”, the implementation of the established peptide screening and sensor fabrication was demonstrated through the development of a second OR-mimetic peptide modified GFET for skatole, a signature VOC from the boar taint. The skatole binding peptides were screened from the OR of the mosquito and functionalized to GFET with the identical method described in chapters 2 and 3. The peptide-modified GFET sensor exhibited good skatole detection including high binding affinity (dissociation constant of 6.8 pM) and enabled to differentiate skatole from its analogs. Moreover, by combining two skatole-binding peptide-modified GFETs and principal component analysis (PCA), the developed system could clearly discriminate skatole from other test VOCs. Finally, the detection of skatole from a pond water sample was investigated. This chapter demonstrated the feasibility of the strategy to develop different OR-mimetic peptide and their use in GFETs sensing.

In Chapter 5, “Development of the bioelectric nose using OR-mimetic peptide-modified GFETs”, the development of bioelectronic nose using an array of multiple OR-mimetic peptide-modified GFET sensors previously fabricated to replicate the natural olfaction for VOCs discrimination was described. In this study, limonene, skatole, benzaldehyde, and hexane were exposed to the sensors to generate unique sets of responses which were analyzed by PCA to establish a pattern recognition system. The bioelectronic nose could detect and distinguish all VOCs from each other with clear clusters while the optimized parameters for the discrimination were obtained. To further explore the differentiation capabilities, trans-*p*-menthene and indole were employed as analogs for limonene and skatole, respectively. The bioelectronic nose successfully distinguished both limonene and skatole from their analogs with distinct clusters as well. These results demonstrate the utility of the developed bioelectronic nose strategy to detect a wide variety of VOCs.

Chapter 6, “Concluding remarks”, summarizes the key findings, implications, and potential future prospects. In brief, this dissertation presents basic knowledge of OR mimetic peptide design, and their utility in GFET for the detection and discrimination of VOCs, and consequently, significant contributions have been made from the perspective of engineering and industrial application. Therefore, this dissertation is considered to be of sufficient value as a doctoral dissertation.