

Multiple surface acoustic wave devices modified with different bitter receptors for chemical sensing

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Abstract:

In this study, a biomimetic taste receptor-based biosensor was developed using a multi-channel surface acoustic wave (SAW) device as transducers and bitter receptors as sensitive elements for chemical sensing. A DNA-directed immobilization method was employed to obtain high-efficient and controllable coupling between the sensitive area of multiple SAW devices and different bitter receptors. SAW device that is a mass-sensitive device was utilized to monitor the responses of a bitter receptor to its specific ligands. The measurement results show that this biosensor can record responsive signals of different bitter receptors when exposed to bitter substances by monitoring the changes in the phase shift of SAW devices. Each SAW detection channel can effectively record the responsive signals from the corresponding bitter receptors, which show good stability and anti-jamming ability. This biosensor can be used for the discrimination of different bitter substances due to the incorporation of multiple bitter receptors as sensitive elements. It is also applicable to the study of the interaction mechanisms between receptors and ligands.

Keywords: bitter receptors, surface acoustic wave, taste biosensor, DNA-directed immobilization, chemical sensing

Introduction

In recent years, biomimetic receptor-based biosensors have attracted more and more attention due to their promising prospects and potential applications in many fields such as biomedicine, food and drug safety, and environmental protection. Within this context, it is of great importance to achieve high-efficient coupling between the sensitive elements and transducers for improving the performance of biosensors. Numerous methods have been reported to facilitate the coupling between the sensitive elements and transducers and improve the signal transduction efficiency. Specifically, a DNA-directed immobilization method has been reported to be successfully applied in the cell-based assays, which is able to realize controllable coupling between cells and sensing chips based on the hybridization of complementary single-stranded DNA (ssDNA) molecules [1,2]. In this study, we are employing

the DNA-directed immobilization method to obtain high-efficient and controllable coupling between multiple SAW devices and different bitter receptors for the development of biomimetic taste receptor-based biosensor towards label-free and highly-sensitive detection and analysis of bitter substances.

Methods

This biosensor utilized four-channel SAW devices as the transducer to monitor the responses of bitter receptors to bitter substances (see Fig. 1). SAW devices were fabricated on the surface of LiNbO₃ substrate by microfabrication process. The bitter receptor proteins were prepared by the expression in cell-free protein expression system of *E. coli*. The sensitive area of SAW devices located in each channel was functionalized with distinct bitter receptors including T2R4, T2R14 and T2R16, while one channel was used as a

reference channel where the sensitive area of SAW device was left bare. A microchamber made from PDMS was sealed with multi-channel SAW devices in order to expose the sensitive area of SAW devices to the liquid environment for the receptor immobilization and detection of bitter substance.

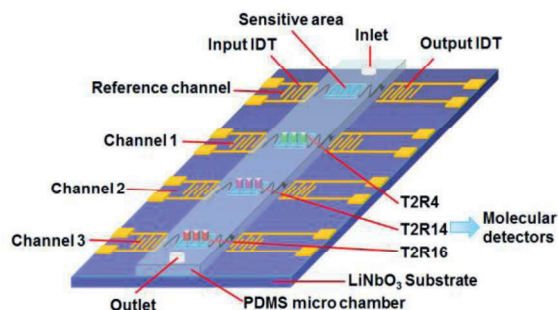


Fig. 1. Schematic diagram of multi-channel surface acoustic wave (SAW) devices modified with different bitter receptors for chemical sensing.

The DNA-directed immobilization method utilized a pair of complementary thiol-modified ssDNA to modify the gold surface of SAW devices and label the bitter receptors, respectively (see Fig. 2). Due to the different ssDNA linked to different types of bitter receptors, which are complementary to the corresponding probe ssDNA immobilized on the sensitive area of SAW devices located at the different channels, so SAW devices of each channel were immobilized with different bitter receptors based on the mechanism of complementary ssDNA hybridization. As a result, bitter receptor protein microarray was constructed for the detection of bitter substances.

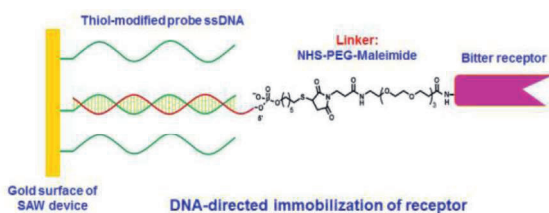


Fig.2. Schematics of DNA-directed immobilization of bitter receptor on the gold surface of the SAW device.

Results and Discussion

Since the multi-channel SAW device has multi-channel simultaneous detection characteristics, it can achieve label-free and highly-sensitive detection of interactions between bitter receptors and bitter substances. Due to the hybridization of complementary ssDNA, the immobilization of bitter receptors on the surface of SAW devices was controlled by the distribution of ssDNA on the sensor surface. In addition, immobilization efficiency was

improved due to the well-oriented of bitter receptors on the sensor surface. The immobilization of bitter receptors was characterized by the fluorescent staining, which indicates higher immobilization efficiency was achieved by DNA-directed immobilization method compared with physical adsorption. When exposed to bitter compounds such as denatonium, this biomimetic taste biosensor can record the responsive signals of different bitter receptors to the bitter compound (see Fig. 3), which show good stability and anti-jamming ability. This DNA-directed immobilization method provides a novel approach for controllable immobilization of receptors on the surface of transducers, which could potentially contribute to the development of receptor array-based biosensors. This biosensor cannot only be used for the discrimination of different bitter substances, but also applicable to the study of the interaction mechanisms between receptors and ligands.

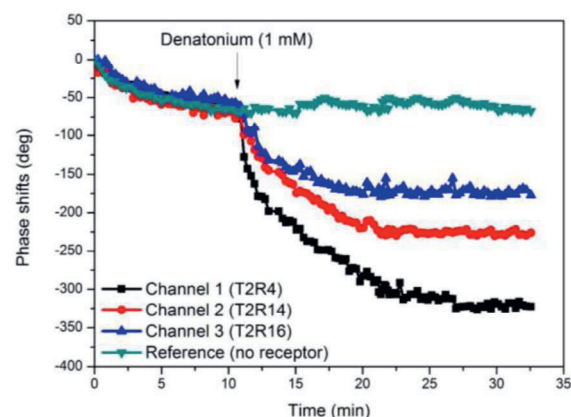


Fig.3. Responses of multi-channel SAW devices modified with different taste receptors to the bitter substance, denatonium (1 mM).

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