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## Visual detection of odorant geraniol enabled by integration of a human olfactory receptor into polydiacetylene/lipid nano-assembly†

A new polydiacetylene lipid/human olfactory receptor nanoassembly was fabricated for the visual detection of an odorant for the first time. The assembly consisted of phospholipid-mixed polydiacetylenes (PDAs) and human olfactory receptors (hORs) in detergent micelles. To overcome the limitations of bioelectronic noses, hOR-embedded chromatic complexes (PDA/hORs) were developed, introducing PDAs that showed color and fluorescence transitions against various stimuli. The chromatic nanocomplexes reacted with target molecules, showing a fluorescence intensity increase in a dose-dependent manner and target selectivity among various odorants. As a result, a color transition of the assembly from blue to purple occurred, allowing the visual detection of the odorant geraniol. Through circular dichroism (CD) spectroscopy and a tryptophan fluorescence quenching method, the structural and functional properties of the hORs embedded in the complexes were confirmed. Based on this first work, future array devices, integrating multiple nano-assemblies, can be substantiated and utilized in environmental assessment and analysis of food quality.

## Introduction

Human olfactory receptors (hORs) are the starting material for olfaction, and transmit a generated signal to the cerebrum by reacting with various odorants in air.<sup>1</sup> The hORs are seventransmembrane receptors that bind to their specific olfactory ligands. Therefore, they are very useful for developing bioelec-

tronic noses to clearly distinguish between target odorants and control molecules.<sup>2</sup> These noses could be applied to a wide range of fields, such as disease diagnosis,<sup>3</sup> analysis of food quality,<sup>4</sup> and environmental monitoring.<sup>5</sup> However, these devices transform the sense of smell to electrical signal, which cannot be recognized by the naked eye immediately. Therefore, various materials have been evaluated to overcome this limitation. A chromatic supramolecule consisting of  $\pi$ -conjugated molecules was used in this study.

Supramolecules could be used in a wide range of fields, including electronic materials, biotechnology, and environmental and chemical engineering.<sup>6</sup> A supramolecular body contains an artificial biomimetic membrane that simulates the structure of the cell membrane. The surface that reacts as a chemical functional group is maximized and can interfere with other ions when dissolved in a solution.8 In particular, polydiacetylene in the supramolecular body shows a chromatic transition from blue to red and a fluorescent transition from non-fluorescent to red-fluorescent against various stimulations, such as temperature, pH, solvent, a molecular recognition process (such as ligand-receptor or antigen-antibody reaction), and mechanical stimulation.9 The properties of these diacetylenes are maintained even in the presence of phospholipid domains in vesicles.<sup>10</sup> In previous studies, a target molecule was detected by embedding a synthetic receptor in supramolecules consisting of phospholipids and polydiacetylene (PDAs),11 and the lipid morphology was confirmed by inserting rhodopsin in the polymerizable lipid.12 In this study, for the first time, a novel PDA lipid bilayer was functionalized successfully with hORs (PDA/hORs). The polymerization of the membrane assembly containing hORs enabled the formation of a robust bilayer and minimally affected the hOR structure and activity. The nano-assembly showed selectivity to the target odorant of the hOR and a color transition from blue to purple, allowing the visual detection of the odorant. This could be applicable in biological and chemical technologies, such as environmental assessment and analysis of food quality.

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