Bio Focus

Water-gated transistors show unprecedented odor discrimination

Animal olfactory systems are very sensitive to minute changes in the conformation of molecules, such as chirality. How this sensitivity arises when the odorant chemicals interact with olfactory receptor proteins in sensory neurons is still unclear. Recently, M.Y. Mulla, L. Torsi, and their colleagues, in a collaborative effort with The University of Manchester that was coordinated by the University of Bari Aldo Moro, used exquisitely sensitive sensors made of water-gated organic field-effect transistors to extract more information about the weak interactions between odorant enantiomers and olfactory receptor proteins.

In the January issue of *Nature Communications* (DOI: 10.1038/ncomms7010), the researchers report functionalizing the gate electrode of field-effect transistors with porcine odorant binding protein. The presence of odorant molecules, here carvone enantiomers, changed the electric response of the transistor by modifying its capacitance. Both enantiomers are detected in the picomolar concentration regime—and they give different responses. "This system allows [us] to gather information about the energetics of the interactions occurring between a ligand and its recognition element when neither of these molecules bears a net charge. It is not easy to find another system that is capable [of detecting] neutral species," says Luisa Torsi.

By analyzing the transistor electric responses in terms of adsorption and dissociation of the odorant molecules onto the detector protein, the researchers extracted the free energies of interaction between the receptor protein and the odorant molecules. These energies turn out to be different for both enantiomers, which explain the differential sensitivity of olfactory proteins. The large capacitance change for one of the two enantiomers suggests that the ligand–protein binding results in a protein conformational change.

As an added advantage, these extremely sensitive biosensors are compatible with flexible substrates and low-cost printing technologies. This makes them interesting for a range of applications such as artificial noses or gas detectors, in addition to being a powerful biophysics research tool. On that front, Torsi says, "The challenges now involve finding systems that can perform sub-femto molar detection in a reliable fashion—and integrating biological recognition elements that are stable and that are really able to perform a recognition task, not only a differential detection."

Indeed, chirality is a very important property in biology in general, and the sensors could also help drug development. "Proteins often preferentially bind one chiral molecule over its mirror image," says Róisín Owens, an expert in bioelectronics, at the École Nationale Supérieure des Mines de Saint-Étienne. "Being able to discriminate between enantiomers is critical for drug development where different enantiomers sometimes have different effects; past examples include thalidomide, where one enantiomer was found to be severely teratogenic." In other words, future bio-electronic sensors could help distinguish between drugs with the intended positive effect on health and their mirror images, which sometimes have strong negative effects.

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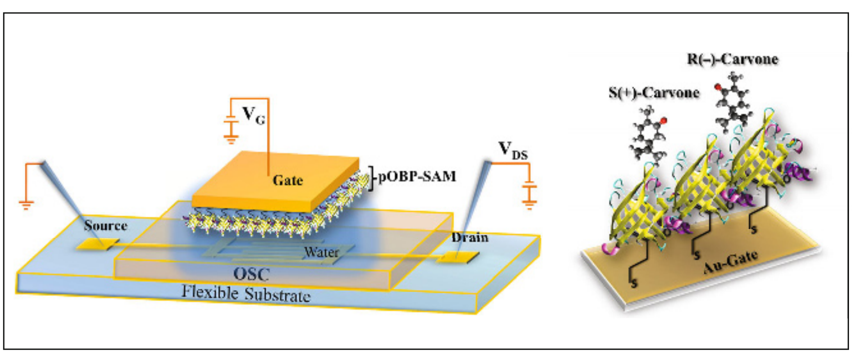

Water-gated bio-organic transistor comprising a porcine odorant binding protein/self-assembled monolayer (pOBP-SAM). OSC is organic semiconductor. Reproduced with permission from *Nat. Commun.* **6** (2015), DOI: 10.1038/ncomms7010. © 2015 Macmillan Publishers Limited.