A SERS Optophysiological probe for the real-time mapping and simultaneous determination in a live mouse brain

With the support by the National Natural Science Foundation of China and East China Normal University, the research team led by Prof. Tian Yang (田阳) at the Shanghai Key Laboratory of Green Chemistry and Chemical Processes, East China Normal University, developed a novel SERS Optophysiological probe for brain research, which was published in *Angew Chem Int Ed* (2019, 58: 5256—5260).

The most widely used tool for recording neuronal activity has been based on electrophysiology with extracellular microelectrodes. The use of this technique has enabled great advances in evaluating brain function. However, electrophysiological technology can only record the electrical signals of neuron-to-neuron communications. As a matter of fact, the generation of electrical signals mainly depends on changes in the chemical signals from neurotransmitters and ions. Therefore, to have a profound understanding of the physiological and pathological processes in a brain, both chemical and electrical signals need to be recorded, but this is still very challenging.

Tian's group is always interested in the development of biosensors for the detection of reactive oxygen species (ROS) and metal ions as well as the pH value in the brain. They proposed the sensing strategy with both current and potential signal outputs for the simultaneous determination of two species in a living system. A series of *in vivo* approaches were summarized in *Acc Chem Res*. However, the usage of an extra voltage or current in electrochemistry might have an influence on brain activity. Therefore, it is an urgent demand to develop new approaches for real-time detection and simultaneous quantification of chemical species in the brain.

Facing the above challenges, they recently designed and developed for the first time a novel SERS optophysiological probe for the real-time mapping and accurate sensing of both CO_3^{2-} and pH in a live mouse brain, as well as in single neurons. The quartz taper was coated with a layer of rough gold film by magnetron sputtering (Au-QT), for SERS determination. 1-(4-Aminophenyl)-2, 2, 2-trifluoroethanone (AT) and 4-mercaptobenzoic acid (MBA) were optimized as the specific recognition elements for CO_3^{2-} and pH, respectively, and co-modified onto Au-QTs. Furthermore, 4-mercaptobenzonitrile (MBN) with C≡N group in the SERS silent region of cells was employed as an inner reference for providing a built-in correction. The SERS microarray containing 8 microprobes with tip sizes of 5 m established a reliable platform for real-time imaging and accurate quantification of CO_3^{2-} and pH in live mouse brain upon middle cerebral artery occlusion. On the other hand, the present SERS nanoprobe with a tip size of 200 nm was successfully applied to determination of CO_3^{2-} and pH in single neurons. This work has opened up a new way to understanding the roles of chemical species in the physiological and pathological processes from the brain to the single neuron level.

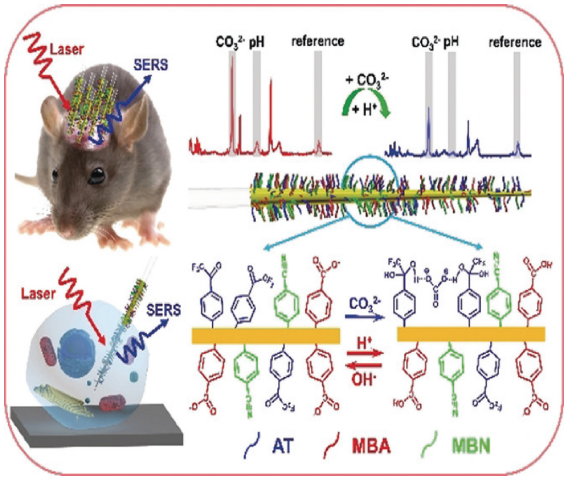

Figure The principle of the developed SERS probe for simultaneously biosensing of CO_3^{2-} and pH in the live brain and single neuron.