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Short peptide, thin layers and the perspective of their use in SERS-based sensors

Protein-mediated processes occurring in complex biological environments involve specific interactions under strictly defined conditions. Protein-derived peptides constitute a large group of biomolecular receptors with the remarkable ability to recognize various molecules and respond through a conformational transition to external stimuli such as local pH or the presence of biologically relevant cations. Coupling of such biology-inspired receptors to plasmonic nanostructures opens a new and fascinating route for creation of sensitive and selective nanosensors utilizing surface-enhanced Raman scattering (SERS) effect. In particular, short peptides are very attractive in this respect due to their bioactivity and the ease with which their structural and functional responses may be tuned according to environmental conditions. This underlies the design flexibility of SERS-based sensors employing peptide-derived receptors.

Design of such sensors requires a deepened understanding of the dynamic structural and physicochemical properties of peptide layers in response to external stimuli. We propose that conformationally labile peptides firmly attached to plasmonic substrate by cysteine (Cys) residue and containing a tryptophan (Trp) Raman probe can be employed as SERS-based sensors to detect for example local pH or concentration of certain biologically relevant ions.

We took the first step to achieve this goal by a comprehensive SERS study of short peptides comprising cysteine and/or tryptophan units. We investigated effects of terminal modifications and the amino acid sequence order in dipeptides composed of Trp and Cys on their SERS signals [1], the accessibility of both thiol moieties to interact with Ag nanoparticles for rigid cyclo(L-Cys-D-Cys) (diCys) structure, and suitability of isotopically labeled Cys (^{13}C and ^{15}N) to improve analysis of vibrational signatures within SERS response [2]. We demonstrated that the SERS spectra of dipeptides consisting of Trp and Cys residues were strongly dominated with the bands due to the vibrations of the Trp moiety. The SERS response was only slightly affected by the peptide sequence and terminal modifications under the fixed experimental conditions; however these two parameters became critical parameters when the effect of the substrate type and excitation wavelength is taken into consideration. We propose that the surface coverage of diCys on silver surface and thus the adsorption mode, which further affects the aggregation of Ag nanoparticles and the availability of the free thiol groups, can be guided by experimental conditions. On the other hand, the use of isotopically-labeled SERS allowed us to probe dynamics within the monolayer composed of L-cysteine and $^{13}C_3$ and ^{15}N L-Cys isotopologues, providing rare insights into murky phase transition unraveled only through this novel methodological approach [2].

Our initial findings allowed us to evaluate the efficiency of short peptide chemisorption and its SERS features, as well as showed the ability of tailoring the peptide adsorption properties with the experimental protocol. A potential of isotopically-edited SERS approach to gain deeper insights into relationship between local structure/conformation and SERS signals of the adsorbed peptide was demonstrated. All of these constitute a valuable introductory step to the informed selection of nature-inspired of stimuli-responsive peptide motifs for SERS nanobiosensors.

References

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