Detection, Identification and Structural Study of Biomolecules by Surface Enhanced Raman Spectroscopy

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The development of reliable, sensitive and specific biosensors is a very active research field. Among all the techniques, the Surface Enhance Raman Scattering (SERS) is one of most sensitive and has been widely used for ultrasensitive chemical analysis down to single molecule detection [1]. SERS is based on the exploitation of the optical properties of metallic nanoparticles and on the electromagnetic field enhancement localised at the vicinity of the nanostructures and created by the excitation of the Localized Surface Plasmon (LSP).

First, by controlling LSP, we are able to produce a highly sensitive sensor. We have determined the sensor characteristics such as its detection limit and its selectivity. We have determined that such sensor could be highly sensitive by reaching some detection limits lowest than the pico-molar. In this work, we have applied this sensor to the detection and the identification of specific proteins and we have been able to detect some specific disease biomarkers in body fluids (serum, saliva) paving the way to the potential disease diagnosis [2,3].

Second, the biosensor specificity is provided by multiple and simultaneous biomolecular recognition events based on weak interactions which give an apparent affinity. Aptamers, single DNA strands, are new bioreceptors intensively used now in biosensor. Through the self-hybridisation of one part of its sequence, the aptamer forms a loop structure exposing some bases that interact specifically with the analyte thanks to electrostatic interactions. It is of primary importance to understand such interaction to optimize the analyte capture and to improve the sensing performances. In addition, molecular interactions are the basis of many biological mechanisms. It is therefore important to have a better understanding of these phenomena and to be able to answer to specific questions as: how does the interaction take place?, is it dynamic or static?, is there any specific conformation for the interaction? To answer to such questions, we study the interaction between aptamer or DNA strand with its analyte or its complementary strand by the combination of SERS and multivariate statistical analysis. We observe the DNA structure and its evolution during the interaction under different experimental conditions (in air or in buffer) and we are able to probe the strand conformations and orientations relatively to the surface [4]. We also study the interactions between two DNA complementary strands (PolyA/PolyT) as well as strands containing mismatch in their sequences (one C base inserted at different positions in the sequence of polyA). We interpret the modification of the SERS spectra by some changes in the orientation and in the flexibility of the DNA strands during the hybridisation. Using Principal Component Analysis, we were able to determine some spectral markers of the hybridisation and of its disruption due to the single base mismatch. This study provides a new approach for the reliable quantification and structural analysis of biological molecules.

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