**New Insight on the Aptamer Conformation and Aptamer/protein Interaction by Surface Enhanced Raman Scattering and Multivariate Statistical Analysis**

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Biosensors are designed to specifically detect analytes. The specificity is then provided by multiple and simultaneous biomolecular recognition events based on weak interactions which give an apparent affinity. Aptamers are new bioreceptors intensively used now in biosensor. They are composed of a single DNA strand that offer many advantages as a high affinity versus analytes, a high stability and a highly reproducible in vitro production with high purity excluding any use of animals or cells. 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 as one of the main drawbacks of biosensor is the biological noise due to unspecific interaction that constrains the detection limit. 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 one aptamer and its analyte (the MnSOD protein) by the combination of Surface Enhanced Raman Scattering and multivariate statistical analysis.[5] We observe the aptamer structure and its evolution during the interaction under different experimental conditions (in air or in buffer). Through the spectral treatment by principal component analysis of a large set of SERS data, we were able to probe the aptamer conformations and orientations relatively to the surface assuming that the in plane nucleoside modes are selectively enhanced. We demonstrate that the aptamer orientation and thus its flexibility relies strongly on the presence of a spacer of 15 thymines and on the experimental conditions with aptamers laying on surface in air and standing in buffer. We reveal that the interaction with the MnSOD induces a large loss of flexibility and freezes the aptamer structure in a single conformation.

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