SERS characterization of transient oligomeric state of amyloidogenic proteins using Ag nanoparticles.

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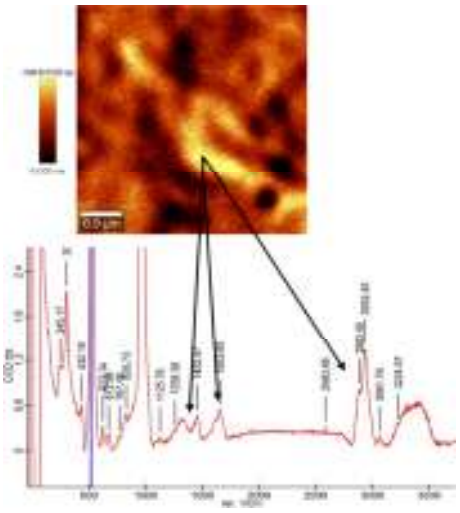
The presence of insoluble fibrillar deposits in the pancreas and in the brain is one of the most common pathological features in patients affected respectively by diabetes mellitus type II and Alzheimer's disease. The fibrillogenesis process of the two proteins β-amyloid peptide (Aβ(1-40)) and islet amyloid polypeptide (IAPP) or amylin follows a nucleation-dependent mechanism. The mechanism comprises a first phase in which monomers form small, soluble, unstructured aggregates, called oligomers [1,2], followed by a second phase, in which unstructured aggregates transform into β-sheet-rich structures that form the mature fibrils through a self-assembling process [3]. Moreover, it has been suggested that the main mechanism for cell cytotoxicity can be ascribed to membrane permeabilization, through the formation of membrane channels by soluble oligomers [4]. Oligomers, are fast transient unstructured species, so experimentally not structurally characterized.
In this work, we highlight an accurate spectral detection of the soluble oligomers by using Surface-Enhanced Raman Scattering (SERS) nanoparticles based on silver, gold and their alloys. Metal colloids were obtained by a pulsed laser ablation process using the 532 nm irradiation wavelength of a Nd:YAG laser. We demonstrate that optimizing the size and the composition of nanostructures we can obtain SERS spectra of proteins at low concentration in the soluble phase. Our data show in the oligomeric species of ABeta (1-40) and IAPP, the presence of both α-helix and β-sheet secondary structures. This data agree with previous molecular dynamics simulation [5]. Moreover, our data evidence oligomeric species of both proteins shared common future secondary structures.



Raman spectrum and Raman imaging of a fibrillary deposit of hIAPP

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