Tip-enhanced Raman spectroscopy to distinguish toxic oligomers from Aβ(1-42) fibrils at the nanometer scale

S. Bonhommeau*, D. Talaga¹, J. Hunel¹, C. Cullin², S. Lecomte²

(1) Institut des Sciences Moléculaires, CNRS UMR 5255, Université de Bordeaux, Bordeaux, France
(2) Institut de Chimie et Biologie des Membranes et Nanoobjets, CNRS UMR 5248, Université de Bordeaux, Bordeaux, France

Tip-enhanced Raman spectroscopy is a powerful technique combining the high sensitivity of surface-enhanced Raman spectroscopy (SERS) and the nanoscale lateral spatial resolution of scanning probe microscopies, such as atomic force microscopy (AFM) and scanning tunneling microscopy (STM). AFM-TERS has been already employed to achieve nanoscale chemical characterization of biochemical and biological samples.¹ However, analyzing amyloid fibrils, consisting of β-sheet-rich peptide aggregates, using TERS remains a challenging task² since the spectral fingerprint of the peptide secondary structure, namely the amide I band, can be missing in amyloid TERS signatures.³

Here, natural Aβ(1-42) fibrils (WT) implicated in Alzheimer’s disease as well as two synthetic mutants forming less toxic amyloid fibrils (L34T) and highly toxic oligomers (oG37C) are chemically characterized at the scale of a single structure (~30 nm) using tip-enhanced Raman spectroscopy (TERS). While the proportion of TERS features associated with amino acid residues is similar for the three peptides, a careful examination of amide I and amide III bands allows us to clearly distinguish WT and L34T fibers organized in parallel β-sheets from the small and more toxic oG37C oligomers organized in anti-parallel β-sheets.⁴ This work opens promising perspectives for the detection of pathological species.

Figure 1. AFM-TERS configuration under 633 nm irradiation and a few TERS spectra observed for toxic oligomers.

References

Corresponding author email: sebastien.bonhommeau@u-bordeaux.fr