TIP-ENHANCED RAMAN SPECTROSCOPY TO DISTINGUISH TOXIC OLIGOMERS FROM $A\beta_{1-42}$ FIBRILS AT THE NANOMETER SCALE

Sébastien Bonhommeau, David Talaga, Julien Hunel
Université de Bordeaux, Institut des Sciences Moléculaires, CNRS UMR 5255, F-33400 Talence, France
Sophie Lecomte, Christophe Cullin
Université de Bordeaux, institut de Chimie et Biologie des Membranes et des Nanoobjets, CNRS UMR 5248, F-33600 Pessac, France
E-mail: sebastien.bonhommeau@u-bordeaux.fr

KEY WORDS: Tip-enhanced Raman spectroscopy, amide bands, amyloid fibrils, oligomers, toxicity

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. However, analyzing amyloid fibrils, consisting of β-sheet-rich peptide aggregates, using TERS remains a challenging task [1] since the spectral fingerprint of the peptide secondary structure, namely the amide I band, can be missing in amyloid TERS signatures [2].

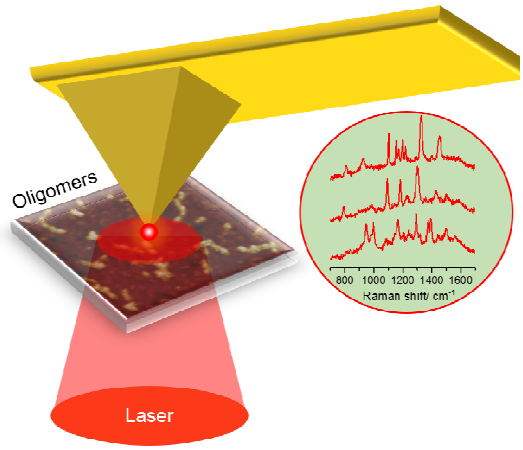

Figure 1: AFM-TERS configuration under 633 nm irradiation and a few TERS spectra observed for toxic oligomers.

Here, natural $A\beta_{1-42}$ 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 [3]. This work opens promising perspectives for the detection of pathological species.

[1] C.C. vandenAkker, T. Deckert-Gaudig, M. Schleeger, K.P. Velikov, V. Deckert, M. Bonn, and G.H. Koenderink, "Nanoscale Heterogeneity of the Molecular Structure of Individual hIAPP Amyloid Fibrils Revealed with Tip-Enhanced Raman Spectroscopy", *Small*, **11**, 4131-4139 (2015).
[2] C. Blum, T. Schmid, L. Opilik, N. Metanis, S. Weidmann, and R. Zenobi, "Missing Amide I Mode in Gap-Mode Tip-Enhanced Raman Spectra of Proteins", *J. Phys. Chem. C*, **116**, 23061-23066 (2012).
[3] S. Bonhommeau, D. Talaga, J. Hunel, C. Cullin, S. Lecomte, "Tip-Enhanced Raman Spectroscopy to Distinguish Toxic Oligomers from $A\beta_{1-42}$ Fibrils at the Nanometer Scale", *Angew. Chem. Int. Ed.*, DOI: 10.1002/anie.201610399 (2017).