2D-IR versus VCD spectroscopy of artificial β-sheet forming fibrils

Jan Helbing[1,*], Roman Marty[2], Holger Frauenrath[2]

[1]Department of Chemistry, University of Zurich, Winterthurerstrasse 190, 8057 Zurich, Switzerland,
[2]Institute of Materials, Ecole Polytechnique Federale de Lausanne (EPFL), 1015 Lausanne, Switzerland
*jan.helbing@chem.uzh.ch

We discuss 2D-IR and VCD spectra of self-assembled nanostructures, which form monomeric right-handed parallel beta sheet helices, but exhibit the 'giant' amide I VCD signals typical of left-handed amyloid-like peptide aggregates. Isotope-labelling and strand-length variations cause dramatic changes in the VCD signal, which are only partially reflected in 2D-IR.

2D-IR spectroscopy allows to determine the position, diagonal and anti-diagonal width of isotope-shifted amide I bands, which encode detailed information about beta-sheet stacking and the position of individual amino acids in peptide aggregates and fibrils[1, 2]. Vibrational circular dichroism (VCD), on the other hand, provides information on the composition and macroscopic chirality of peptide aggregates, primarily based on the observation that stacked beta-sheets in amyloid-like fibrils with an overall left-handed morphology give rise to left-handed amide I couplets, which become very intense as the fibrils grow in size[3]. We have studied, by VCD and 2D-IR spectroscopy, self-assembled nanostructures, which form highly reproducible, monomeric right-handed parallel beta sheet helices, but exhibit the 'giant' amide I VCD signals typical of left-handed amyloid-like peptide aggregates[4]. Isotope-labelling and strand-length variations cause dramatic changes in the VCD signal, which are only partially reflected in the linear and 2D-IR spectra. Although both 2D-IR and VCD signals of the amide I band of peptides and proteins can usually be understood in terms of the same vibrational exciton model, we find that a model, which can account for the achiral 1D and 2D spectra, cannot reproduce the intensity of the chiral signal and its strong isotope dependence. In view of these results, chiral 2D-IR spectroscopy would be a highly desirable tool, which is, however, still out of reach, despite significant experimental efforts.

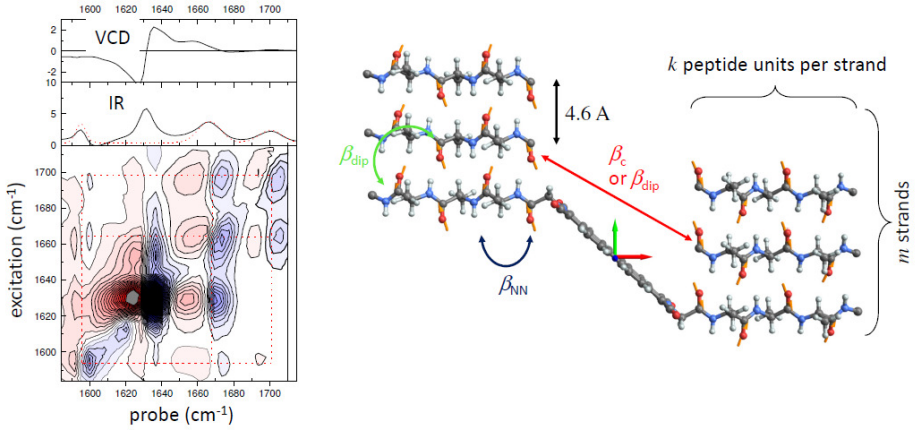

Fig.1 (Left) VCD, FTIR and 2D-IR spectrum of the unlabeled parallel beta-sheet helices. (Right) The helices consist of self-assembling perylene bisimides cores substituted on both sides by oligopeptide and (not shown) polymer chains, which prevent aggregation. The number of peptide units (k=3,4,5) was varied and ^{13}C=O isotope labels were introduced at various distances from the core.

[1] C.T. Middleton et al., Nat Chem 4 (2012) 355-360.
[2] L. Wang et al., J. Am. Chem. Soc. 133 (2011) 16062.
[3] D. Kurouski, et al.,Biophys. J. 103 (2012) 522.
[4] R. Marty, et al., J. Phys. Chem. B 118 (2014) 11152-11160.