

# Illuminating Biomolecular Complexity: X-ray Free Electron Lasers and Vibrational Spectroscopies for Protein, Aggregates, and Cellular Architectures



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## FTIR (micro-)spectroscopy in situ: Diagnostic Potential and Insights into Amyloid Deposits

Fourier transform infrared (FTIR) (micro-)spectroscopy is a label-free and non-destructive vibrational tool that has been successfully applied to study not only the amyloid structural properties and aggregation mechanisms directly in cells, tissues, or biofluids, but also to gain new insights into the mechanisms of amyloid formation and toxicity[1]. In particular, the use of an infrared microscope allows measuring *in situ* the IR absorption from selected areas of the sample, enabling to explore the colocalization of amyloid deposits with other biomolecules[1].

We employed FTIR microspectroscopy to analyze unfixed human tissues - cardiac and adipose - from patients affected by systemic light chain amyloidosis[2]. We detected the *in situ* marker band of the aggregates, ascribable to amyloid deposits. The possibility to measure unfixed tissue sections made it possible to detect important peculiarities in the spectral features of other biomolecules in cardiac tissues, in areas enriched with aggregates, suggesting a role in particular of lipids in amyloid deposition *in vivo*[2].

We then applied attenuated total reflection (ATR)-FTIR investigation - coupled to multivariate analysis - to the analysis of adipose tissue aspirates from patients affected by systemic amyloidosis[3]. We found that the ATR-FTIR approach can differentiate fat aspirates containing amyloid deposits from control specimens with high sensitivity and specificity. Notably, discrimination between amyloid-affected and negative samples was obtained on the basis of the whole spectrum, pointing out that resident lipids are intrinsic features of amyloidosis-affected subcutaneous fat[3].

After our initial studies[2,3], independent groups published works on the potential use of FTIR spectroscopy for the detection and typing of cardiac amyloidosis. The results of subsequent studies[4] confirmed our findings on a larger cohort of patients, emphasizing FTIR spectroscopy as a promising diagnostic method. Here, the scientific background[1,5] and the FTIR spectroscopic approach[1-3] are presented for the detection of cardiac amyloidosis in a clinical setting on the one hand, and for gaining new insights into amyloid deposits *in situ* on the other.

### References:

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### Scholarship eligibility

no

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