Conformational analysis of lipid membrane mimetics modified with Aβ42 peptide by Raman spectroscopy and computer simulations

Mamatkulov K.,

Zavatski S.[1],

Arynbek Y.,

Esawii H. A.,

Burko A.[1],

Bandarenka H.[1],

Arzumanyan G.

2025

[1]Belarusian State University of Informatics and Radioelectronics, 6 P. Brovki Street, Minsk, 220013, Belarus.

Keywords: Raman spectroscopy, MDDFT, peptide secondary structure, conformational states.

Abstract: Peptide-lipid interactions play an important role in maintaining the integrity and function of the cell membrane. Even slight changes in these interactions can induce the development of various diseases. Specifically, peptide misfolding and aggregation in the membrane is considered to be one of the triggers of Alzheimer's disease (AD), however its exact mechanism is still unclear. To this end, an increase of amyloid-beta (Aβ) peptide concentration in the human brain is widely accepted to gradually produce cytotoxic Aβ aggregates (plaques). These plaques initiate a sequence of pathogenic events ending up in observable symptoms of dementia. Understanding the mechanism of the Aβ interaction with cells is crucial for early detection and prevention of Alzheimer's disease. Hence, in this work, a

comprehensive Raman analysis of the Aβ42 conformational dynamics in water and in liposomes and lipodiscs that mimic the membrane system is presented. The obtained results show that the secondary structure of Aβ42 in liposomes is dominated by the α–helix conformation, which remains stable over time. However, it comes as a surprise to reveal that the lipodisc environment induces the transformation of the Aβ42 secondary structure to a β-turn/random coil. Our Raman spectroscopy findings are supported with molecular dynamics (MD) and density functional theory (DFT) simulations, showing their good agreement.

Publication source:

Conformational analysis of lipid membrane mimetics modified with Aβ42 peptide by Raman spectroscopy and computer simulations / K. Mamatkulov, S. Zavatski, Y. Arynbek [et al.] // Journal of Biomolecular Structure and Dynamics. – 2025. – Volume 43, Issue 17. – P. 9994–10007. – DOI : https://doi.org/10.1080/07391102.2024.2330706.