ZAJEDNIČKI SEMINAR

utorak, 22.12.2015., 14:00 sati (točno)

PMF-Fizički odsjek, Bijenička cesta 32, Predavaonica 201

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Physical determinants of amyloid aggregation: traversing scales using computer simulations

The assembly of normally soluble proteins into large fibrils, known as amyloid aggregation, is associated with a range of pathologies, including Alzheimer's and Parkinson's diseases. It has proven to be very challenging to experimentally characterise the mechanisms of amyloid formation; this is crucial for influencing the pathological processes in a rational manner. Computer simulations, in combination with quantitative experiments, can provide invaluable insight in this case.

Substantial evidence shows that disordered pre-fibrillar oligomers − not the fully grown amyloid fibrils − are cytotoxic and involved in pathological processes. Yet, their relationship to fibrils is not well understood. Using computer simulations, we showed that at physiological conditions, small disordered oligomers serve as nucleation centres for fibrils, and are crucial on-pathway species to amyloid formation [1].

Furthermore, recent experiments have revealed that amyloid fibrils are able to catalyse formation of their copies from soluble peptides. By combining simulations and kinetic theory, with biosensing experiments and kinetic measurements of Alzheimer's Aβ40 peptide aggregation, we proposed a mechanistic explanation for the self-replication of protein fibrils. We find that this intricate process is governed by a single physical determinant − the adsorption of monomeric proteins onto the surface of fibrils [2]. Such mechanistic understanding not only has implications for future efforts to control pathological protein aggregation, but is also of interest for the rational assembly of nanomaterials, where achieving self-replication is one of the unfulfilled goals.

References:

[1] A. Šarić, Y. C. Chebaro, T. P. J. Knowles and D. Frenkel, *PNAS* 111, 17869 (2014)

[2] A. Šarić, G. Meisl, A. K. Buell, T. C. T. Michaels, S. Linse, T. P. J. Knowles and D. Frenkel, under review (2015).

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Anđela Šarić is a Human Frontier Science Program Fellow in the Department of Chemistry, University of Cambridge. She received a diploma in Chemistry from the University of Zagreb, and a PhD in Chemical Physics (with distinction) from Columbia University, New York. She uses computer simulations to address physical mechanisms of biological processes where collective behaviour arises. Her research interests thus far included physics of biological membranes, self-assembly of active matter, and pathways of amyloid aggregation. In 2016 she will join the University College London Department of Physics and the Institute for the Physics of Living Systems as a junior group leader.