THE PHYSICS COLLOQUIUM

Thursday 11 July 2024, 4:00 p.m.
Nijenborgh 4, Lecture Hall 5111.0080

Cracking the Code: A Computational Expedition into Neurodegenerative Proteins and Innovative Therapies

Ioana M. ILIE

University of Amsterdam

Protein misfolding and aggregation are associated with the onset of neurodegenerative disorders such as Alzheimer's, Parkinson's and Creutzfeld-Jakob's disease. To date no cure exists for neurodegenerative diseases and therapeutic interventions give limited symptomatic relief, rather than prevention. Different aggregates are associated with neurotoxicity. A better understanding of the physicochemical properties that govern the assembly mechanism of the early oligomeric species will aid in understanding their role in toxic propagation.

Here, I present our computational efforts to understand the aggregation mechanisms of polypeptides associated with neurodegenerative diseases from a multiscale perspective. First, we investigate the effects of antibody binding to the cellular prion protein. Next, I introduce a novel coarse-grained model for amyloidogenic polypeptides and use Brownian dynamics simulations to gain insight into the physical mechanisms of assembly into oligomeric species [3,4]. Lastly, I present a novel iterative approach to design cyclic peptides that bind to soluble proteins with the aim of inhibiting the toxic propagation [4].

[1] IMI et al, Biophys. J. **121**, 2813-2825 (2022)
[2] IMI & Caflisch, **1870**, 140827 BBA-Prot. Proteom. (2022)
[3] Mayer et al., in preparation
[4] Zhou et al, Adv. Sci. 2402740 (2024)
[5] de Raffele & IMI, Chem. Comm. **60** 632–645 (2024)

Join us for coffee starting 3:30 p.m. Refreshments will be served after the lecture.
For more information contact the host: Loredana Protesescu (l.protesescu@rug.nl)
Website: http://www.rug.nl/research/vsi/colloquia/