Coarse-grained molecular dynamics of intrinsically disordered proteins

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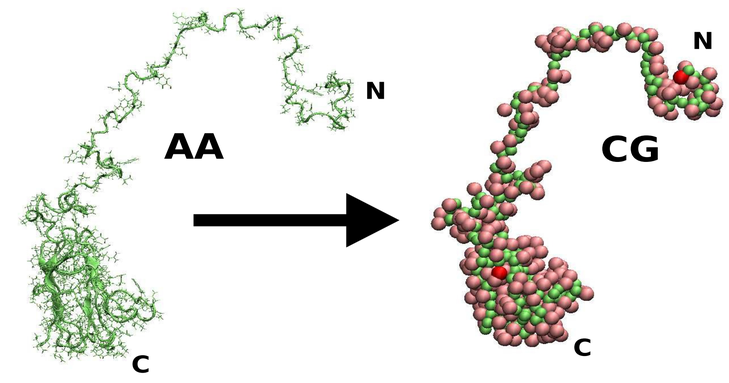
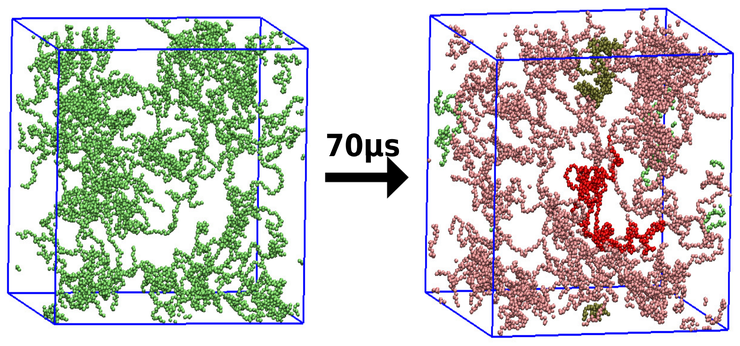
Abstract

Intrinsically disordered proteins (IDPs) at physiological conditions have no stable structure in extended parts of their polypeptide chains. We use molecular dynamics (MD) methods to study conformations and interactions of IDPs. Since IDPs typically exhibit large conformational fluctuations on time scales of microseconds or longer, we use coarse-grained (CG) models, where groups of atoms are represented by single beads, which significantly reduces the computation time. Firstly, we employ our locally developed CG Cα-based model [1] to study aggregation of α-synuclein. In particular, we investigate how α-synuclein aggregation depends on protein concentration and temperature. Secondly, use Martini 3 model [2] to determine the conformational ensemble of galectin-3. We follow the approach of Thomasen et al. [3] and rescale water-protein interactions to obtain a conformational ensemble consistent with data from small angle X-ray scattering experiments.

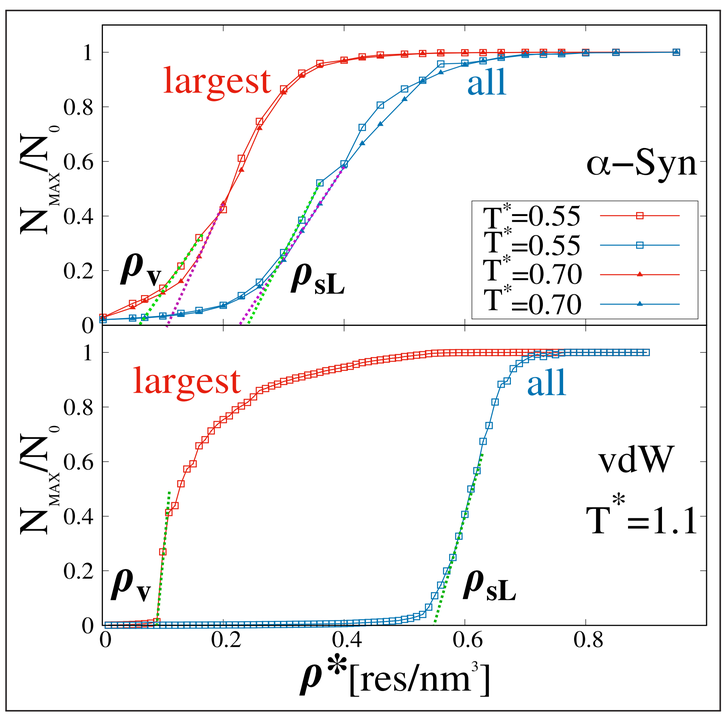
AA→CG (galectin-3)



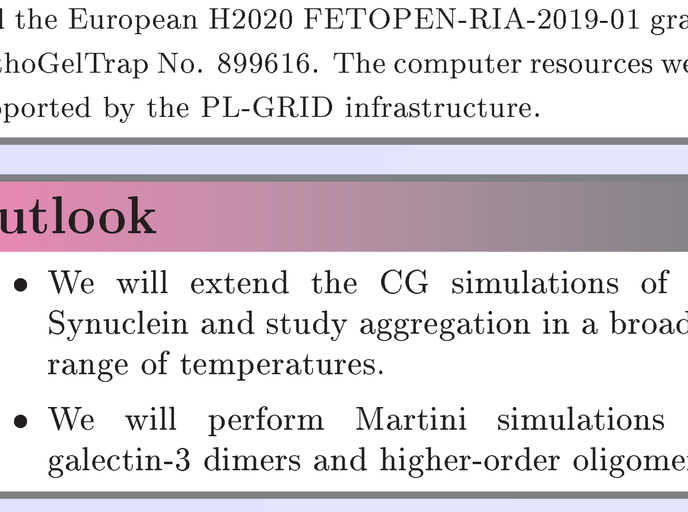
Clusterisation α-Syn (CG)



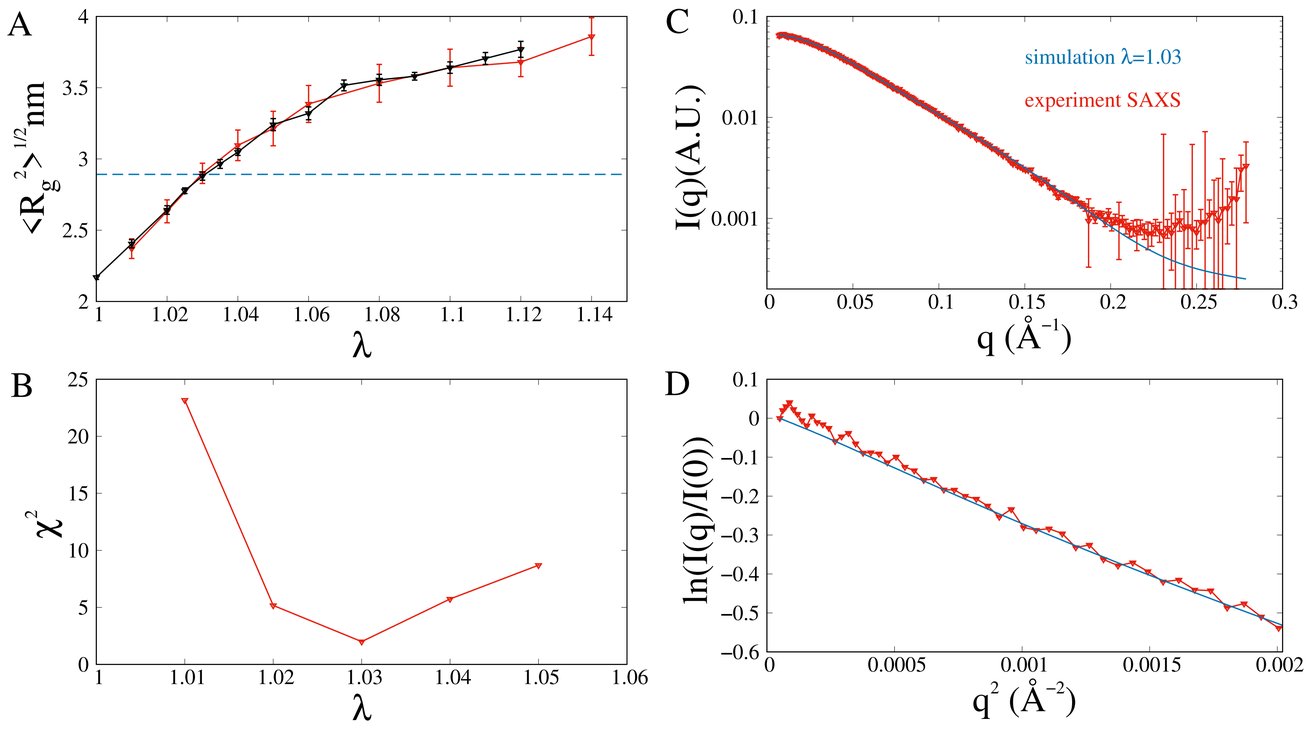
Cluster size (CG and vdW)



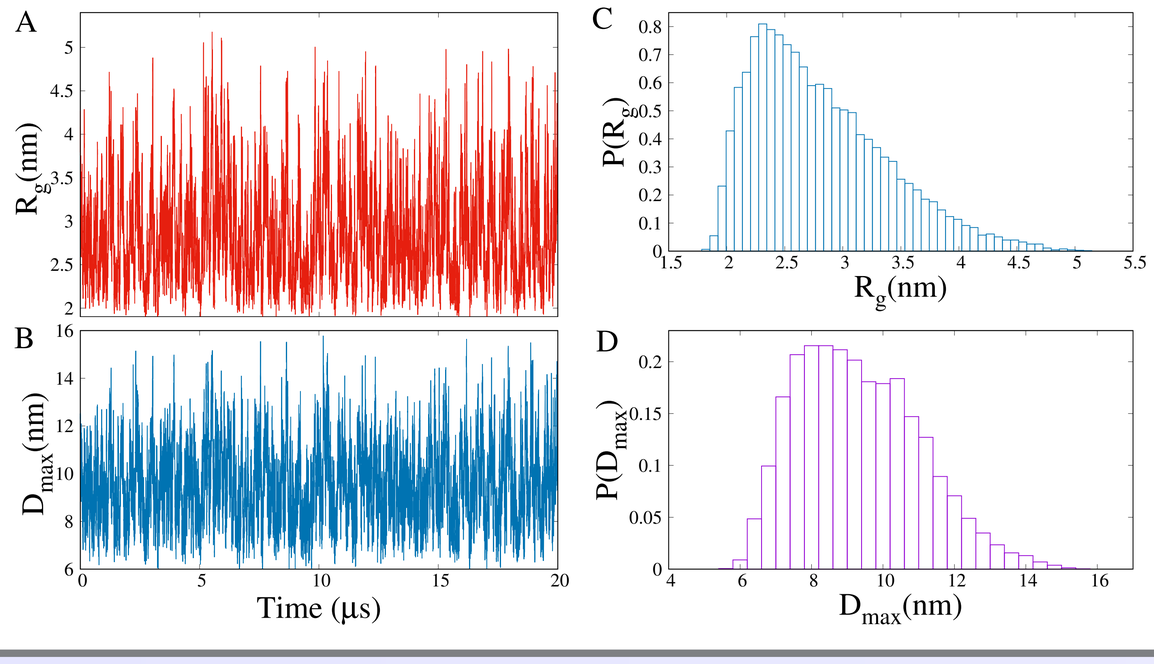
Single peptide



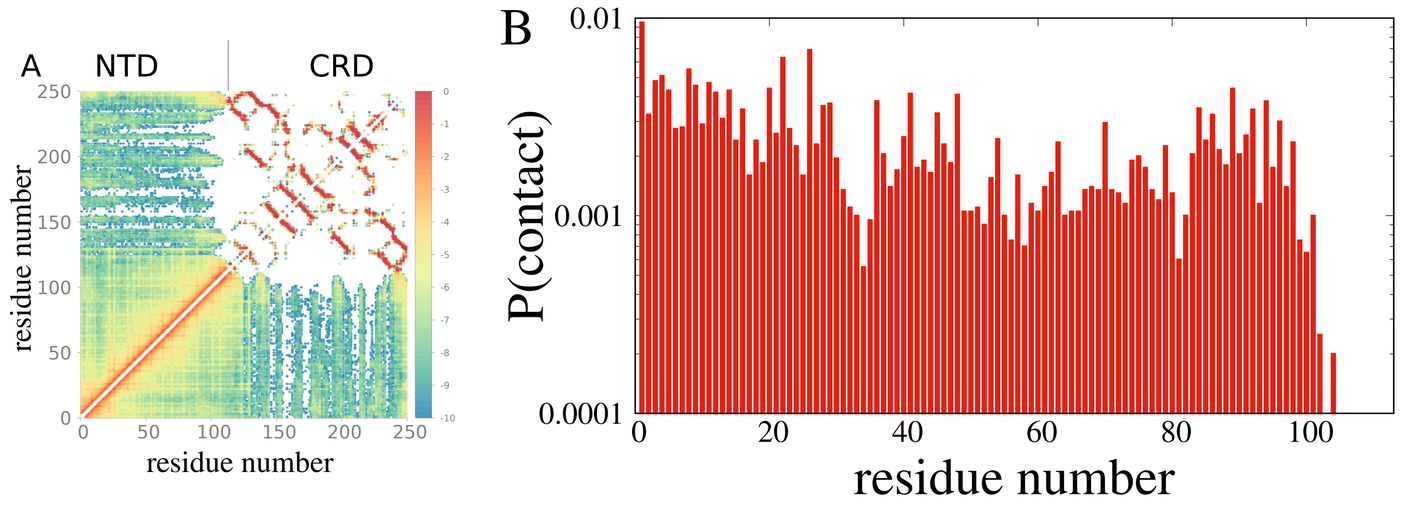
Comparison to SAXS experiment



Fluctuations



Contact map



Acknowledgements

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Outlook

- We will extend the CG simulations of α-Synuclein and study aggregation in a broader range of temperatures.
- We will perform Martini simulations of galectin-3 dimers and higher-order oligomers.

References

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[4] Pham Dinh Quoc Huy, Mateusz Chwastyk and Marek Cieplak. Front. Chem. 10: 1646,(2023)