Conformational dynamics of galectin-3 based on the Martini 3 model

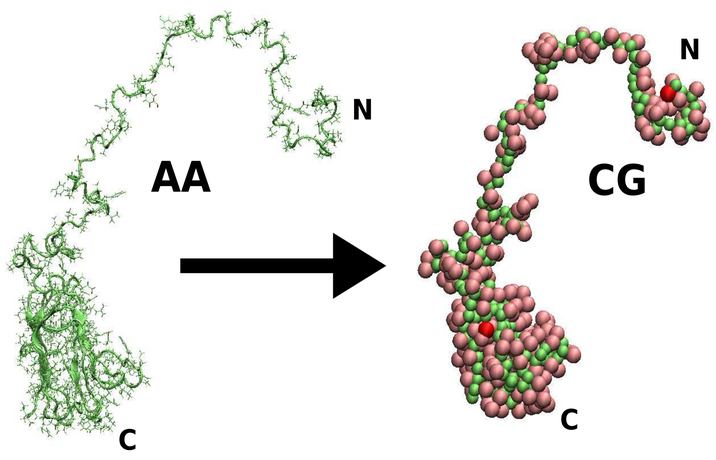
M. M. Anila[1], P. Rogowski[1], B. Różycki[1]

[1] *Institute of Physics, Polish Academy of Sciences, Aleja Lotników 32/46, 02-668 Warsaw, Poland.*

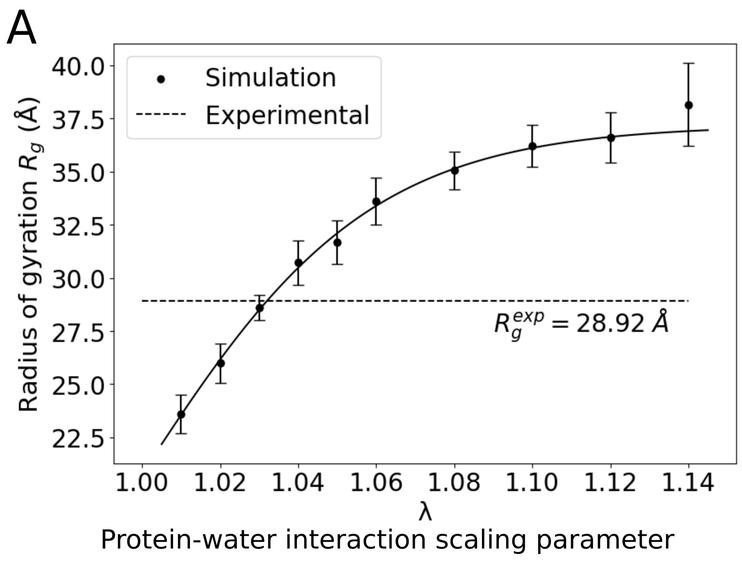
Abstract

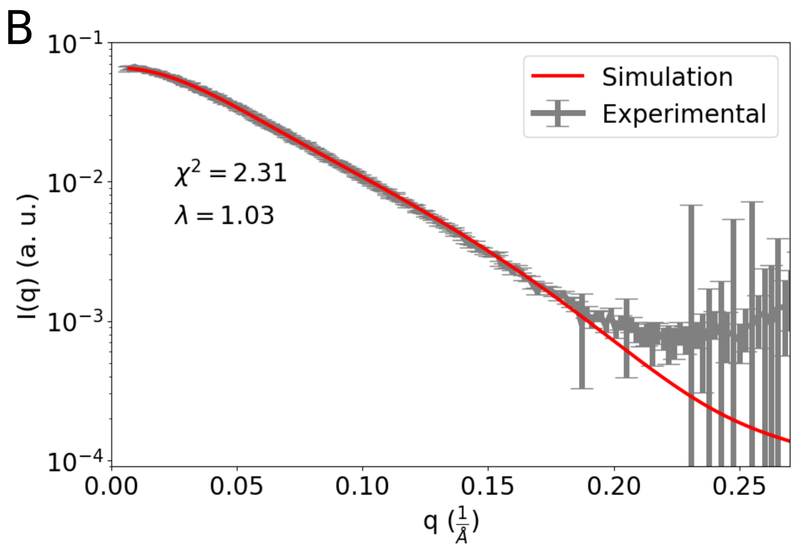
We characterize conformations of galectin-3, which is mixed-folded protein comprising an intrinsically disordered N-terminal domain (NTD) and a carbohydrate recognition domain (CRD). We perform molecular dynamic simulations using the Martini 3 force field [1] and a cubic box of side length of 20 nm. We follow the methodology of Thomasen et al. [2] to rescale protein-water interactions, and obtain a conformational ensemble fully consistent with data from small angle X-ray scattering experiments [3]. Our simulation results show that galectin-3 exhibits large-scale fluctuations between compact and extended conformations. Most frequent contacts are formed by aromatic residues within the NTD. It appears that self association of galectin-3 molecules is mostly mediated via the NTD.

Coarse-grained representation

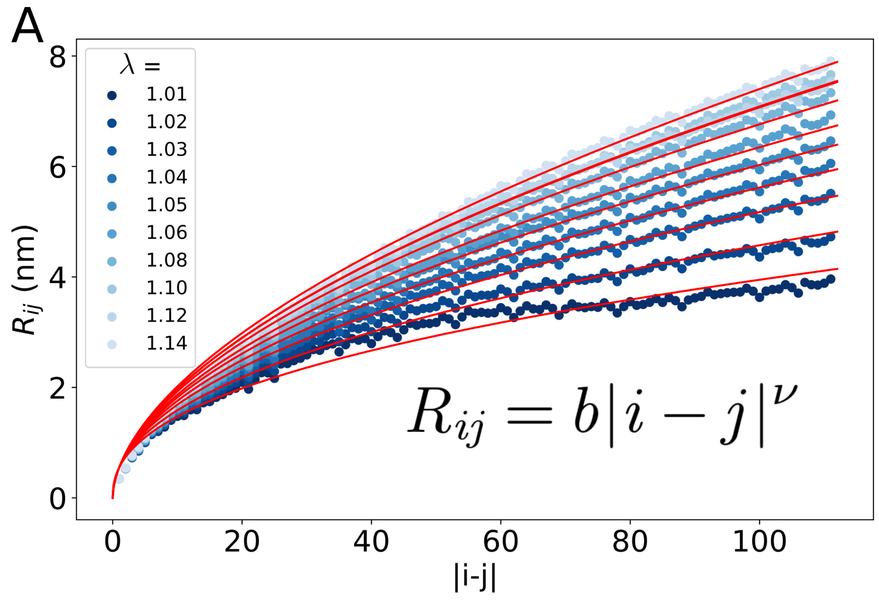


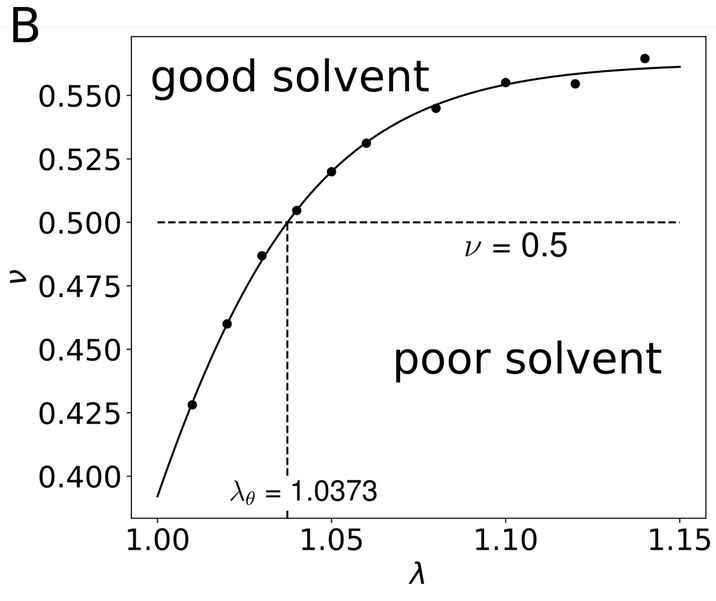
SAXS: experiment and simulations



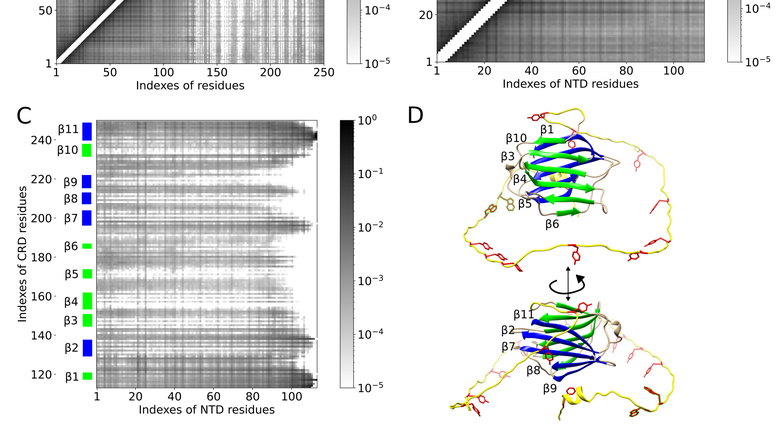


Scaling of average intra-molecular distances in the NTD

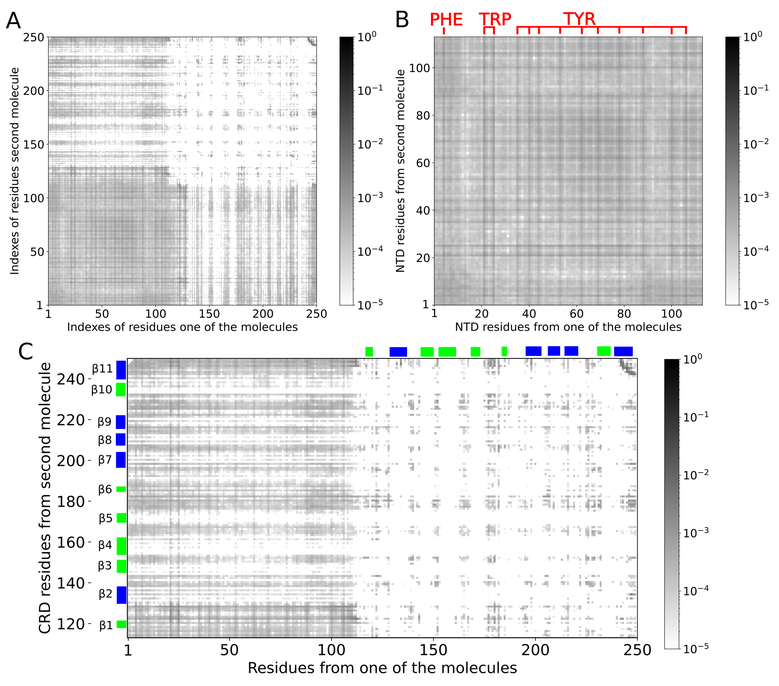




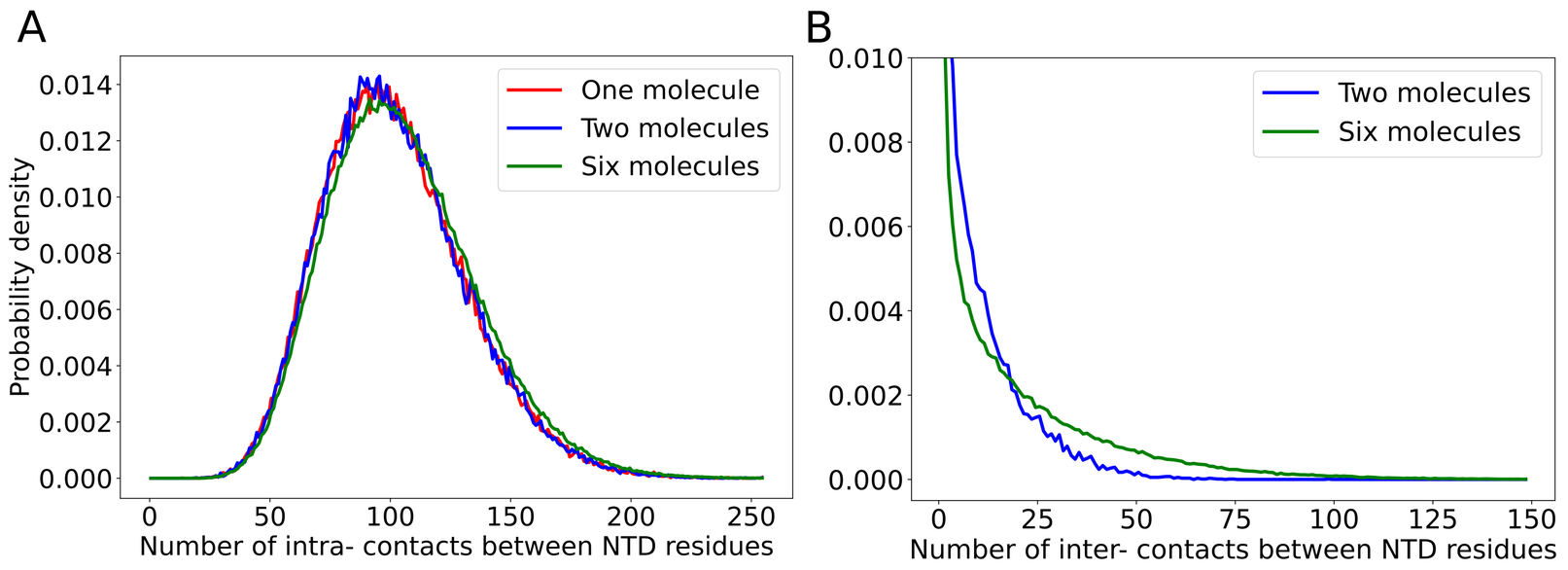
Intra-molecular contacts



Inter-molecular contacts



Effect of protein concentration



References

[1] P. C. T. Souza et al. Nature Methods 18, 382-388 (2021).

[2] F. E. Thomasen et al. J. Chem. Theory Comput. 18, 2033-2041, (2022).

[3] Y. H. Lin et al. J. Biol. Chem. 292, 17845-17865 (2017).

Outlook and Acknowledgements

Our goal is to simulate biomolecular condensates of galectin-3 in the context of clathrin-independent endocytosis.

This research has received support from the National Science Centre (grant No. 2020/39/B/NZ1/00377). We acknowledge the Polish high-performance computing infrastructure PLGrid for awarding this project access to the LUMI supercomputer (grant No. PLL/2023/04/016485).