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GRK 2516 Soft Matter Seminar

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Research seminar of the DFG Research Training Group GRK 2516 (https://grk2516.uni-mainz.de).

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Single-chain and condensed-state behavior of hnRNPA1 from molecular simulations

Intrinsically disordered proteins (IDPs) are essential components for the formation
of membraneless organelles, which play key functional and regulatory roles
within biological systems. These complex assemblies form and dissolve spontaneously
over time via liquid-liquid phase separation of IDPs. Mutations in their amino acid
sequence can alter their phase behavior, which has been linked to the emergence
of severe diseases such as cancer and neurodegenerative diseases including amyotrophic
lateral sclerosis. In this work, we study the conformation and phase behavior
of a low-complexity domain of heterogeneous nuclear ribonucleoprotein A1
(hnRNPA1), using coarse-grained implicit solvent molecular dynamics simulations [1].
We systematically analyze how these properties are affected by the number of aromatic
residues within the examined sequences. We find a significant compaction
of the chains and an increase in the critical temperature with increasing number of
aromatic residues within the IDPs. Comparing single-chain and condensed state simulations,
we find much more collapsed polymer conformations in the dilute systems,
even at temperatures near the estimated θ-temperature of the solution. These observations
strongly support the hypothesis that aromatic residues play a dominant
role for condensation, which is further corroborated by a detailed analysis of the intermolecular

contacts, and conversely that important properties of condensates are captured in coarse-grained simulations. Interestingly, we observe density inhomogeneities within the condensates near criticality, which are driven by electrostatic interactions.
Finally, we find that the relatively small fraction of hydrophobic residues in the IDPs results in interfacial tensions which are significantly lower compared to typical combinations of immiscible simple liquids.

[1] Dignon et al., PLOS Comput. Biol. 14, e1005941 (2018)

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