Molecular entropic forces and scaling laws in chaperone-driven nanofilament unbundling

Miguel Rubi

University of Barcelona, Diagonal 647, Barcelona, Spain

Entropic forces are central to nanoscale phenomena ranging from colloidal self-assembly to biomolecular disaggregation. Here, we combine an exact analytical theory with a coarse-grained computational approach to derive general scaling laws for tether-mediated entropic forces in nanofilament bundles. We find that a single dimensionless parameter, the ratio of excluded-volume radius to tether length, determines whether filaments are pushed apart or, paradoxically, pulled together, challenging the assumption that entropic forces invariably promote disaggregation. Applied to amyloid α-synuclein disaggregation by Hsp70, we identify two classes of entropic effects (intra- and inter-protofilament) and show that only highly efficient chaperone systems, requiring co-chaperone networks and ATP hydrolysis, can overcome the free energy barrier of lateral protofilament association. These results, confirmed by Brownian dynamics simulations and supported by high-speed atomic force microscopy data, offer predictive insights for biophysics, soft matter, nanotechnology, and the design of therapies targeting protein-aggregation diseases.

[1] J. M. G. Vilar, J. M. Rubi, and L. Saiz, "Chaperone-Driven Entropic Separation of Amyloid Nanofilament Bundles," Phys. Rev. X 15, 1 (2025).

[2] J. M. G. Vilar, J. M. Rubi, and L. Saiz, "Scaling Laws and Paradoxical Metastable States in Nanofilament Entropic Separation," J. Chem. Phys. 164, 124905 (2026).