Membrane curvature sensing by model biomolecular condensates

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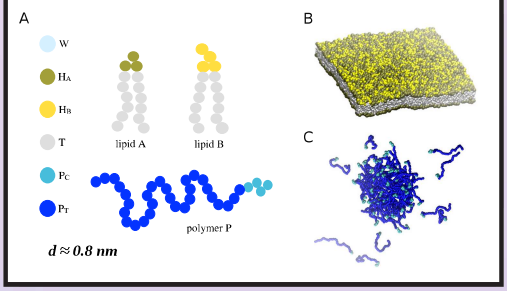
Abstract

Biomolecular condensates (BCs), comprised mainly of intrinsically disordered proteins, form through liquid–liquid phase separation within biological cells. Despite considerable research on BCs in the cytosol and nucleus, their behavior at cellular membranes remains largely unexplored. Galectin-3, a mixed-folded protein consisting of an intrinsically disordered N-terminal domain (NTD) and a carbohydrate recognition domain (CRD), plays pivotal roles in various biological processes such as immune responses, cell migration, and signaling. It has been demonstrated that galectin-3 interacts with glycosphingolipids on the cell membrane, facilitating clathrin-independent endocytosis [1]. Using dissipative particle dynamics (DPD) simulations, we explore how polymer models resembling galectin-3 sense and respond to membrane curvature. Our findings suggest a generic mechanism by which BCs sense membrane curvature, potentially influencing such cellular processes as endocytosis [2].

DPD Model



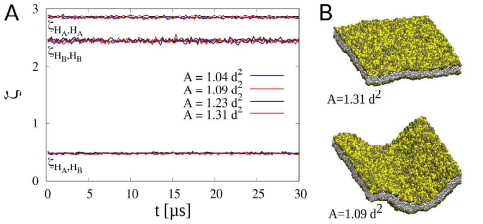
Absence of polymers

Coordination number

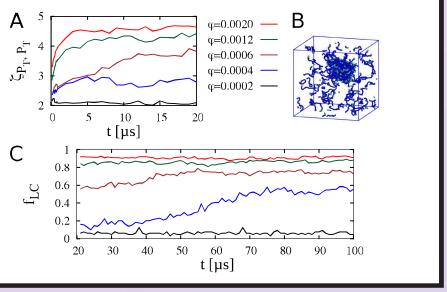
$$\zeta_{X,Y} = \frac{n_{X,Y}}{2(n_X + n_Y)} \quad 1)$$

Projected area per lipid

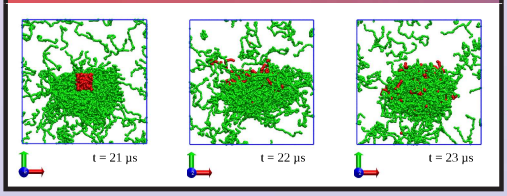
$$A = \frac{2L^2}{N_{\mathrm{lipA}} + N_{\mathrm{lipB}}} \quad 2)$$



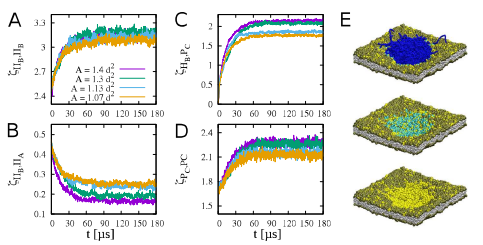
Absence of lipids



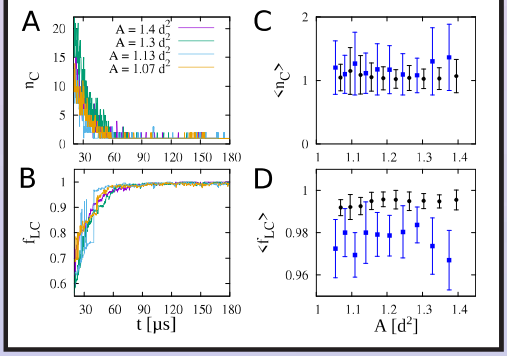
Fluidity of nanodroplets



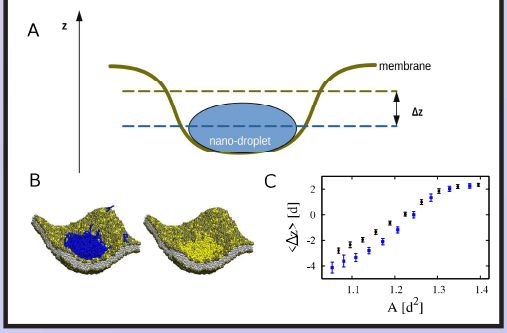
With lipids and polymers



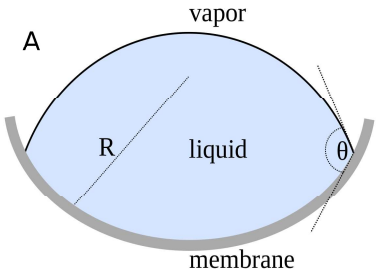
Clusterization of polymers



Immersion depth



Toy-model



Interfacial energy

$$U = A_{\mathrm{lv}}\sigma + A_{\mathrm{lm}}(\sigma_{\mathrm{lm}} - \sigma_{\mathrm{vm}}) = \sigma(A_{\mathrm{lv}} - A_{\mathrm{lm}}\cos\theta) \quad 4)$$

$$\Delta U = U(\theta, r_0/R) - U(\theta, 0) \quad 5)$$

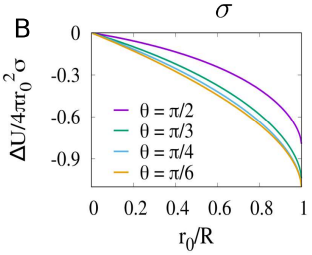
Bending energy

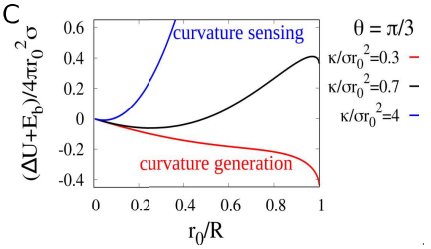
$$E_{\mathrm{b}} = 2\kappa \int M^2 \mathrm{d}A = \frac{2\kappa}{R^2} A_{\mathrm{lm}} \quad 6)$$

Total energy = $\Delta U + E_{\mathrm{b}}$ 7)

Young's equation

$$\cos\theta = \frac{\sigma_{\mathrm{vm}} - \sigma_{\mathrm{lm}}}{\sigma} \quad 3)$$





References

[1] R. Lakshminarayan et al. Nature Cell Biology 16(6), 592-603 (2014).

[2] M. M. Anila et al. Soft Matter 19(20), 3723-3732 (2023).

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Conclusion

Our results of the coarse-grained simulations and analytical calculations indicate together towards a generic mechanism of membrane curvature sensing by biomolecular condensates.