

Peer Review

Review of: "Separation of Sticker–Spacer Energetics Governs the Coalescence of Metastable Condensates"

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In this manuscript, the authors present a computational study on the fusion of polymer droplets, comparing two scenarios: heterotypic polymers and homopolymers. For heterotypic polymers, fusion is dominated by specific interactions, whereas for homopolymers, non-specific interactions play the key role. The authors identify two distinct physical mechanisms underlying droplet fusion. In heterotypic polymers, fusion can be kinetically arrested when specific interactions are strong due to sticker saturation. For homopolymers, a high non-specific energy leads to kinetic arrest caused by an excessively high droplet density. This study is crucial for a deeper understanding of the rich behaviors of bio-condensates.

The manuscript is well written, and I only have some doubts regarding the explanation of entropy in Fig. 5C. As the authors explained: this is not the thermodynamic entropy, and therefore it has different units compared to potential energy $E_{\text{potential}}$. During the fusion process, the potential energy decreases slightly, primarily due to the decrease of E_{contact} as shown in Fig. S11. Essentially, the slight decrease in $E_{\text{potential}}$ also facilitates the fusion process. How can we compare the contributions of energy and entropy, and how can we determine when the contribution of entropy plays a decisive role?

Additionally, in the discussion part, the authors mentioned that the exchangeability of stickers, determined by entropy, is the driving force of fusion. This scenario is akin to the “mixing of two ideal gases,” where entropy drives the gas molecules to explore more volume. However, I am curious: during the fusion of two droplets, the total volume actually decreases. Why, then, is the entropic change due to the transition from intra-cluster bonds to inter-cluster bonds analogous to the case of two ideal gases mixing?

Declarations

Potential competing interests: No potential competing interests to declare.