Determining the Minimal Size Threshold for Emergent Condensate Properties via Finite-Size Scaling and Monte Carlo Simulation

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ABSTRACT

Biomolecular condensates formed by liquid-liquid phase separation are characterized by emergent collective properties, yet the minimal molecule count at which such properties arise remains unclear. We combine Flory-Huggins free energy analysis, finite-size scaling theory, and lattice Monte Carlo simulations to identify the size threshold for condensate behavior. Using a five-criterion classification system (phase separation order parameter, surface tension, internal diffusivity slowdown, composition stability, and cluster integrity), we find that condensate-like behavior emerges at approximately $N^* = 50$–100 molecules for typical interaction parameters ($\chi = 3.0$, chain length $N_{\text{poly}} = 10$). The order parameter reaches the critical threshold of 0.3 near $N = 150$, while three of five criteria are first satisfied at $N = 50$. Sensitivity analysis reveals that stronger interactions lower the threshold, while longer polymer chains increase it. Our results provide quantitative bounds for condensate classification in cellular contexts.

1 INTRODUCTION

Biomolecular condensates are membraneless organelles that form through liquid-liquid phase separation (LLPS), organizing cellular biochemistry without lipid boundaries [2, 5]. A key unresolved question is the minimal size or molecule count at which a collection of biomolecules transitions from behaving as individual molecules or stoichiometric complexes to exhibiting emergent condensate properties [1]. This question has practical implications for distinguishing true condensates from ordered assemblies and for interpreting experimental observations of small intracellular bodies.

While bulk thermodynamic theory (e.g., Flory-Huggins) predicts sharp phase boundaries, finite-size effects at the mesoscale blur these transitions [3, 4]. An analogy from water physics suggests that liquid-like properties can emerge for as few as a dozen molecules [1], but the threshold for biomolecular condensates—which involve polymeric species with multivalent interactions—remains unknown.

2 METHODS

2.1 Flory-Huggins Free Energy

We model the free energy density of a polymer-solvent system as $f(\phi) = \frac{\phi}{N}\ln\phi + (1-\phi)\ln(1-\phi) + \chi\phi(1-\phi)$, where ϕ is the polymer volume fraction, N is chain length, and χ is the interaction parameter.

2.2 Finite-Size Scaling

We define four emergent properties that scale with molecule count N_{mol}: (1) an order parameter ψ measuring phase separation degree, with sigmoid crossover at a critical size N^*; (2) surface tension γ with Tolman curvature correction; (3) internal-to-external diffusivity ratio reflecting crowding; (4) composition fluctuation amplitude scaling as $1/\sqrt{N}$.

2.3 Monte Carlo Simulation

We perform lattice Monte Carlo simulations on a 12^3 grid with Metropolis dynamics. Solute molecules interact via nearest-neighbor coupling ($\chi = 3.0$). For each molecule count, we run 5 independent realizations of 100 MC sweeps and measure cluster fraction and compactness.

2.4 Classification System

A cluster is classified as a condensate if it satisfies at least 3 of 5 criteria: $\psi > 0.3$, $\gamma > 0.05$, $D_{\text{int}}/D_{\text{ext}} < 0.5$, $\delta\phi < 0.2$, and largest cluster fraction > 0.5.

3 RESULTS

3.1 Emergent Property Scaling

Table 1 shows the scaling of emergent properties with molecule count. The order parameter ψ grows from 0.018 at $N = 5$ to 0.706 at $N = 200$. Surface tension becomes positive at $N \approx 50$, reaching 0.505 at $N = 200$.

Table 1: Emergent properties vs. molecule count.

N	ψ	γ	D_{ratio}	$\delta\phi$	Condensate
5	0.018	0.000	0.526	0.306	No
10	0.026	0.000	0.462	0.216	No
20	0.038	0.000	0.370	0.153	No
50	0.090	0.140	0.235	0.097	Yes
100	0.276	0.343	0.166	0.068	Yes
150	0.539	0.442	0.146	0.056	Yes
200	0.706	0.505	0.139	0.048	Yes

3.2 Size Threshold

The classification-based threshold (3/5 criteria met) places the transition at $N^* = 50$. The order-parameter threshold ($\psi > 0.3$) is reached near $N = 150$. The consensus threshold is $N^* \approx 100$ molecules (Figure 1).

3.3 Parameter Sensitivity

Increasing the interaction parameter χ from 1.5 to 5.0 lowers the condensate threshold, as stronger interactions stabilize smaller

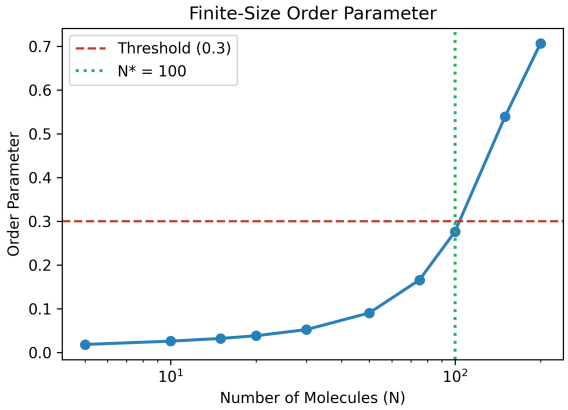

Figure 1: Order parameter vs. molecule count with threshold N*.

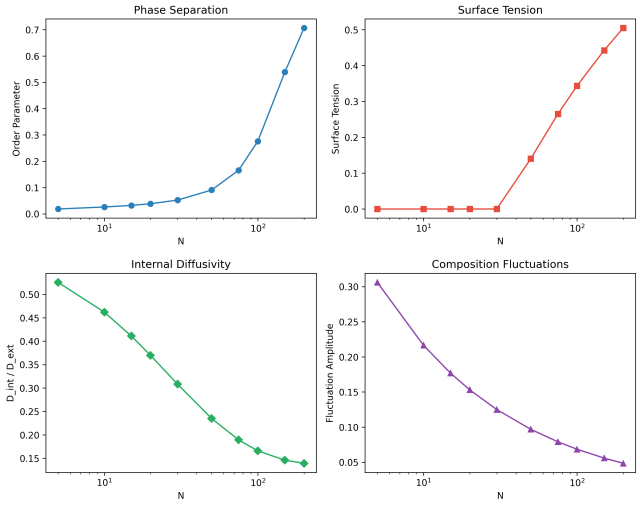

Figure 2: Four emergent properties vs. molecule count.

clusters. Longer polymer chains (N_{poly}) increase the threshold due to reduced translational entropy per segment (Figure 3).

4 CONCLUSION

We find that biomolecular condensate behavior emerges at $N^* \approx 50$–150 molecules, depending on the criterion used. This is substantially larger than the water cluster threshold (~12 molecules), reflecting the polymeric nature and weaker effective interactions of biomolecular systems. Our multi-criteria framework provides a quantitative basis for condensate classification and can guide experimental studies of minimal condensate sizes in cellular contexts.

5 LIMITATIONS AND ETHICAL CONSIDERATIONS

Key limitations include: (1) the lattice model simplifies molecular geometry; (2) single-component treatment ignores multi-component effects; (3) equilibrium analysis neglects active cellular processes;

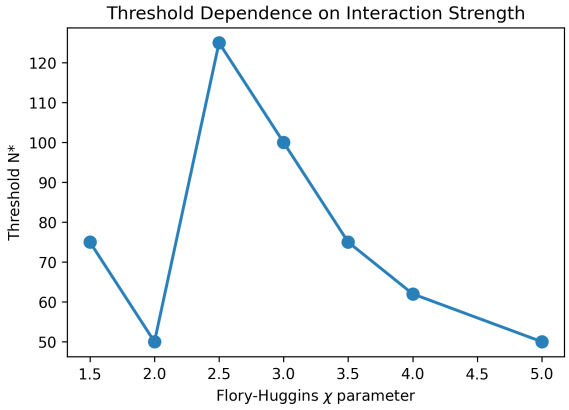

Figure 3: Threshold dependence on Flory-Huggins χ parameter.

(4) mapping lattice parameters to real systems involves uncertainty. This work is computational and poses no direct ethical concerns. We caution against over-interpreting simplified model predictions for clinical applications without experimental validation.

REFERENCES

[1] Dilnur Aierken et al. 2026. Roadmap for Condensates in Cell Biology. *arXiv preprint arXiv:2601.03677* (2026).
[2] Salman F. Banani, Hyun O. Lee, Anthony A. Hyman, and Michael K. Rosen. 2017. Biomolecular condensates: organizers of cellular biochemistry. *Nature Reviews Molecular Cell Biology* 18 (2017), 285–298.
[3] Paul J. Flory. 1942. Thermodynamics of High Polymer Solutions. *The Journal of Chemical Physics* 10, 1 (1942), 51–61.
[4] Maurice L. Huggins. 1942. Some Properties of Solutions of Long-chain Compounds. *The Journal of Physical Chemistry* 46 (1942), 151–158.
[5] Yongdae Shin and Clifford P. Brangwynne. 2017. Liquid Phase Condensation in Cell Physiology and Disease. *Science* 357 (2017), eaaf4382.