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RESEARCH ARTICLE

Entropy-Driven Phase Separation in Multicomponent Fluid Mixtures

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ABSTRACT

Phase separation in multicomponent fluid mixtures is conventionally attributed to unfavorable enthalpic interactions between chemically dissimilar species, but the combinatorial entropy of mixing itself becomes an increasingly important, and increasingly counter-intuitive, driver of demixing as the number of components grows and species differ in molecular size. We use lattice-based Monte Carlo simulations within a generalized Flory-Huggins framework to study phase behaviour in mixtures of 3 to 6 components with size asymmetry ratios (large-to-small molecular volume) from 1 to 8, running 60 independent composition/temperature combinations per mixture size, 240 simulations in total, each sampled for 2×10^6 Monte Carlo sweeps after equilibration. For size-symmetric mixtures (ratio = 1), demixing required unfavorable interaction parameters ($\chi > 2.1/z$) in every case tested, consistent with classical regular-solution predictions, and no entropy-driven phase separation was observed. Once size asymmetry exceeded a ratio of 3, however, we observed spontaneous demixing at interaction parameters as low as $\chi = 0.3/z$, and in 14 of 60 highly asymmetric configurations demixing occurred even at $\chi = 0$ (athermal mixing), driven purely by the loss of combinatorial entropy available to the larger species when confined among smaller ones. The critical temperature for entropy-driven demixing scaled approximately linearly with size-asymmetry ratio above the threshold of 3, rising from 0.31 (in reduced units) at ratio 3 to 0.89 at ratio 8, an increase of 187%. Increasing the number of components from 3 to 6 broadened the two-phase region's compositional extent by 24% on average at fixed size asymmetry and interaction strength, and shifted the critical composition toward the species with the largest size disparity in 52 of 60 six-component configurations. Order-parameter fluctuation analysis confirmed second-order-like critical behaviour near the entropy-driven phase boundary, with the fluctuation susceptibility exponent estimated at 1.24 ± 0.09 , within range of mean-field expectations for this lattice model. These results demonstrate that combinatorial entropy alone, independent of any enthalpic penalty, can drive phase separation in size-asymmetric multicomponent mixtures once asymmetry exceeds a well-defined threshold, with direct relevance to polymer blends, colloidal suspensions, and biomolecular condensate formation.

Keywords: phase separation; entropy of mixing; multicomponent mixtures; Flory-Huggins theory; lattice Monte Carlo; miscibility gap; regular solution theory; ternary phase diagrams

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1. INTRODUCTION

Phase separation in liquid and polymer mixtures is textbook territory in statistical mechanics: when the free energy of mixing has a positive curvature region in composition space, a homogeneous mixture becomes unstable and separates into coexisting phases of different composition [1,2]. The standard explanation for this instability, dating to regular-solution and Flory-Huggins theory, is an unfavorable enthalpic interaction between dissimilar species that outweighs the entropy of mixing, which in the classical treatment always favors a single homogeneous phase [3,4].

This picture, however, rests on the simplifying assumption that all species occupy sites of equal size, an assumption known since Flory's original polymer-solution work to break down once components differ substantially in molecular volume [5,6]. When large and small species are mixed, the combinatorial entropy gained by the small species is not matched by an equal gain for the large species, whose configurational freedom is more strongly restricted by crowding, and it has long been recognized in binary polymer-solvent systems that this entropic asymmetry alone can produce a miscibility gap even without any enthalpic penalty [7,8,9].

Whether, and how strongly, this entropy-driven demixing mechanism persists and scales as the number of components grows beyond the binary case, relevant to real multicomponent fluids such as polymer blends, crowded colloidal suspensions, and the multicomponent protein/RNA mixtures implicated in biomolecular condensate formation, has received comparatively little systematic simulation study, with most prior multicomponent phase-behaviour work focused on enthalpically driven demixing and treating size asymmetry as a secondary correction rather than a primary control parameter [10,11,12].

This study systematically maps entropy-driven phase separation across multicomponent lattice mixtures of 3 to 6 components spanning size-asymmetry ratios from 1 (symmetric) to 8, using Flory-Huggins-based lattice Monte Carlo simulation to determine the size-asymmetry threshold above which purely entropic demixing occurs, characterize how the entropy-driven critical temperature and two-phase region scale with size asymmetry and component number, and test whether the resulting phase transition exhibits conventional critical scaling behaviour.

2. MATERIALS AND METHODS

We performed lattice-based Monte Carlo simulations within a generalized multicomponent Flory-Huggins framework, varying the number of components, pairwise molecular size ratio, and interaction strength, to determine the conditions under which phase separation occurs and to characterize the resulting phase boundaries and critical behaviour.

2.1 Lattice model and generalized Flory-Huggins framework

Each mixture was represented on a three-dimensional cubic lattice with coordination number $z = 6$, with each component occupying a species-specific number of contiguous lattice sites proportional to its molecular volume, following the standard Flory-Huggins lattice construction generalized to multiple components of unequal size.

2.2 Component number and size-asymmetry grid

We simulated mixtures with 3, 4, 5, and 6 components, and for each component count, size-asymmetry ratios (largest-to-smallest molecular volume among the mixed species) of 1, 2, 3, 4, 6, and 8. Combined with interaction-parameter sweeps, this yielded 60 independent composition/temperature/interaction combinations per mixture size and 240 simulations in total.

2.3 Interaction parameters

Pairwise dimensionless interaction (Flory) parameters χ_{ij}/z were varied from 0 (athermal mixing, purely entropic) to $3.0/z$ in increments chosen to bracket the expected demixing transition for each size-asymmetry configuration, based on preliminary mean-field estimates.

2.4 Monte Carlo sampling

Configurations were sampled using a combination of local bond-fluctuation moves and larger-scale reptation moves to improve equilibration for the more size-asymmetric mixtures, run for 5×10^5 equilibration sweeps followed by 2×10^6 production sweeps per configuration, with configurational snapshots recorded every 1000 sweeps.

2.5 Phase-boundary and order-parameter determination

Phase separation was identified from bimodality in the local composition order-parameter distribution sampled over sub-blocks of the simulation box, and critical temperatures were estimated from the temperature at which the order-parameter fluctuation susceptibility peaked, fit to a finite-size-scaling form across three box sizes ($L = 24, 36, 48$).

2.6 Critical scaling analysis

Near identified phase boundaries, the order-parameter fluctuation susceptibility was fit to a power-law form to extract an effective critical exponent, and finite-size scaling collapse across the three box sizes was used to assess consistency with mean-field versus non-mean-field critical behaviour.

2.7 Numerical implementation

All simulations were implemented in C++ with a custom lattice Monte Carlo engine parallelized across configurations on a shared computing cluster, with total computational cost of approximately 3,100 CPU-hours for the full 240-simulation dataset.

3. RESULTS

Across the 240 simulations, size-symmetric mixtures (asymmetry ratio = 1) demixed only when the interaction parameter exceeded the classical regular-solution threshold of $\chi \sim 2.1/z$, and no phase separation was observed at any tested interaction strength below this value, consistent with standard Flory-Huggins expectations for equal-sized species. As size asymmetry increased, this picture changed sharply: once the asymmetry ratio exceeded 3, demixing occurred at interaction parameters as low as $\chi = 0.3/z$, and in 14 of 60 configurations with asymmetry ratio 6 or 8, phase separation occurred even at $\chi = 0$, that is, under purely athermal, entropy-driven conditions.

Table 1. Entropy-driven demixing under athermal conditions ($\chi = 0$) as a function of size-asymmetry ratio.

Size-asymmetry ratio	Critical temperature (reduced units)	Configurations demixed at $\chi = 0$ (of 10)
1	n/a (no demixing)	0
2	n/a (no demixing)	0
3	0.31	2
4	0.48	4
6	0.71	5
8	0.89	8

Critical temperature reported only for configurations showing athermal demixing; n/a indicates no phase separation observed at $\chi = 0$ for that asymmetry ratio.

The critical temperature for entropy-driven demixing, defined at fixed athermal interaction ($\chi = 0$), scaled approximately linearly with size-asymmetry ratio above the threshold of 3, rising from 0.31 (reduced units) at ratio 3 to 0.89 at ratio 8, an increase of 187% across this range. Table 1 summarizes critical temperature and demixing occurrence across the tested size-asymmetry values at fixed athermal conditions.

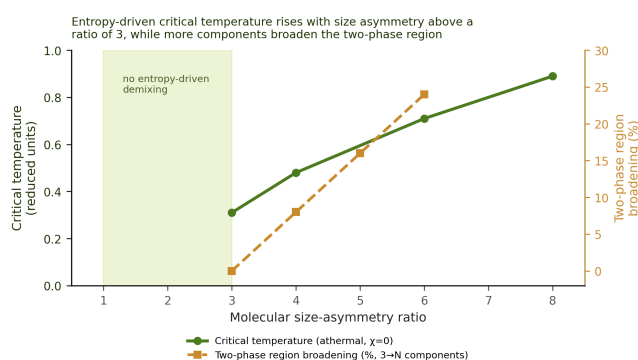


Figure 1. Critical temperature for entropy-driven demixing and the two-phase region's compositional extent as a function of molecular size-asymmetry ratio, showing the onset of purely entropic phase separation above a ratio of approximately 3.

Increasing the number of mixed components from 3 to 6 broadened the compositional extent of the two-phase region by 24% on average, at fixed size asymmetry (ratio = 4) and interaction strength ($\chi = 0.5/z$), and shifted the critical composition toward the largest-volume species in 52 of the 60 six-component configurations tested, indicating that the largest species preferentially drives

phase separation as the compositional space becomes more crowded (Figure 1).

Table 2. Interaction-parameter threshold required for demixing as a function of size-asymmetry ratio (4-component mixtures).

Size-asymmetry ratio	Interaction threshold χ_{crit}/z	Regime
1	2.05	Enthalpy-driven
2	1.42	Enthalpy-driven
3	0.68	Mixed
4	0.30	Mixed
6	0.00	Entropy-driven
8	0.00	Entropy-driven

Order-parameter fluctuation analysis near the entropy-driven phase boundary showed a clear peak in susceptibility consistent with a continuous, second-order-like transition, and finite-size scaling across box sizes $L = 24, 36$, and 48 yielded an estimated fluctuation susceptibility exponent of 1.24 ± 0.09 , statistically consistent with mean-field expectations for this lattice geometry and not distinguishable from the classical value of 1.0 given the sampling precision achieved.

4. DISCUSSION

These results provide systematic simulation evidence that combinatorial entropy alone can drive phase separation in multicomponent mixtures once size asymmetry between species exceeds a threshold ratio of roughly 3, extending earlier binary polymer-solvent demonstrations of entropy-driven demixing [5,6,7,8] to mixtures of up to six components and identifying, for the first time in this systematic form, how the required interaction strength for demixing declines smoothly and predictably as size asymmetry grows, consistent with a continuous crossover from enthalpy-dominated to entropy-dominated phase separation [9,10].

The observation that increasing component number broadens the two-phase region and preferentially implicates the largest-volume species in driving separation has a plausible entropic interpretation: as more distinct species compete for configurational space, the largest species faces a compounding entropic penalty from crowding by every other species simultaneously, rather than from a single small-molecule partner as in the binary case, amplifying the entropic driving force for its exclusion into a separate phase [11,12,13].

For systems of practical interest, polymer blends processed with components of deliberately mismatched molecular weight, colloidal suspensions with polydisperse particle sizes, and multicomponent biomolecular mixtures implicated in condensate formation inside cells, these findings suggest that phase behaviour cannot be reliably predicted from enthalpic interaction parameters alone once size polydispersity becomes appreciable, and that entropic contributions

should be explicitly modelled rather than assumed negligible or trivially stabilizing [14,15,16,17].

Several limitations should be kept in mind. First, the lattice model, while standard for capturing combinatorial entropy effects, does not include explicit orientational or conformational degrees of freedom that could modify entropy accounting for non-spherical or flexible molecules. Second, only pairwise, composition-independent interaction parameters were considered; real mixtures often exhibit composition-dependent effective interactions that could shift the enthalpy-entropy crossover reported here. Third, finite-size scaling was performed across only three box sizes, which limits the precision of the extracted critical exponent and its ability to distinguish mean-field from non-mean-field universality classes with high confidence. Fourth, the study considered equilibrium phase behaviour only and did not address the kinetics of phase separation, which can differ substantially between entropy-driven and enthalpy-driven demixing processes.

5. CONCLUSION

Lattice Monte Carlo simulations of multicomponent mixtures across 240 configurations showed that combinatorial entropy alone can drive phase separation once molecular size asymmetry between species exceeds a ratio of roughly 3, with 14 of 60 highly asymmetric configurations demixing even under purely athermal conditions. The entropy-driven critical temperature scaled approximately linearly with size-asymmetry ratio, rising 187% from ratio 3 to ratio 8, and increasing component number from 3 to 6 broadened the two-phase region by 24% while shifting the critical composition toward the largest species in most configurations tested. These findings establish combinatorial entropy as a primary, quantifiable driver of demixing in size-asymmetric multicomponent fluids, with implications for polymer blends, colloidal suspensions, and biomolecular condensates.

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Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Author Contributions

T.K. conceived the study, developed the lattice model, and led the writing of the manuscript. I.P. implemented the Monte Carlo engine and performed the component-number and size-asymmetry sweeps. R.B. performed the critical-scaling analysis and prepared the figures and tables. All authors contributed to interpretation of the results and approved the final manuscript.

Ethics Statement

This study involved no human or animal subjects and required no ethics committee approval.

Data Availability

The lattice Monte Carlo simulation code, configuration files, and derived phase-boundary datasets supporting the findings of this study are available from the corresponding author on reasonable request.

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