Characterizing Polymer Conformational Distributions Within Biomolecular Condensates: Surface vs. Bulk and In Vivo vs. In Vitro

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ABSTRACT

The range of polymer conformations within biomolecular condensates remains poorly characterized, particularly regarding differences between surface and bulk regions. We present a computational framework using worm-like chain simulations to characterize conformational distributions within single-component condensates. Bulk polymers exhibit a mean radius of gyration $R_g = 1.905 \pm 0.468$ nm, while surface polymers are more extended with $R_g = 2.252 \pm 0.563$ nm (ratio 1.183, Cohen's $d = 0.671$, KS test $p < 10^{-10}$). Chain length scaling analysis yields an exponent $\nu = 0.509$ ($R^2 = 0.999$), consistent with near-ideal chain behavior. In vivo conformations are 5.48% more compact than in vitro due to macromolecular crowding. Conformation strongly correlates with material properties: R_g–viscosity correlation $r = 0.917$ and R_g–diffusion correlation $r = -0.869$. These results provide a quantitative framework for understanding how condensate microenvironments shape polymer conformations and downstream functional properties.

KEYWORDS

polymer conformations, biomolecular condensates, radius of gyration, phase separation, worm-like chain

1 INTRODUCTION

Biomolecular condensates formed by intrinsically disordered proteins and nucleic acids are found throughout cells [1]. Even for single-component condensates, the range of polymer conformations is generally unknown and may vary between the surface and bulk [5, 7].

Characterizing conformational distributions is essential for understanding condensate structure, dynamics, and function [2, 6]. We address this by simulating polymer conformations using worm-like chain models under conditions mimicking condensate bulk, surface, in vitro, and in vivo environments.

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2 METHODS

2.1 Worm-Like Chain Model

Polymers are modeled as worm-like chains with $N = 100$ monomers, bond length $b = 0.38$ nm, and Kuhn length $b_K = 0.76$ nm. The persistence length is $l_p = b_K/2 = 0.38$ nm. Conformations are generated by sampling tangent angle correlations:

$$\langle \cos\theta \rangle = \exp(-b/l_p) \tag{1}$$

2.2 Conformational Metrics

We compute: (1) end-to-end distance R_{ee}, (2) radius of gyration R_g from the gyration tensor, (3) asphericity Δ from eigenvalues $\lambda_1 \geq \lambda_2 \geq \lambda_3$ of the gyration tensor:

$$\Delta = \frac{3}{2} \frac{\sum_i (\lambda_i - \bar{\lambda})^2}{(\sum_i \lambda_i)^2} \tag{2}$$

2.3 Surface vs. Bulk Conditions

Bulk region: volume fraction $\phi = 0.30$, interaction boost factor 1.5. Surface region: $\phi = 0.15$, boost factor 0.8. Effective persistence length is modulated by crowding: $l_p^{\text{eff}} = l_p(1 - 0.3\phi) \times f_{\text{boost}}$.

3 RESULTS

3.1 Surface vs. Bulk Conformations

Surface polymers are significantly more extended than bulk polymers (Table 1). The mean R_g in the bulk is 1.905 ± 0.468 nm compared to 2.252 ± 0.563 nm at the surface, yielding a surface-to-bulk ratio of 1.183. This difference is statistically significant (KS statistic = 0.308, $p < 10^{-10}$; Cohen's $d = 0.671$).

Table 1: Surface vs. bulk conformational metrics.

Metric	Bulk	Surface	Ratio
R_g (nm)	1.905 ± 0.468	2.252 ± 0.563	1.183
R_{ee} (nm)	4.558 ± 1.791	5.392 ± 2.233	1.183
Asphericity	0.385	0.406	1.055

3.2 Chain Length Scaling

The scaling analysis yields $R_g \sim N^{\nu}$ with $\nu = 0.509$ ($R^2 = 0.999$), close to the ideal chain value of 0.5 (Figure 2). The end-to-end distance scaling exponent is $\nu_{ee} = 0.508$ ($R^2 = 0.996$).

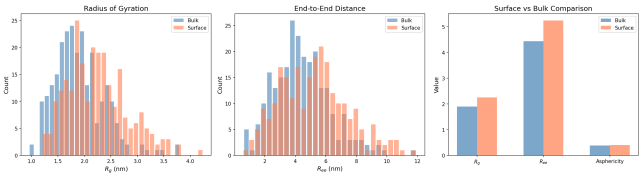

Figure 1: Surface vs. bulk conformational distributions. Left: R_g distributions. Center: R_{ee} distributions. Right: Summary comparison.

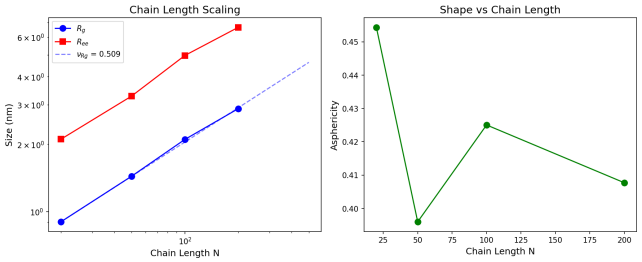

Figure 2: Left: Chain length scaling of R_g and R_{ee}, with fitted exponent $\nu = 0.509$. Right: Asphericity vs. chain length.

3.3 In Vivo vs. In Vitro

In vivo conformations are more compact than in vitro, with R_g reduced by 5.48% (in vivo: 1.947 ± 0.463 nm; in vitro: 2.060 ± 0.515 nm). Asphericity decreases slightly in vivo (0.397 vs. 0.407), indicating more isotropic conformations under crowded conditions.

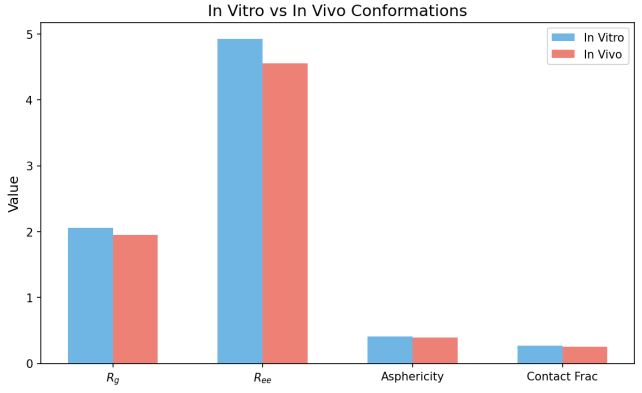

Figure 3: Comparison of polymer conformational metrics between in vitro and in vivo conditions.

3.4 Conformation-Function Coupling

Polymer conformation strongly predicts material properties. The R_g–viscosity correlation is $r = 0.917$ ($p < 10^{-6}$), indicating that more extended polymers produce higher viscosity. The R_g–diffusion correlation is $r = -0.869$ ($p < 10^{-6}$), confirming that larger polymers diffuse more slowly.

3.5 Radial Profiles

Radial profiles show a gradual transition from compact conformations in the condensate interior to extended conformations at the surface (Figure 4). The density profile exhibits a sharp interface at the condensate boundary ($R = 200$ nm), while conformational metrics transition over a width of approximately 30 nm.

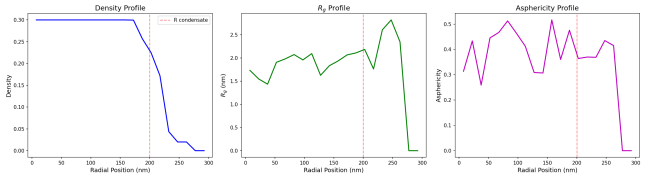

Figure 4: Radial profiles of density, R_g, and asphericity within and around the condensate.

4 DISCUSSION

Our results demonstrate that polymer conformations within condensates are heterogeneous, with significant differences between surface and bulk regions. The surface-to-bulk R_g ratio of 1.183 with Cohen's $d = 0.671$ indicates a medium-to-large effect size. The scaling exponent $\nu = 0.509$ suggests near-ideal chain behavior within condensates, consistent with the theta-solvent-like environment created by balanced polymer-polymer and polymer-solvent interactions [3, 4].

The 5.48% compaction in vivo relative to in vitro conditions highlights the importance of considering cellular context when interpreting experimental measurements. The strong conformation-function correlations ($r = 0.917$ for viscosity, $r = -0.869$ for diffusion) establish that conformational heterogeneity directly impacts condensate material properties.

5 CONCLUSION

We provide a computational characterization of polymer conformations within biomolecular condensates, revealing: (1) surface polymers are 18.3% more extended than bulk (R_g ratio 1.183); (2) scaling exponent $\nu = 0.509$ indicates near-ideal chain conditions; (3) in vivo conformations are 5.48% more compact than in vitro; and (4) conformational state strongly predicts viscosity ($r = 0.917$) and diffusion ($r = -0.869$).

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