

Molecular Simulation of the Shape Deformation of a Polymersome

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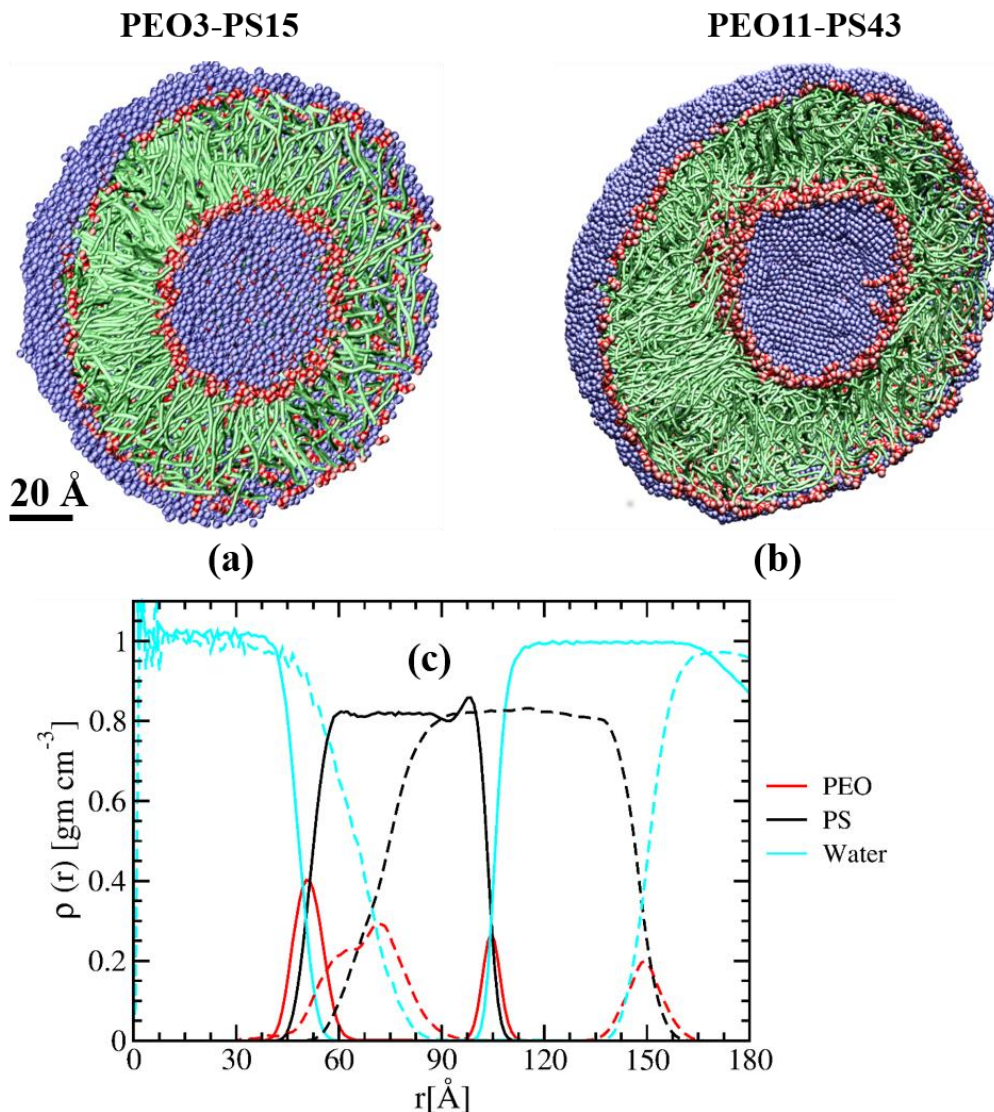
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Properties of Polymersome

Structural Properties

The final configurations of smaller PEO₃-PS₁₅ and PEO₁₁-PS₄₃ polymersomes are shown in **SI 1(a)** and **(b)** respectively. From the snapshots it is clear that both the polymersomes remain stable



SI 1. (a) Snapshots of PEO₃-PS₁₅ and PEO₁₁-PS₄₃ polymersome after 100 ns. PEO is pink, PS is green. Water within 10 Å from the polymersome are shown in blue. (b) The density profile of PEO, PS, and water from the center of mass of the polymersome averaged over last 90 ns. Data for PEO₃-PS₁₅ and PEO₁₁-PS₄₃ are shown in solid and dotted lines respectively.

during simulation. In contrast to the PEO₃-PS₁₅ membrane, the polymers in the hydrophobic core of both the polymersomes are highly entangled. The average density of PEO, PS, and water over last 90 ns from the center of mass of the polymersomes is included in **SI 1 C**. Density profiles reveal many interesting structural features. First of all, irrespective of chain length, PEO density in the outer membrane leaflet is lower than the inner leaflet, due to the differences in the mean curvature of the interfaces, in particular due to the small radius of this initial polymersome conformation. However, experimental characterization of the scaling of the PEO brush length by SAXS and TEM has shown for much longer PEO-poly(butylene oxide)(PBO) copolymers, the PEO brush is symmetric and scales linearly with PEO length. Thus, the initial configuration of polymers in the outer and inner leaflet will need to be optimized further. But, recently Keyes *et al.*¹ explored the packing of lipid molecules in lipid wrapped nanoparticles computationally. Like us, they also found that the smaller vesicles are asymmetric. The outer leaflet of small vesicle contains more lipid molecules than the inner one. Temperature induced shape change of polymersome from symmetric to asymmetric is also reported previously²⁻³. It can be further seen from the figure that with increasing polymer chain length both core size and overall radius of the polymersome also increases simultaneously. For instance, while the average core and overall radius of PEO₃-PS₁₅ polymersome are 50 Å and 110 Å respectively, in the case of PEO₁₁-PS₄₃ these values are 60 Å and 150 Å. Similarly, the width of the hydrophobic core (d) also increases with increasing polymer chain length keeping a localized density of PS around 0.8 g/cm⁻³. The average d values for two different polymersomes are shown in **Table-2**. The Corresponding data for bilayers are also included in the table for comparison. Notably, for PEO₁₁-PS₄₃, the hydrophobic core radii of both bilayer and polymersome are quite similar to each other. In contrast, d is significantly lower for the PEO₃-PS₁₅ polymersome than the corresponding membrane due to

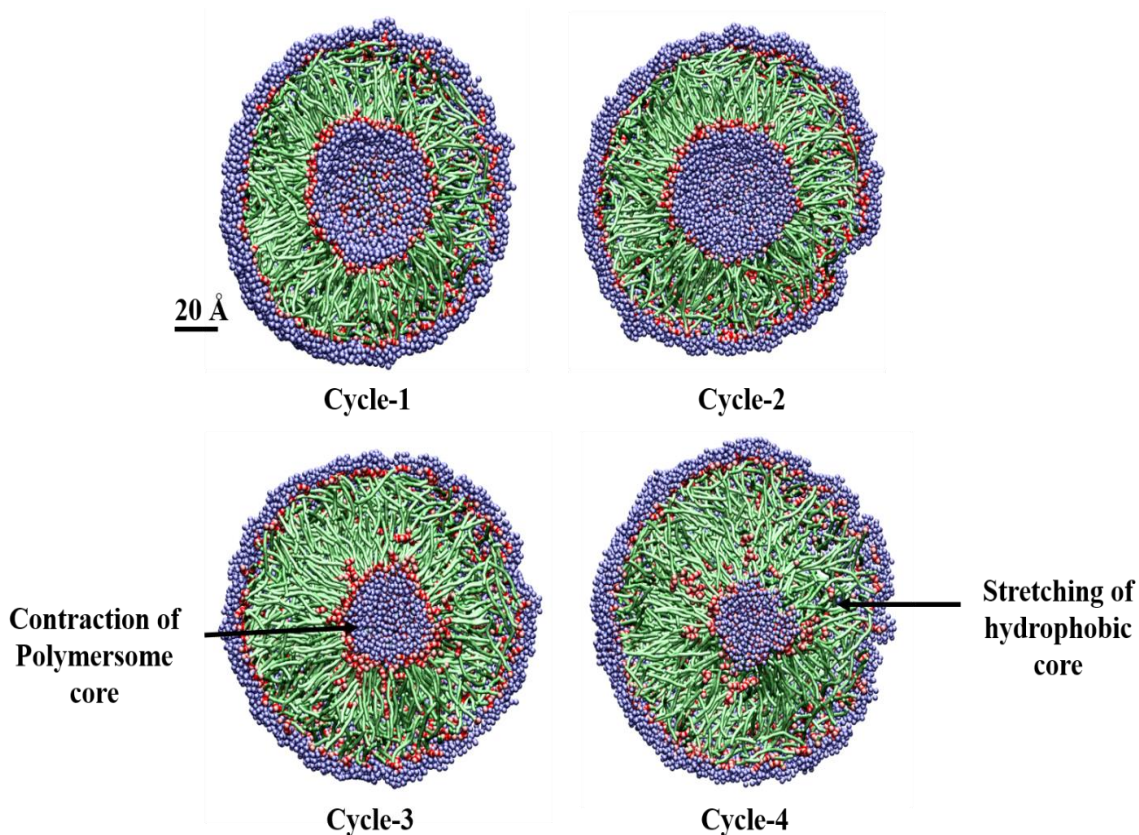
minimum overlap between its two leaflets. In the polymersome, the polymers are entangled with each other, with much more overlap between the outer and inner leaflets. As a result, the hydrophobic core radius decreases in the PEO₃-PS₁₅ polymersome compared to the membrane.

SI Table 1: Average width of the hydrophobic core (d) of the PEO-PS self-assemblies

Chain Length	d [Å]	
	Membrane	Polymersome
PEO3-PS15	75.2 (± 2.3)	45.0 (± 0.99)
PEO11-PS43	70.8 (± 0.9)	67.4 (± 4.5)

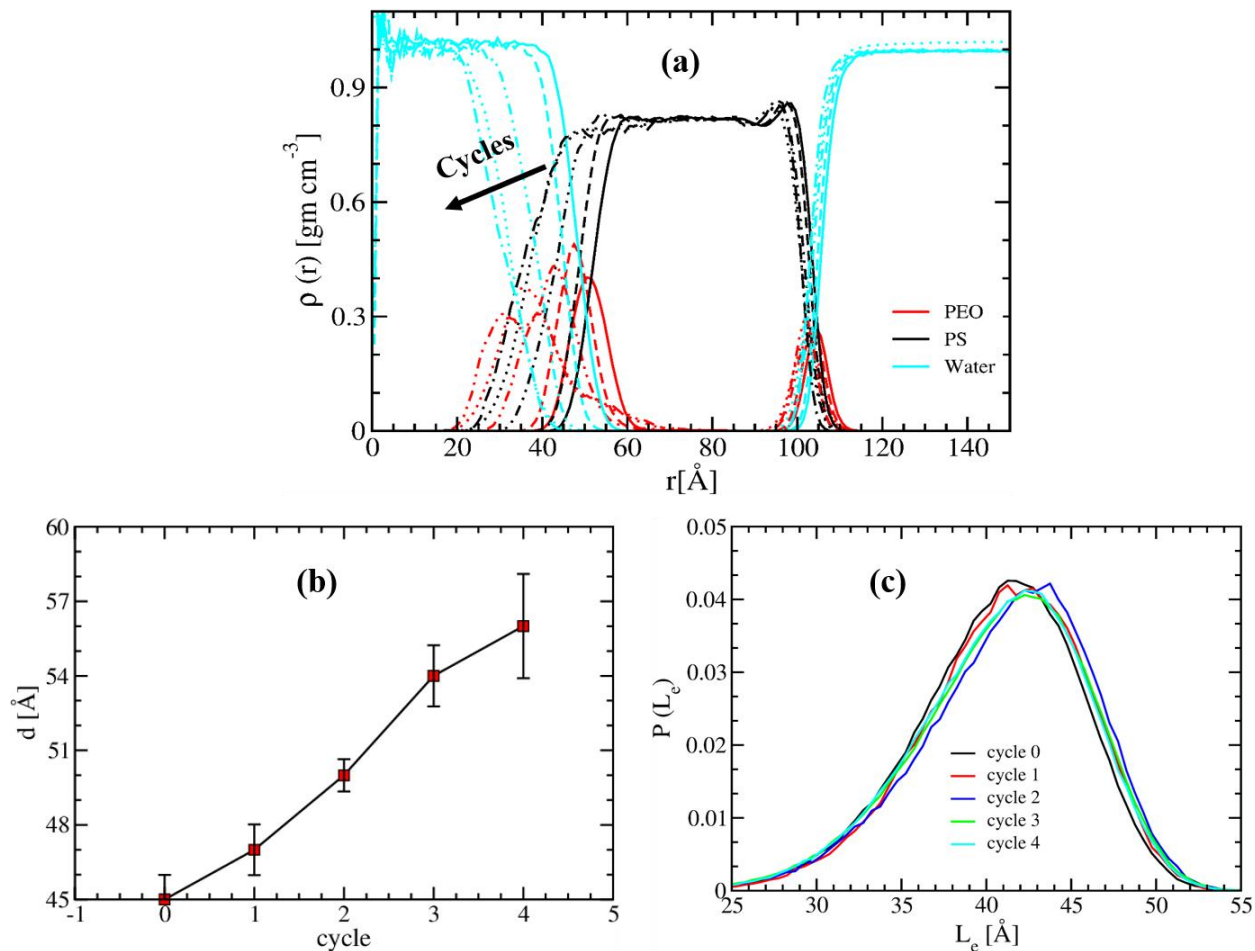
Solvent Induced Shape Change

To mimic the diffusion of THF molecules from the inside to outside of the polymersome, we take the final structure of the polymersome after 100 ns simulation time, then randomly select for water within 10 Å of the inner hydrophobic core, place those water molecules at least 20 Å away from the outer radius of the polymersome and equilibrate for 30 ns until the inner hydrophobic core radius is fixed, and next repeat the cycle. Four cycles (Cycle 1, Cycle 2, Cycle 3, and Cycle 4) are performed so far. The final snapshot after each cycle is shown in **SI 2**. From the figure it is clear that the radius of the inner hydrophobic core contracts after each cycle and substantially after Cycle



SI 2. Snapshot of the smaller PEO₃-PS₁₅ polymersome after Cycle1, Cycle 2, Cycle 3 and Cycle 4. PEO is silver and red, PS is green. Water within 10 Å from the polymersome are shown in blue.

3. Furthermore, the contraction after Cycle 3 indicates that the contraction of the inner core radius is anisotropic. This reveals that shape deformation of polymersomes could propagate starting from the inner core. Apart from the contraction of the inner core, the snapshots also demonstrate the

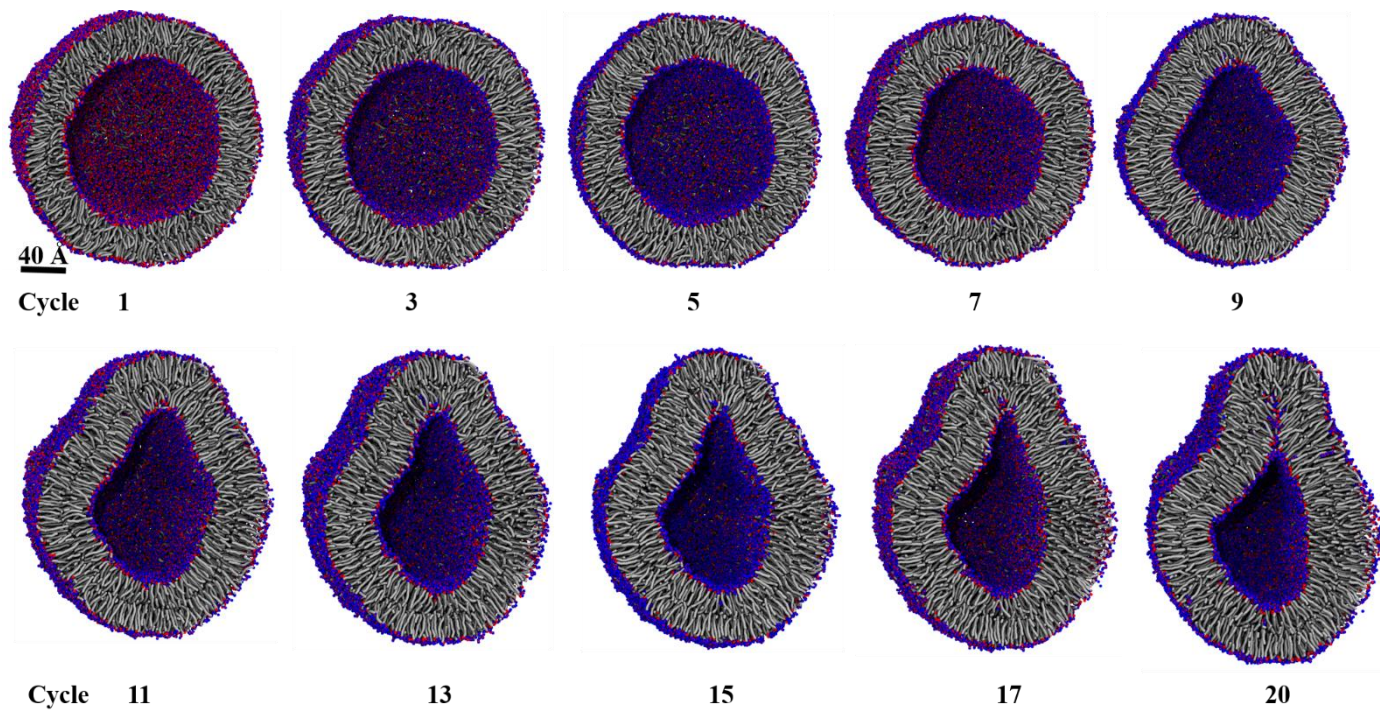


SI 3. Density profile of PEO, PS, and water from the center of mass of the smaller PEO₃-PS₁₅ polymersome after 50 ns (solid line), 10 ns of water dehydration-Cycle 1 (dashed line), another 10 ns of water dehydration-Cycle 2 (dot-dashed line), another 10 ns of water dehydration-Cycle 3 (dotted line) and another 10 ns of water dehydration-Cycle 4 (dash-dotted line). The inner radius of the PEO contracts and spreads out. (b) Variation of hydrophobic core radius during different water dehydration-Cycle. (c) Distribution of end-to-end distance (P_{L_c}) of each polymer during different water dehydration-Cycle.

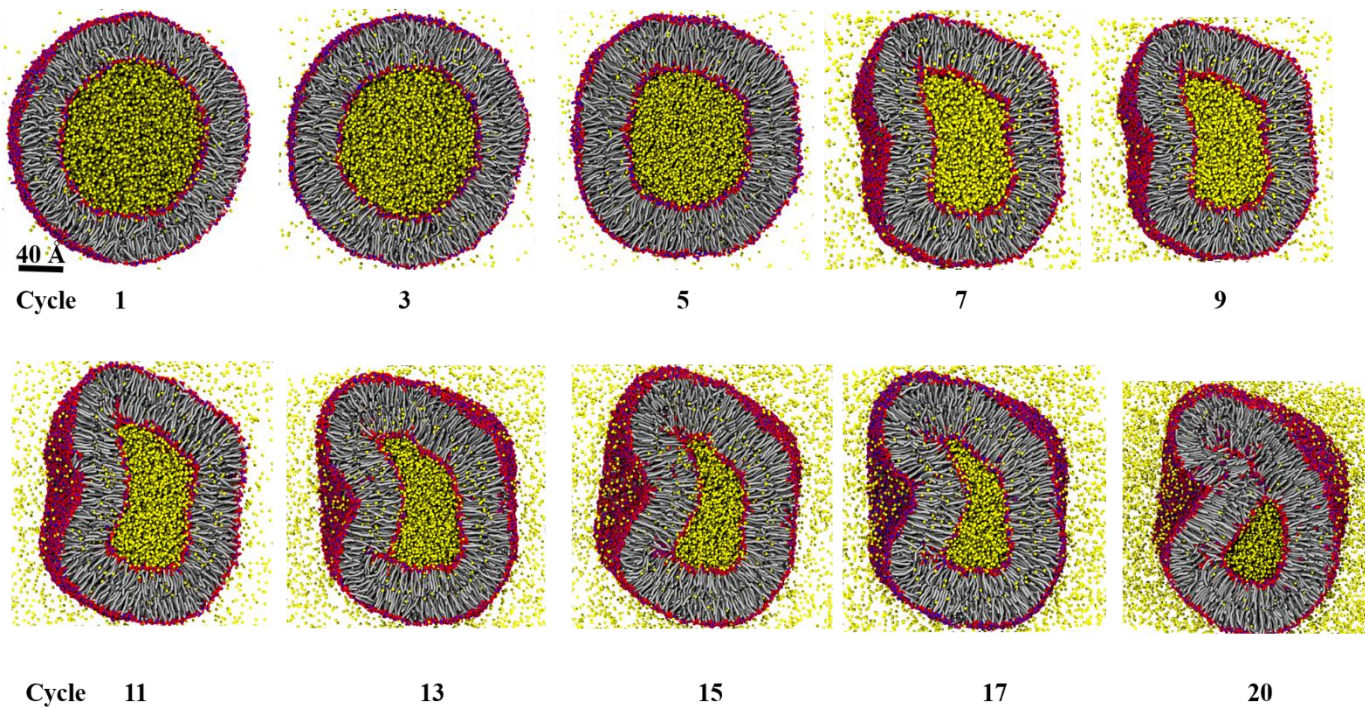
stretching of the hydrophobic core of the polymersome due to diffusion of solvent molecules from the inner core.

Next, to explore the structural changes of the polymersome during different cycles, we compute the density profiles of both polymers and water molecules from the center of the polymer assemblies, as shown in **SI 3 (a)**. Contraction of the inner core is again clearly visible from the density profile. The figure also suggests that while inner core starts to shrink, the position of the

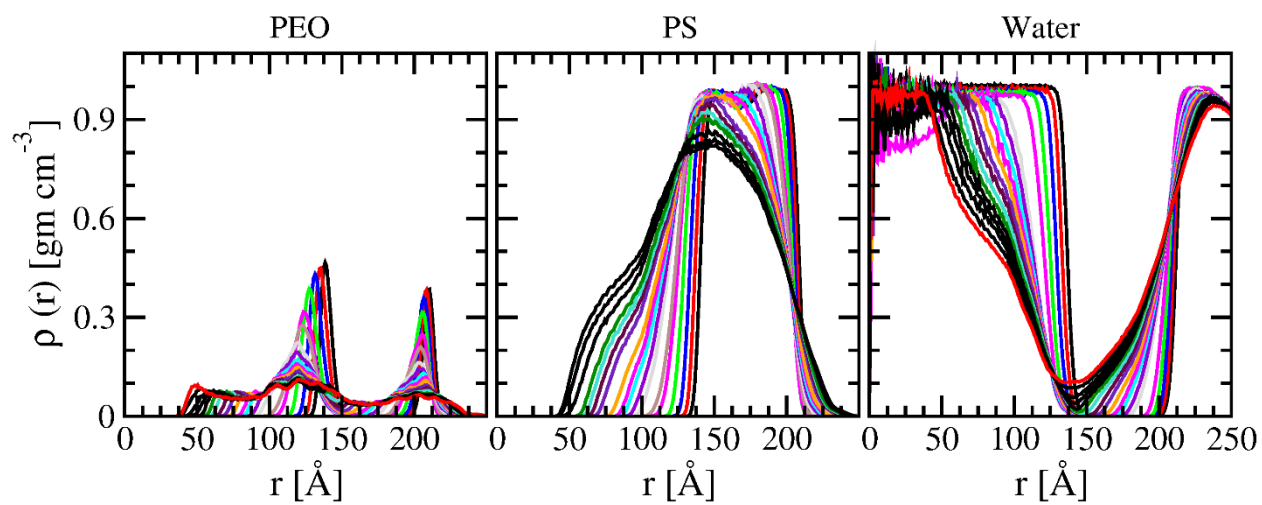
outer leaflet remains almost the same (anisotropic contraction) and it is only possible when hydrophobic core began to expand. Variation of the hydrophobic core width during different cycles is shown in **SI 3(b)**. Stretching of the hydrophobic core is also evident from the distributions of the end-to-end (P_{Le}) distances of the PEO-PS polymers, as shown in **SI 3(c)**. Hence, due to stretching of the individual polymers, the inner core of the polymersome can contract anisotropically.



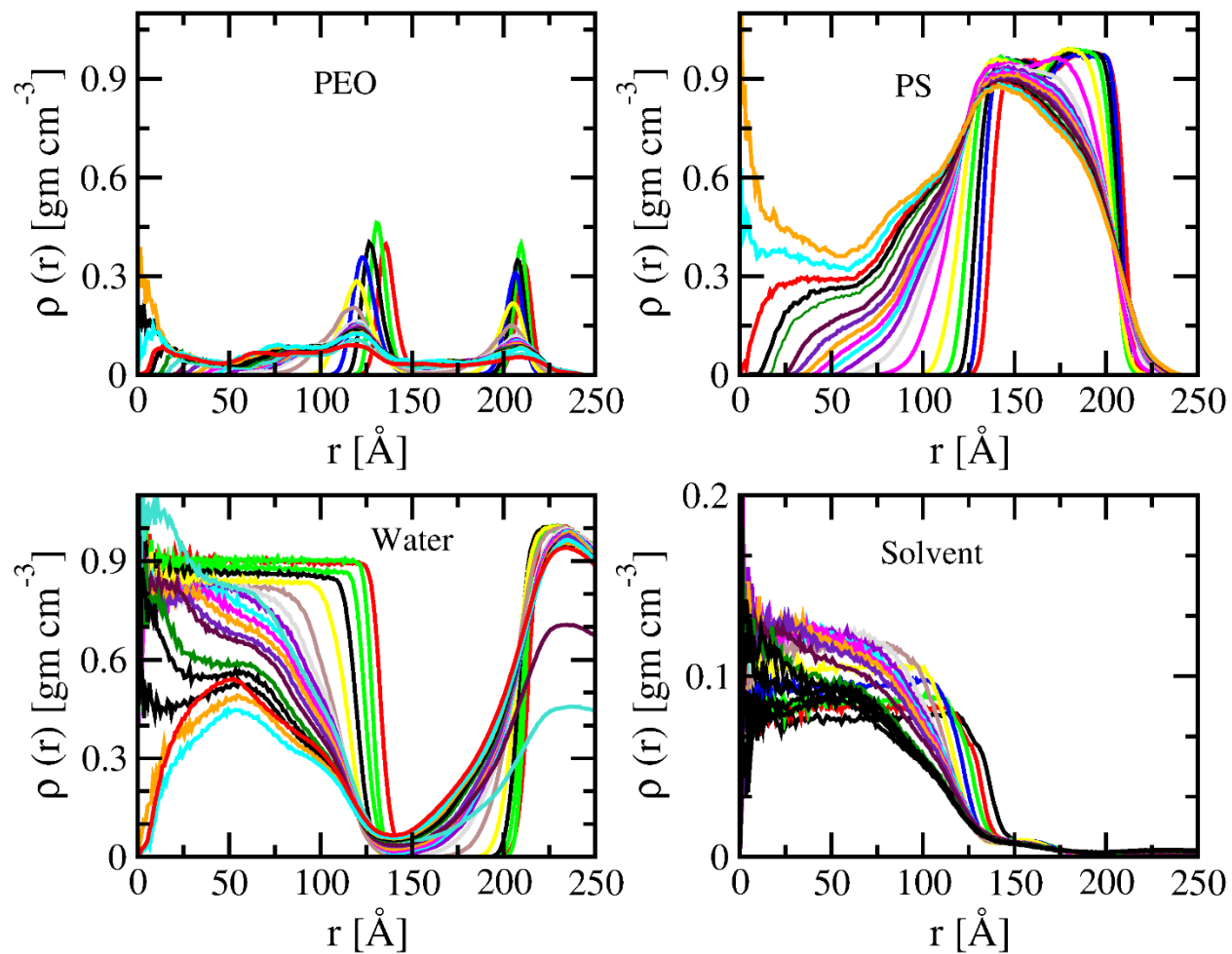
SI 4. Snapshot of the larger PEO₃-PS₁₅ 40 nm diameter polymersome after different cycles. PEO is in blue and red, PS is in gray. Initially, up to Cycle 7, the polymersome is mainly spherical in shape. Then, the polymer membrane starts to bend and forms a non-spherical geometry.



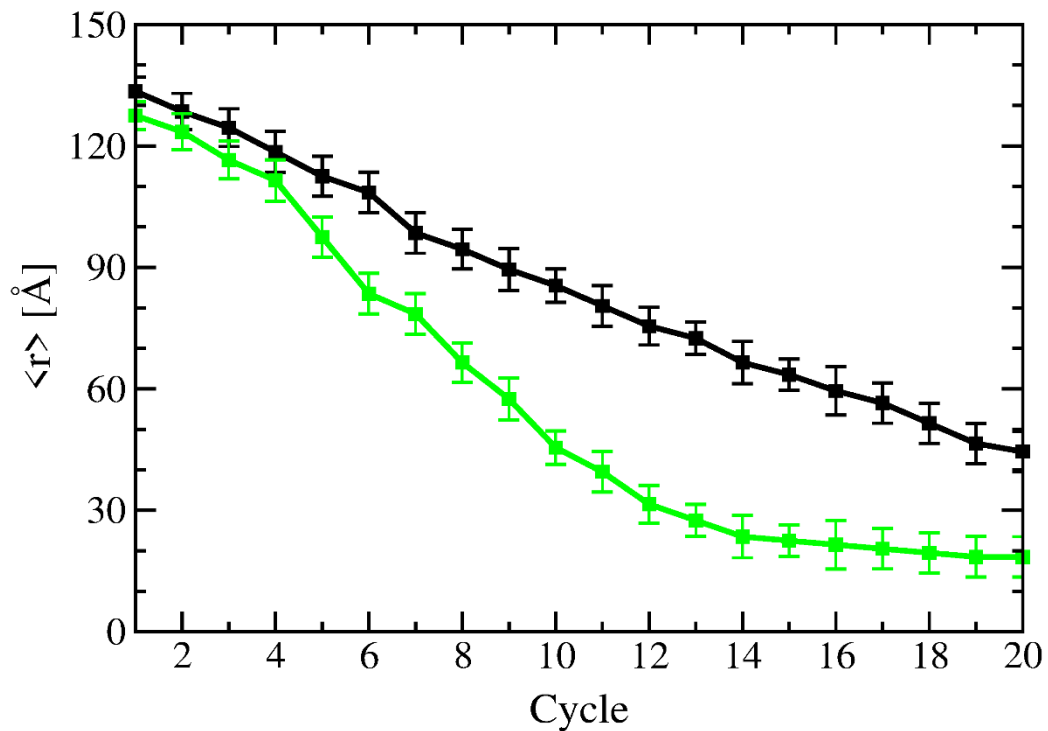
SI-5. Snapshots of the larger PEO₃-PS₁₅ 40 nm diameter polymersome after different cycles in presence of 20 % hydrophobic solvent. PEO is in blue and red, PS is in gray. Hydrophobic solvent is in yellow.



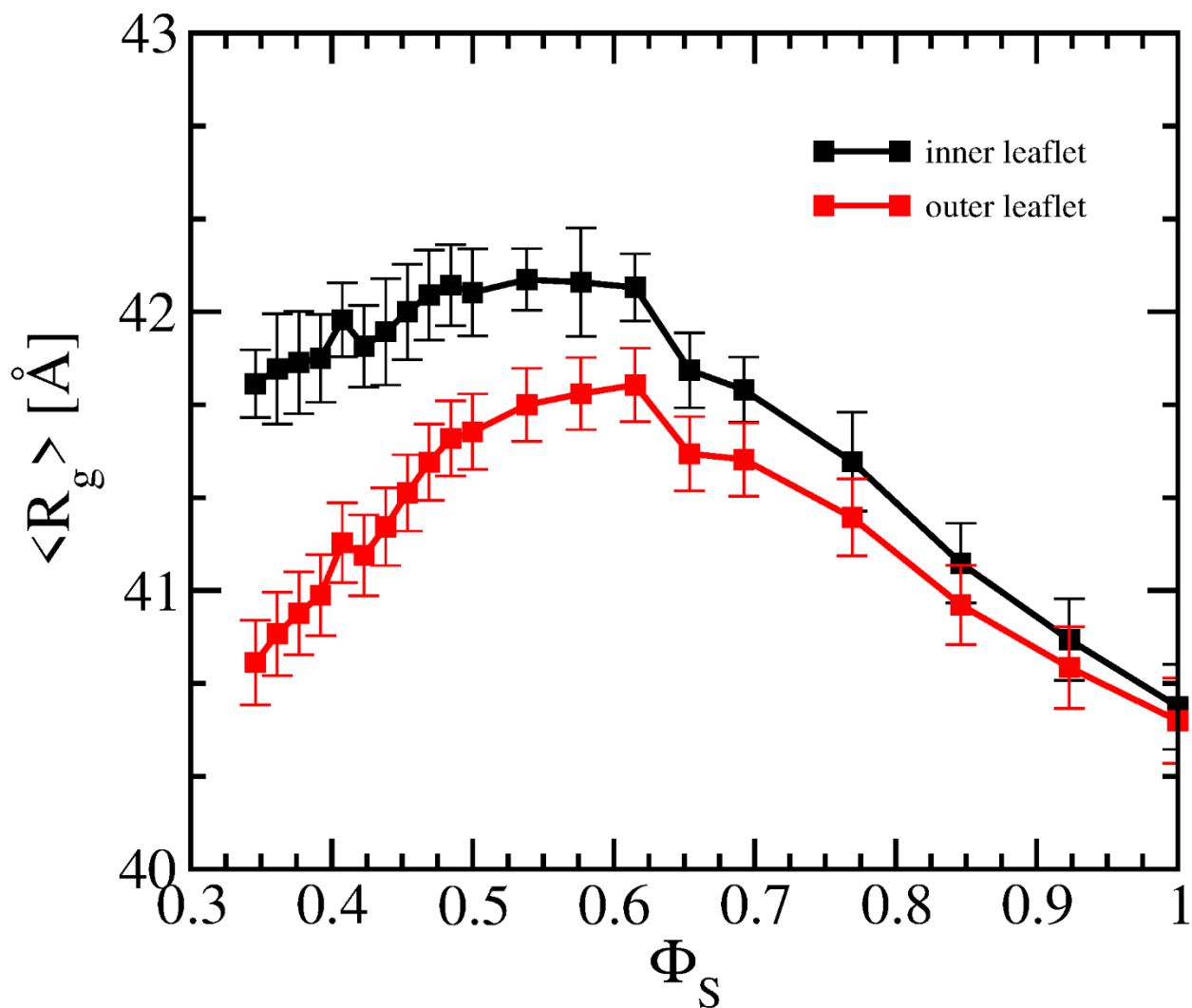
SI 6. Density profiles of PEO, PS and water from the center of the larger PEO₃-PS₁₅ 40 nm diameter polymersome after each cycle.



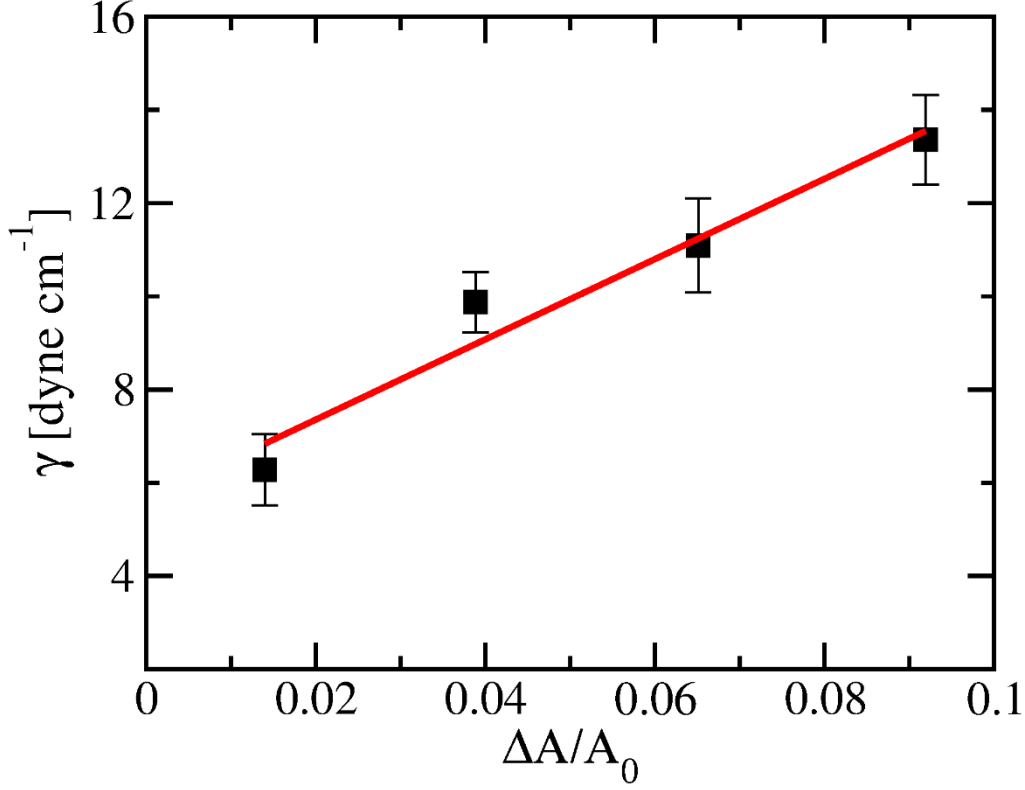
SI 7. Density profiles of the PEO, PS and water from the center of the larger PEO₃-PS₁₅ 40 nm diameter polymersome after each cycle in presence of 20 % hydrophobic solvent.



SI 8. Variation of inner core radius (r) of the larger PEO₃-PS₁₅ polymersome after each cycle. Black line represents the r in presence of only water and green line in the presence of 20 % hydrophobic solvent.



SI-9. Variation of the average radius of gyration (R_g) of the PS chains present in the different leaflets of the polymersome. The relatively larger R_g value of the PS chains present in the inner leaflet suggest the asymmetric contraction of the polymersome.



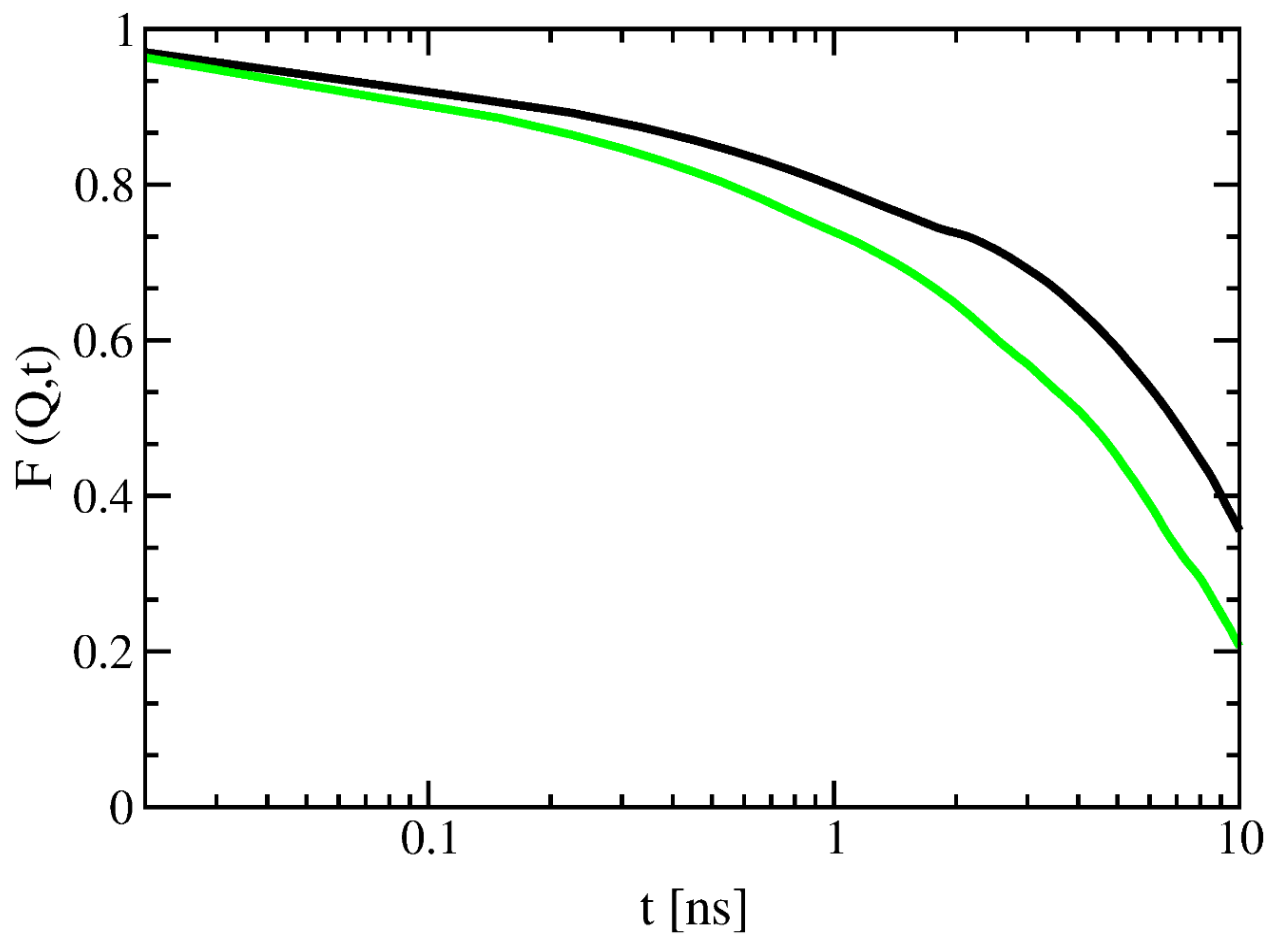
SI 10. Surface tension vs area of expansion of PEO₃PS₁₅ bilayers in the presence of 20% model hydrophobic solvent.

Dynamical properties of PEO-PS polymers are investigated by calculation self-intermediate scattering function ($F(Q,t)$). $F(Q,t)$ can be represent as

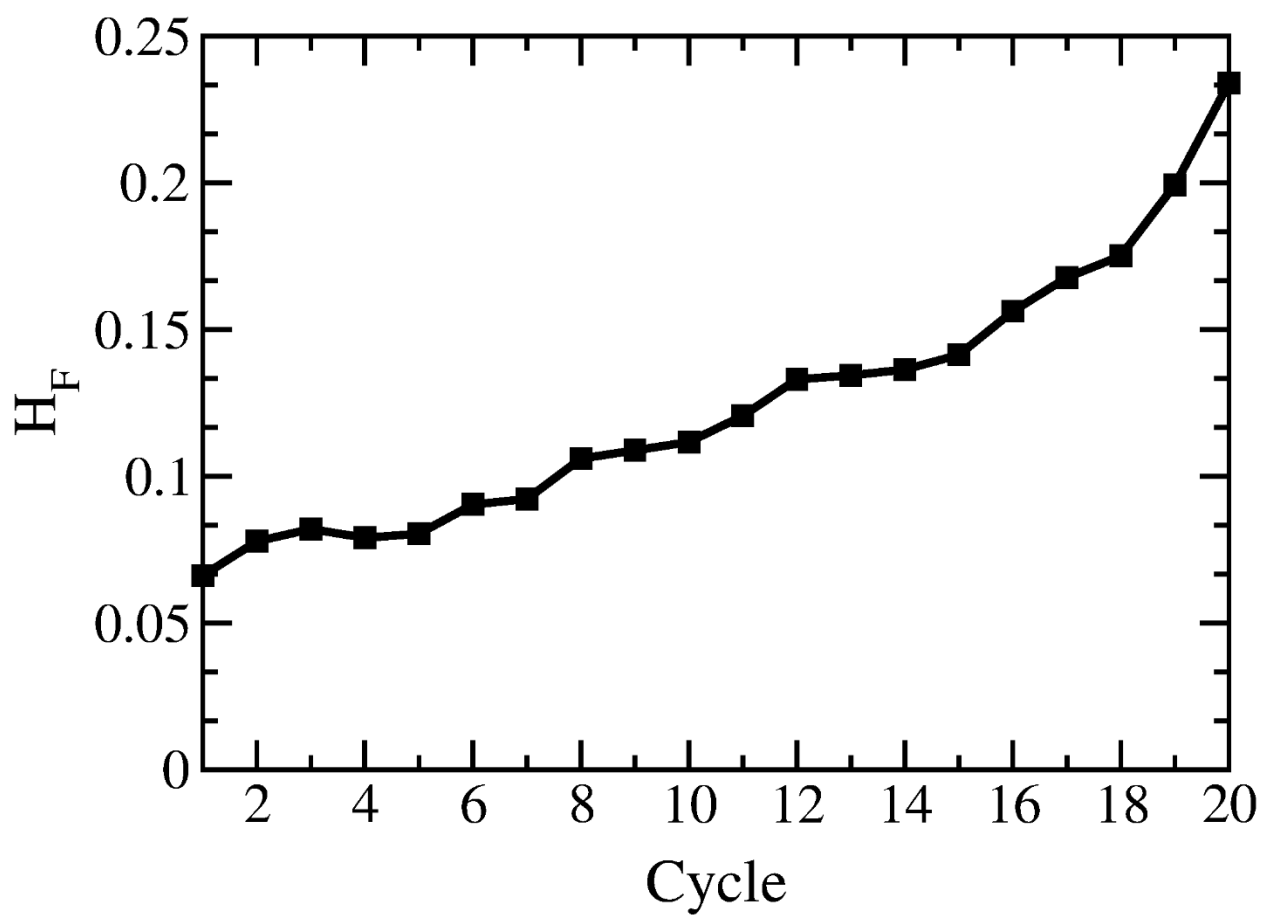
$$F(Q,t) = \langle \exp(-iQ(\mathbf{r}_i(t) - \mathbf{r}_i(0))) \rangle$$

where Q is the wave vector, and $\mathbf{r}_i(t)$ and $\mathbf{r}_i(0)$ denote position vectors of the center of mass of each PS chain at time t and $t = 0$, respectively. The value of $|Q|$ is taken to be 1 \AA^{-1} in the calculations. Faster relaxation of $F(Q,t)$ in the presence of 20 % model hydrophobic solvent suggesting more liquid-like behavior of PS chain in compared to aqueous medium. Relaxation

time of the scattering functions are 6 ns and 10 ns in the presence and absence of hydrophobic solvent respectively.



SI 11. Relaxations of self-intermediate scattering function ($F(Q,t)$) in presence of only water (black line) and in presence of 20 % hydrophobic solvent (green line). This is calculated for the last cycle.



SI 12. Fractions of model hydrophobic solvent (H_F) buried inside the hydrophobic core of the polymersome for different cycles.

Parameters

Atom Type	Atom Type	ϵ (kcal/mol)	LJ type	σ (Å)
W	W	0.895	12-4	4.371
EOT	EOT	.437	9-6	4.25
EOT	W	.57	12-4	4.31
EO	EO	.4050	9-6	4.25
EO	W	.57	12-4	4.31
EOT	EO	.42	9-6	4.25
I	I	.4491	9-6	3.713
I	W	.70	9-6	3.95
I	EOT	.44	9-6	3.89
I	EO	.44	9-6	3.89
I	B	.374	9-6	3.967
B	B	0.312	9-6	4.221
B	W	0.25	9-6	4.085

SI Table 2. Coarse grained parameters for non-bonded interactions in PEO-PS-water systems. EOT and EO parameters are taken from Shinoda et al, Molecular Simulation, 2007. The parameters of the interfacial bead I is taken from Loverde et al., Advanced Materials, 2012. Parameters for the backbone and ring PS beads, B, are taken from Drenscko et. al, Molecular Simulation, 2017. ϵ is the depth of the Lennard-Jones potential well and σ is the finite distance at which the inter-particle potential is zero. All are other parameters are determined using the mixing rule.

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