Supporting Information

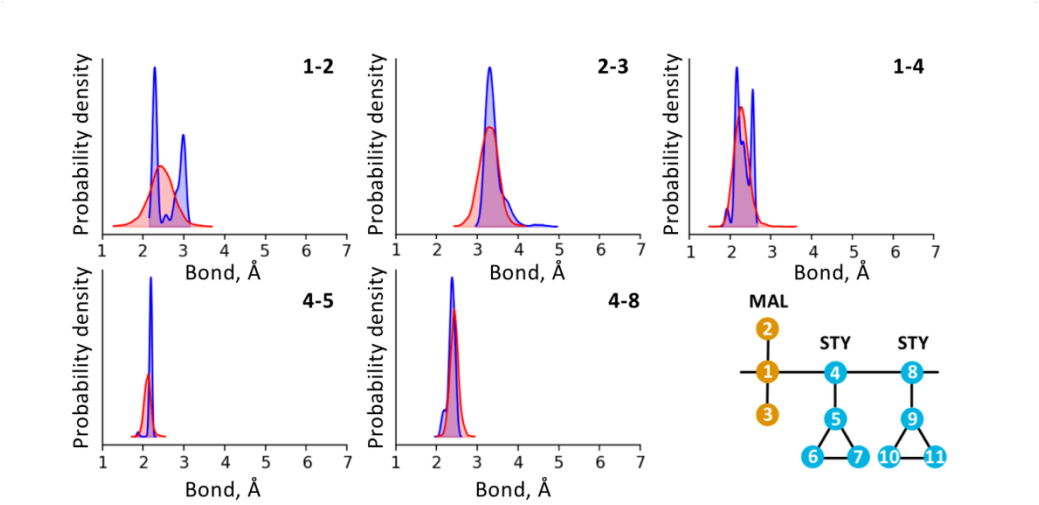

Figure S1. Distributions of the bond terms from the AA simulation (blue histogram) and from the CG simulation of SMA polymer in aqueous solution with the final set of optimized parameters (red histogram). The numbers correspond to the beads numbered on the scheme.

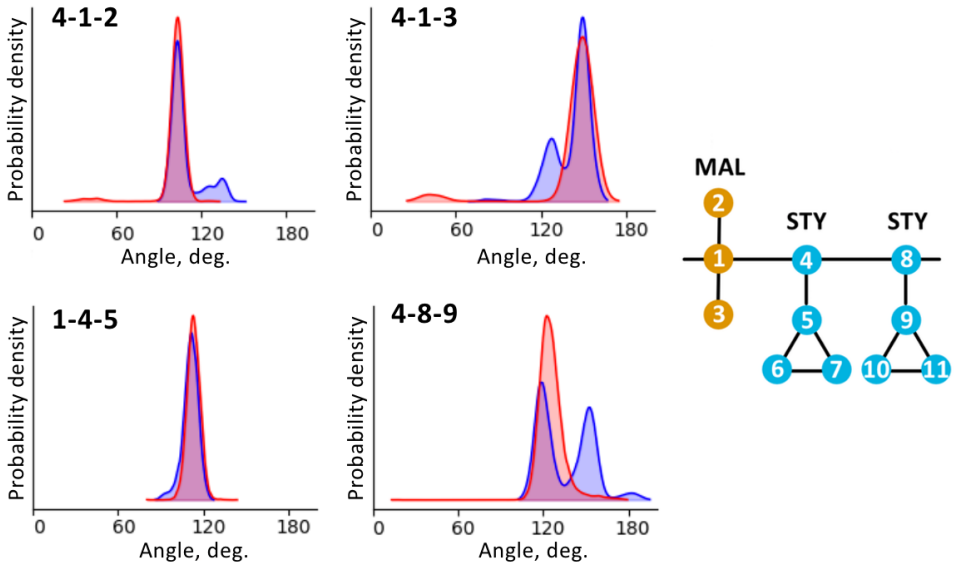

Figure S2. Distributions of the angle terms from the AA simulation (blue histogram) and from the CG simulation of SMA polymer in aqueous solution with the final set of optimized parameters (red histogram). The numbers correspond to the beads numbered on the scheme.

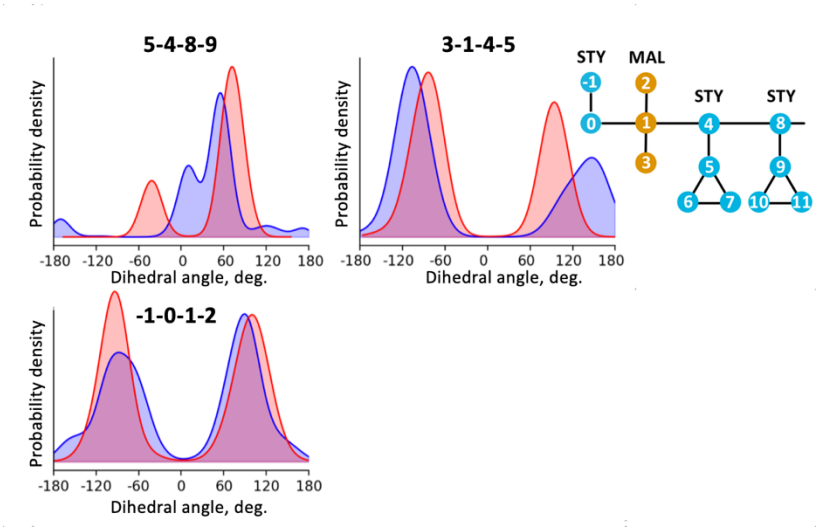

Figure S3. Distributions of the dihedral terms from the AA simulation (blue histogram) and from the CG simulation of SMA polymer in aqueous solution with the final set of optimized parameters (red histogram). The numbers correspond to the beads numbered on the scheme.

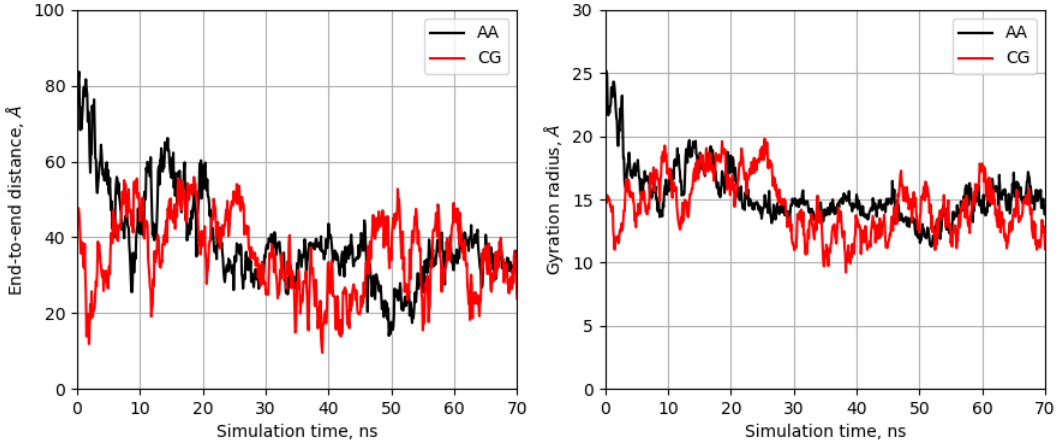

Figure S4. Comparison of the end-to-end distance (left) and gyration radius (right) of a SMA copolymer in aqueous solution as calculated for all-atom (AA) and coarse-grained (CG) models.

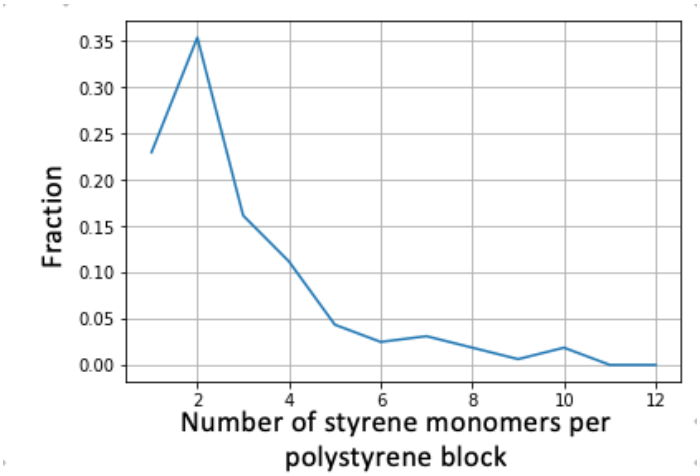

Figure S5. Distribution of sizes of styrene blocks (in monomers) in the generated sequences of statistical copolymers.

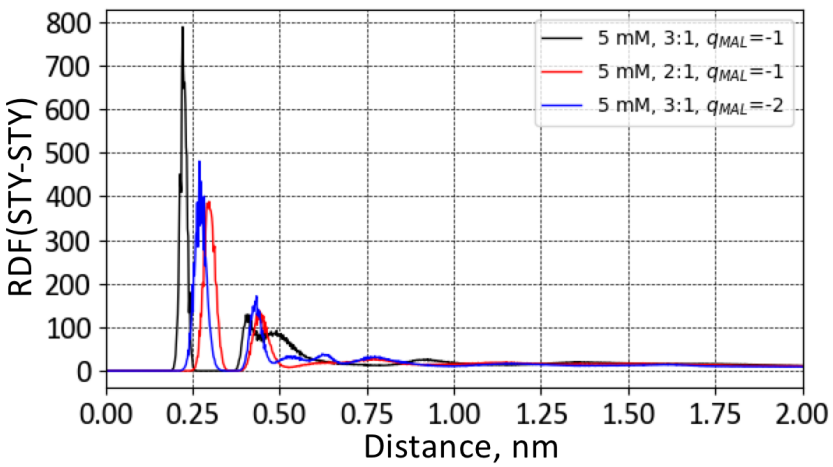

Figure S6. Radial distribution function for styrene side chains (intermolecular) for different SMA copolymer species.

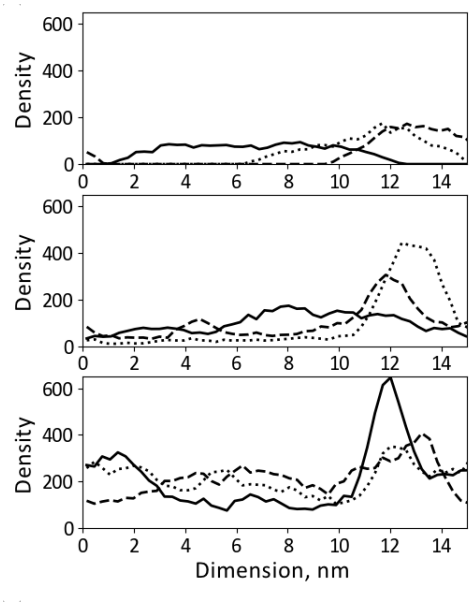

Figure S7. SMA copolymer density profiles along dimensions of the cubic simulation box (solid, dashed and dotted lines correspond to x, y and z, respectively) for the systems with 5 (top), 10 (middle) and 20 (bottom) mM concentration of SMA copolymers.

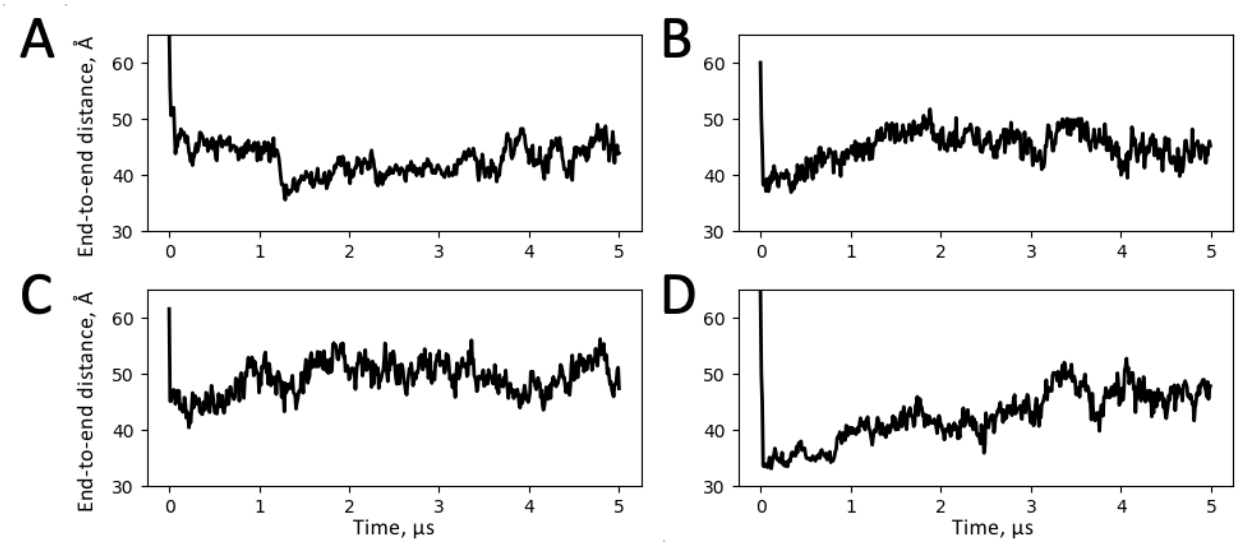

Figure S8. End-to-end distance of individual copolymers averaged over all the simulated 2:1 (**A, C**) and 3:1 (**B, D**) SMA copolymers during the 5 μs-long simulations with DMPC bilayer (data for two replica simulations are shown for each system).

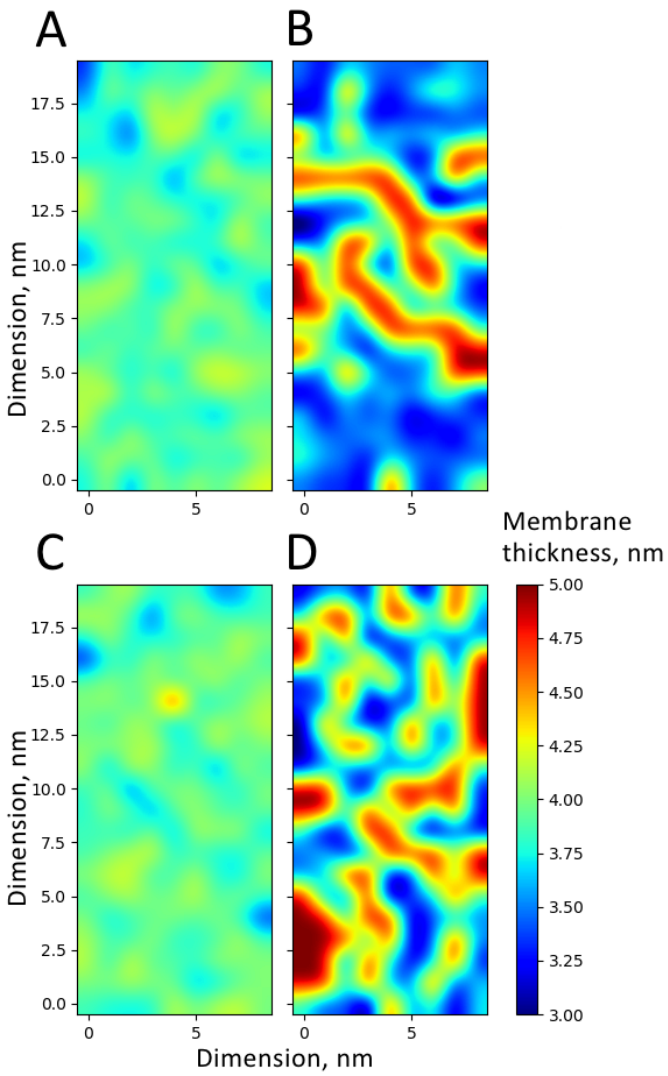

Figure S9. Representative 2D density plots of membrane thickness before (**A, C**) and after (**B, D**) adsorption of 2:1 (top) and 3:1 (bottom) SMA copolymers onto the DMPC bilayer.

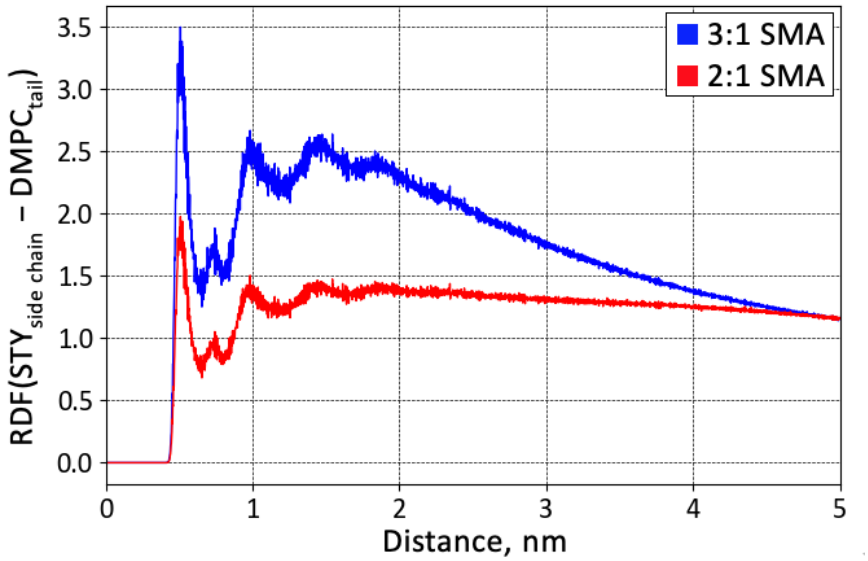

Figure S10. Radial distribution function for CG beads, corresponding to the hydrophobic lipid tails, and side chains of styrene. RDFs are calculated from the last 1 μs of 5-μs-long simulations of 2:1 and 3:1 SMA copolymers with DMPC bilayer.

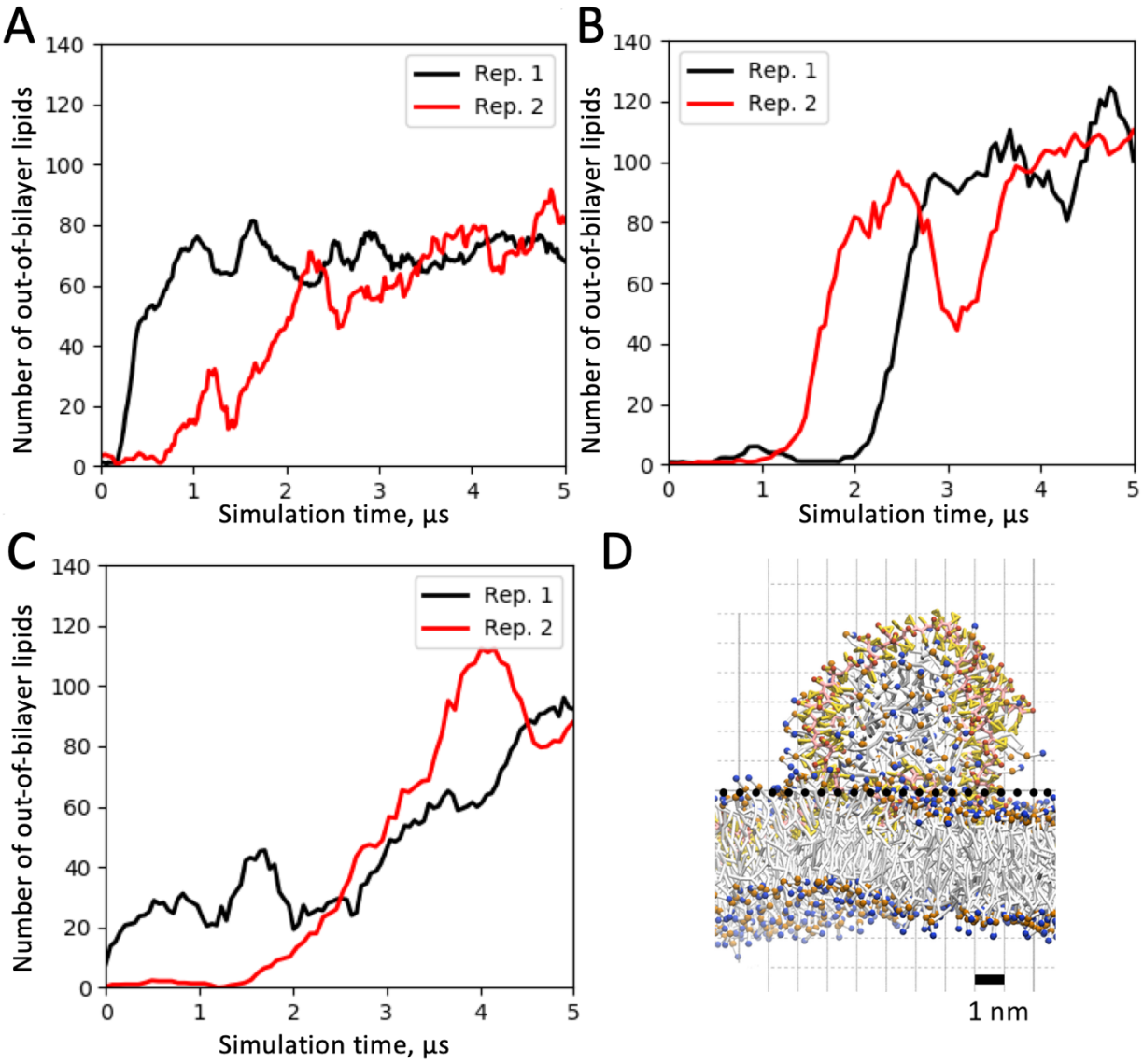

Figure S11. Number of lipid molecules in the disc-shaped protrusion stabilized by periodic (**A**), statistical (**B**) and length-dispersed (**C**) SMA copolymers with 3:1 molar ratio of styrene:MA residues estimated as a number of lipids outside the bilayer plane (schematically shown as a dotted line in panel **D**). Results for two replica simulations are shown for each system.

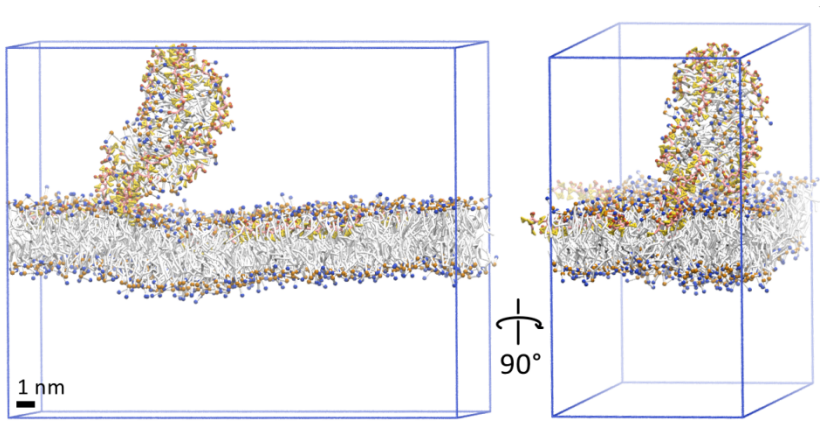

Figure S12. Further detachment of the disc-shaped protrusion stabilized by SMA copolymers with 3:1 ratio of styrene:MA residues after 1 μs-long simulation with the polarizable water model, which extended the preceding 5 μs-long simulation with the standard MARTINI water model.

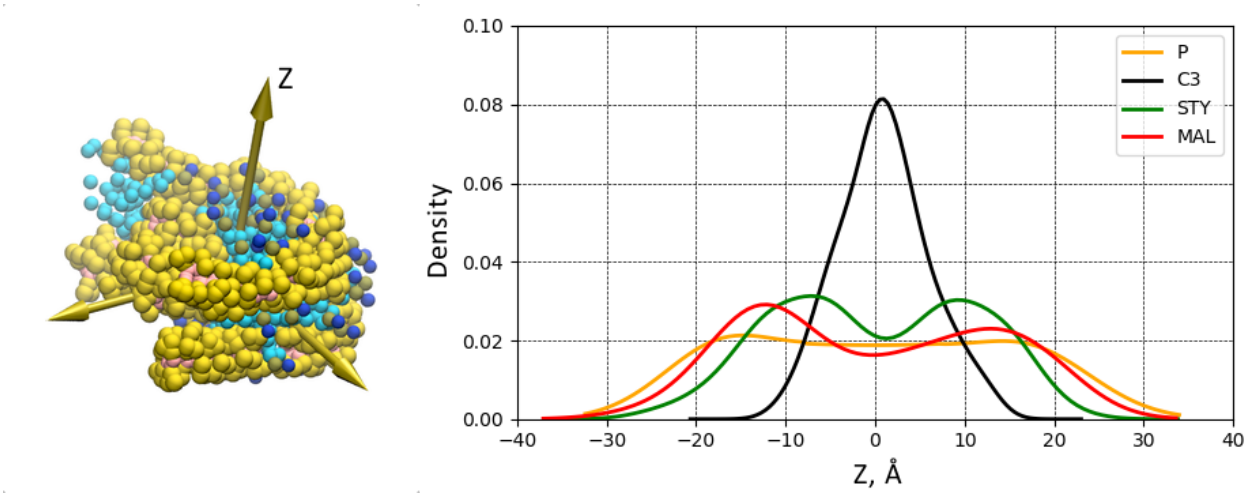

Figure S13. Density profiles along Z direction corresponding to the third principal moment of inertia of the SMALP-like protrusion (shown on the left with yellow and rose spheres of the SMA copolymer and blue, red and cyan spheres of DMPC). P, DMPC phosphate; C3, terminal groups of acyl chains; STY, styrene; MAL. maleic acid.

Table S1. Monomer sequences and molecular weights of SMA copolymers used in the simulations.

Styrene:MA ratio, polymer type	*Number of monomers*	*Monomer sequence*	*M_w, kDa*	*Simulation IDs*
3:1, periodic	104	$(SSSM)_{26}$	11.6	8
3:1, periodic	52	$(SSSM)_{13}$	5.8	1, 2, 3, 5, 6, 6c, 8
3:1 periodic	26	MSSSMSSSMSSSMSSSMSSSMSSSMS	2.9	8
3:1, periodic	13	MSSSMSSSMSSSM	1.4	8
3:1, periodic	12	$(SSSM)_3$	1.3	10
2:1, periodic	51	$(SSM)_{17}$	5.7	4, 7, 7c
3:1, statistical	52	MSSMSSMSSSMSSMSSSSSSSSMSSSSSSMSSSSSSSSSSMSMSSSSSMSSM, MSSMSMSSMSSMSSSMSSMSMSMSMSMSMSSSSSSSMSSSSSSSSSSSMSSMS, SSSMSMSSSSSSMSSMSSSMSSSSSMSMSSMSSMSSSSSSMSSSMSSSMSSSMSM, MSMSSMSSSMSSSSSMSSSMSSSSSSSMSSMSSSSSSSMSSSSMSSSSMSSSM, MSMSSMSSMSSMSMSSSSSMSSSMSSMSSSSSSSSMSSSSSSSSSSMSMSSSSM, MSSSSMSSMSSSSMSSMSSSSSSSSMSSSSSMSMSSMSSMSSMSSMSSM, MSSSMSSSSSMSSMSSSSSMSSSSMSMSSSSSSSSMSMSSMSMSMSSSSS, MSSMSSSSMSSMSSSSSMSSSSSSMSMSSMSSMSSSSMSSSMSMSMSS, MSMSSMSSMSSSMSSSMSSSMSSSSSMSSMSMSSMSSMSSSSSSSSSSSSSM, MSSMSMSSSMSSSSSMSSMSSSSSMSSMSSMSSMSMSSSSSMSSMSSSMSMSMS, MSMSSMSSSMSMSMSSSSSSSSSSSMSMSSSSSSSSMSSSSSMSSSMSSSSSS, MSSSSSSSMSSSMSSMSSSMSSMSSMSSSSMSSMSMSMSSMSSSSSSMSSMSS

Table S2. Relative fraction of three-styrene units in SMA copolymers (according to Fig. 7 from ref. 1) with different styrene:MA ratios and their solubilizing efficiency (estimated as (1 – normalized optical density at pH=7.0) from Fig. 6 from ref. 1).

Styrene:maleic acid ratio	***Relative fraction of three-styrene units***	***Solubilizing efficiency***
1.4:1	0.05	0.45
2:1	0.2	1
3:1	0.2	1
4:1	0.13	0.65

References

1. Scheidelaar, S.; Koorengevel, M. C.; van Walree, C. A.; Dominguez, J. J.; Dörr, J. M.; Killian, J. A. Effect of Polymer Composition and pH on Membrane Solubilization by Styrene-Maleic Acid Copolymers. *Biophys. J.* **2016**, *111* (9), 1974–1986.