Electronic Supplementary Material (ESI) for Nanoscale.

Supporting Information for:

Polymer Stiffness Governs Template Mediated Self-Assembly of Liposome-Like Nanoparticles: Simulation, Theory and Experiment

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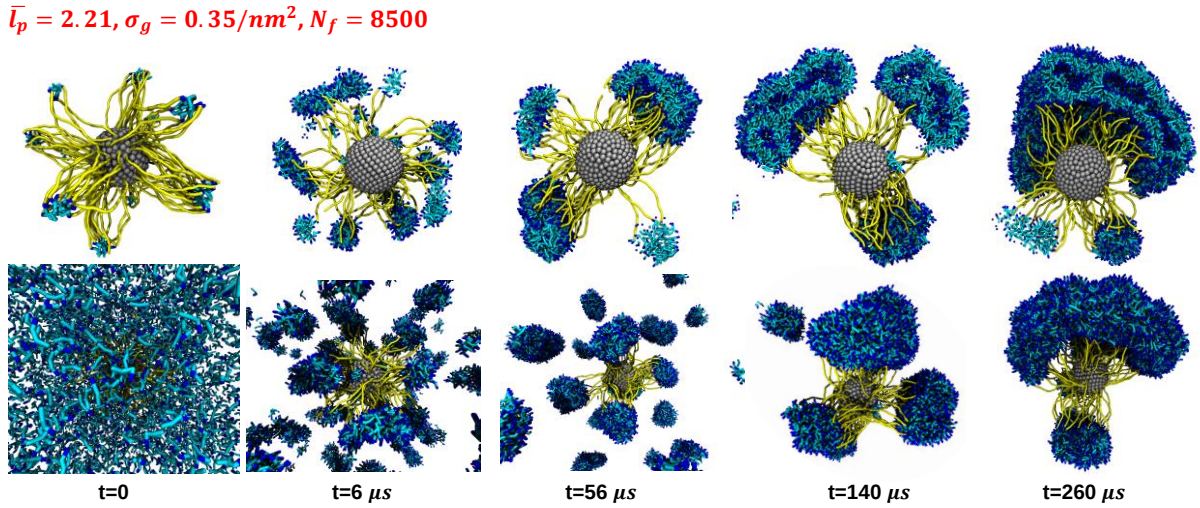

Figure S1. Self-assembly of TMLs at $\bar{l_p} = 2.21, \sigma_g = 0.35 \text{ / nm}^2$, $N_f = 8500$. To investigate the effect of free lipid number, we increased the free lipid number to 8500. All other conditions are the same as the one in Figure 2 (B) in the main text. A partially encapsulated TML is also found when the free lipid number is increased.

2. Synthesis of CPLS NPs

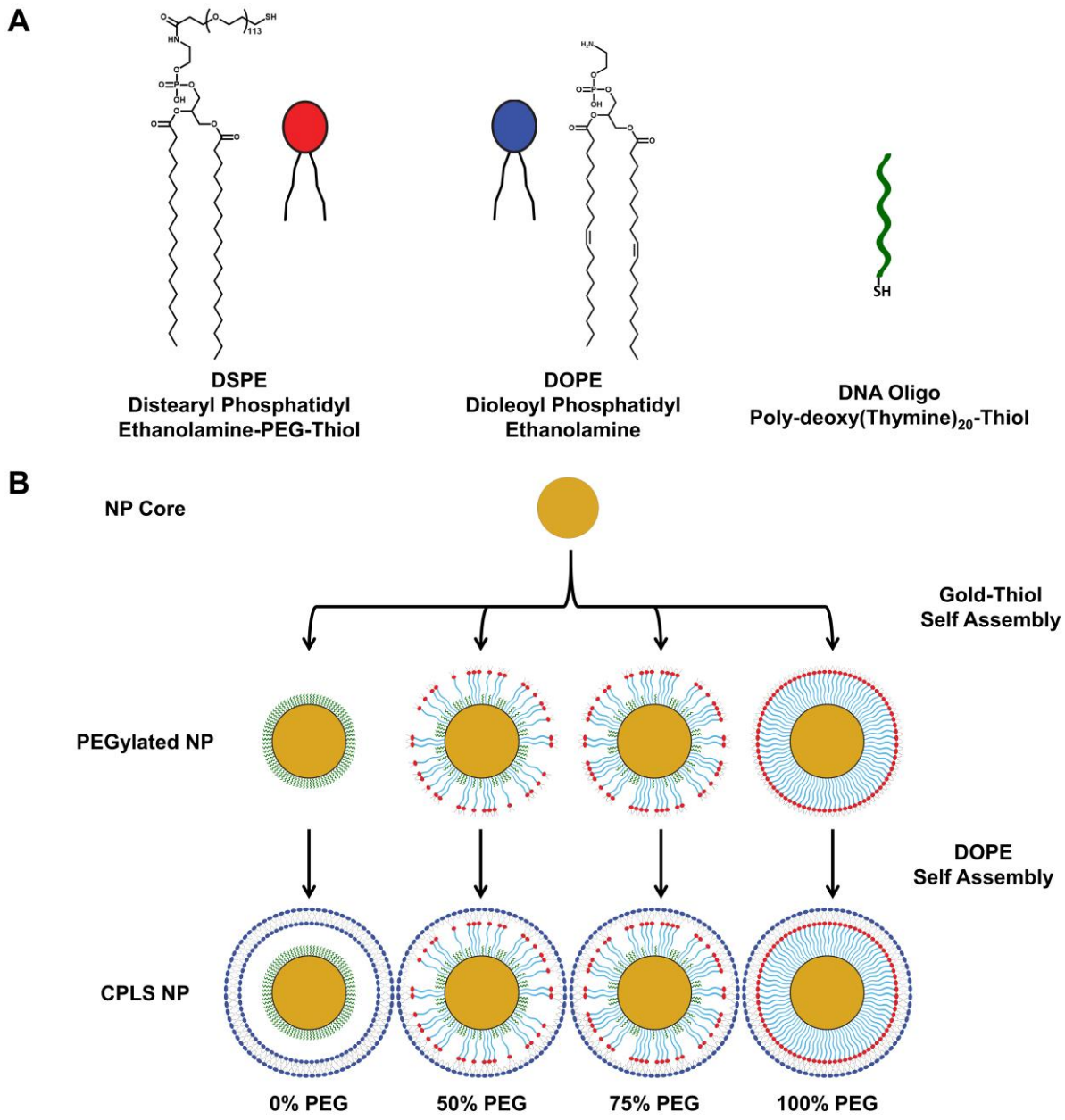

Figure S2. (A) Legend for scheme. (B) Schematic Representation of the synthesis of CPLS NPs with variable amounts of SH-PEG-DSPE and polyT DNA backfill. The thiolated polymers adsorb to the surface of the Au NP. To achieve the 100%, 75%, 50%, and 0% conditions, relative concentrations of the SH-PEG-DSPE and the thiolated DNA oligonucleotide were controlled with respect to the concentration of the ~30 nm Au core, in a 10,000:1 molar ratio of the combined ligands to the Au core. The free lipid DOPE was added to the PEGylated NPs through thin film hydration in a 2,500:1 molar ratio of DOPE to the Au core.

3. Characterization of CPLS NPs

The CPLS NPs observed in TEM images were counted and sorted into four categories following these parameters: *Perfectly Encapsulated* is defined as having a thick white halo, which can be slightly amorphous (i.e. not a rigid sphere); *Budding* is defined as a thick white halo, including at least one contiguous bulge; *Anchored Vesicles* is defined as either a thin or thick white halo around the inorganic core, but must include at least two small white spheres non-contiguously or non-continuously arrayed around the core; *No Encapsulation* is defined as a thin white shell which matches almost perfectly the core morphology, must have zero white spheres arrayed around the core. Particles which contained multiple cores per lipid shell were not counted. Particles which did not fit into the above parameters were not counted. In instances where multiple cores could be observed sharing white spheres and ownership could not be differentiated, all particles were declared Anchored Vesicles. The following TEM images are representative of each 100%, 75%, 50%, and 0% grafting density of SH-PEG-DSPE.

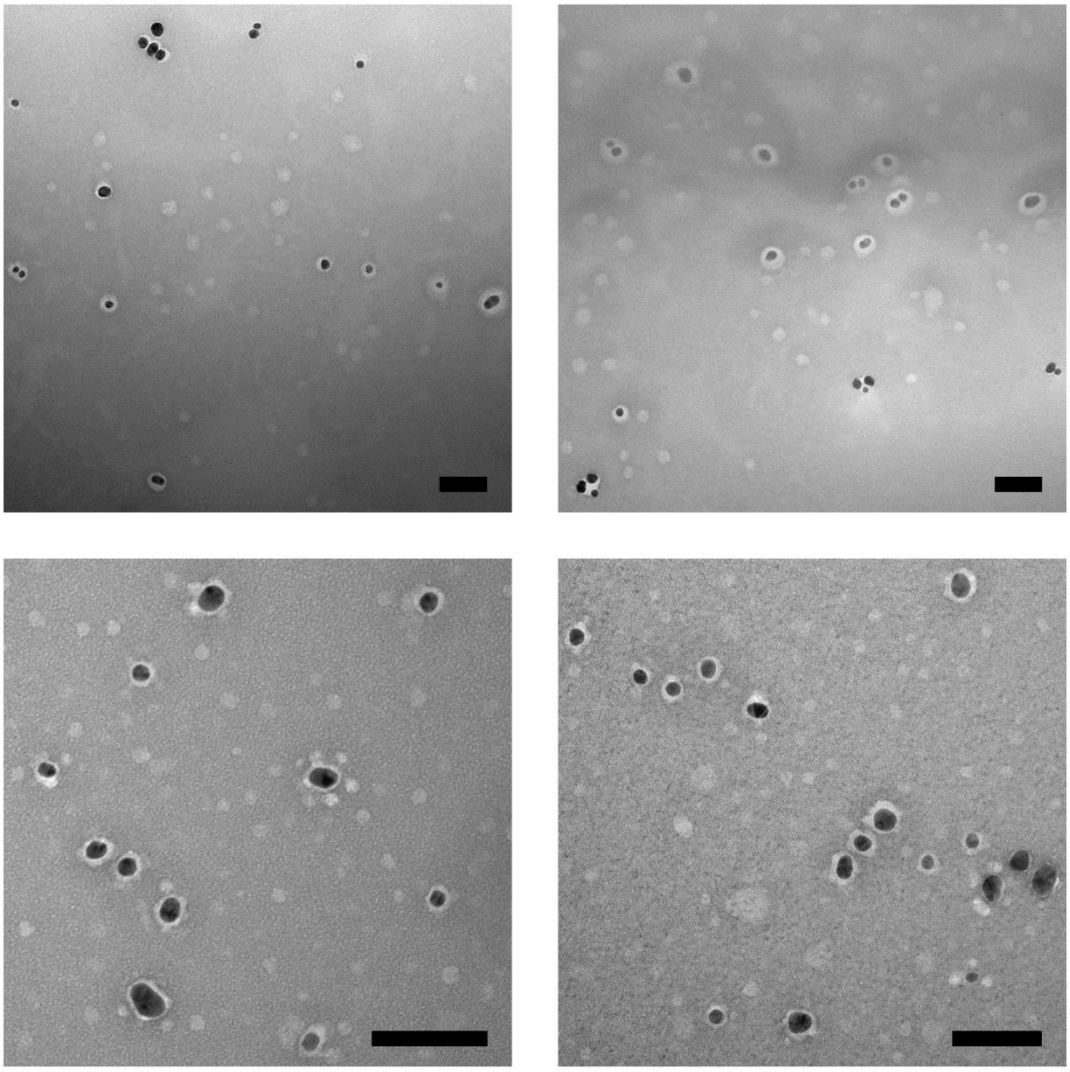

Figure S3. TEM images of the CPLS NPs with 100% PEGylated lipid. Samples were stained with 0.5% uranyl acetate solution. All scale bars 100 nm.

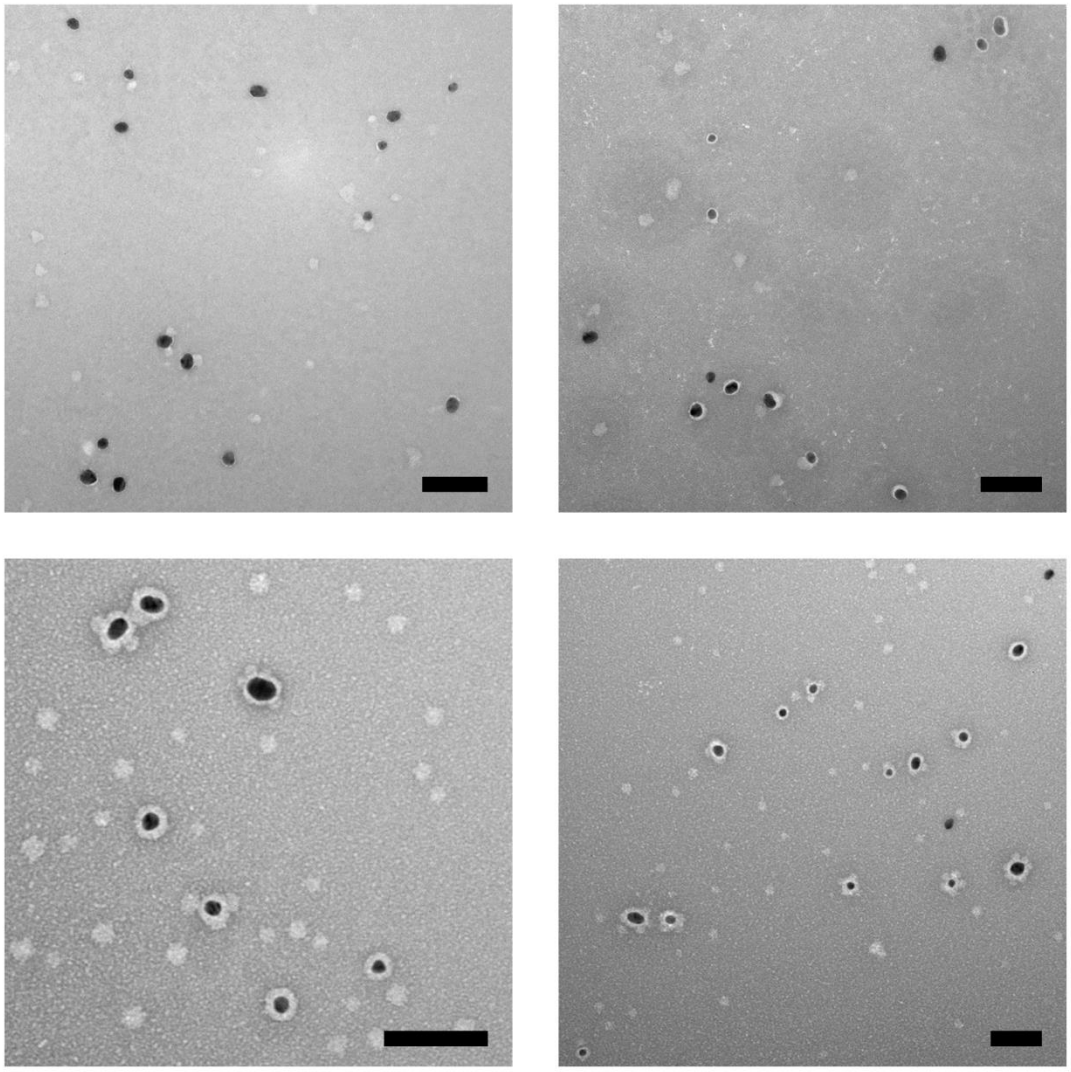

Figure S4. TEM images of the CPLS NPs with 75% PEGylated lipid. Samples were stained with 0.5% uranyl acetate solution. All scale bars 100 nm.

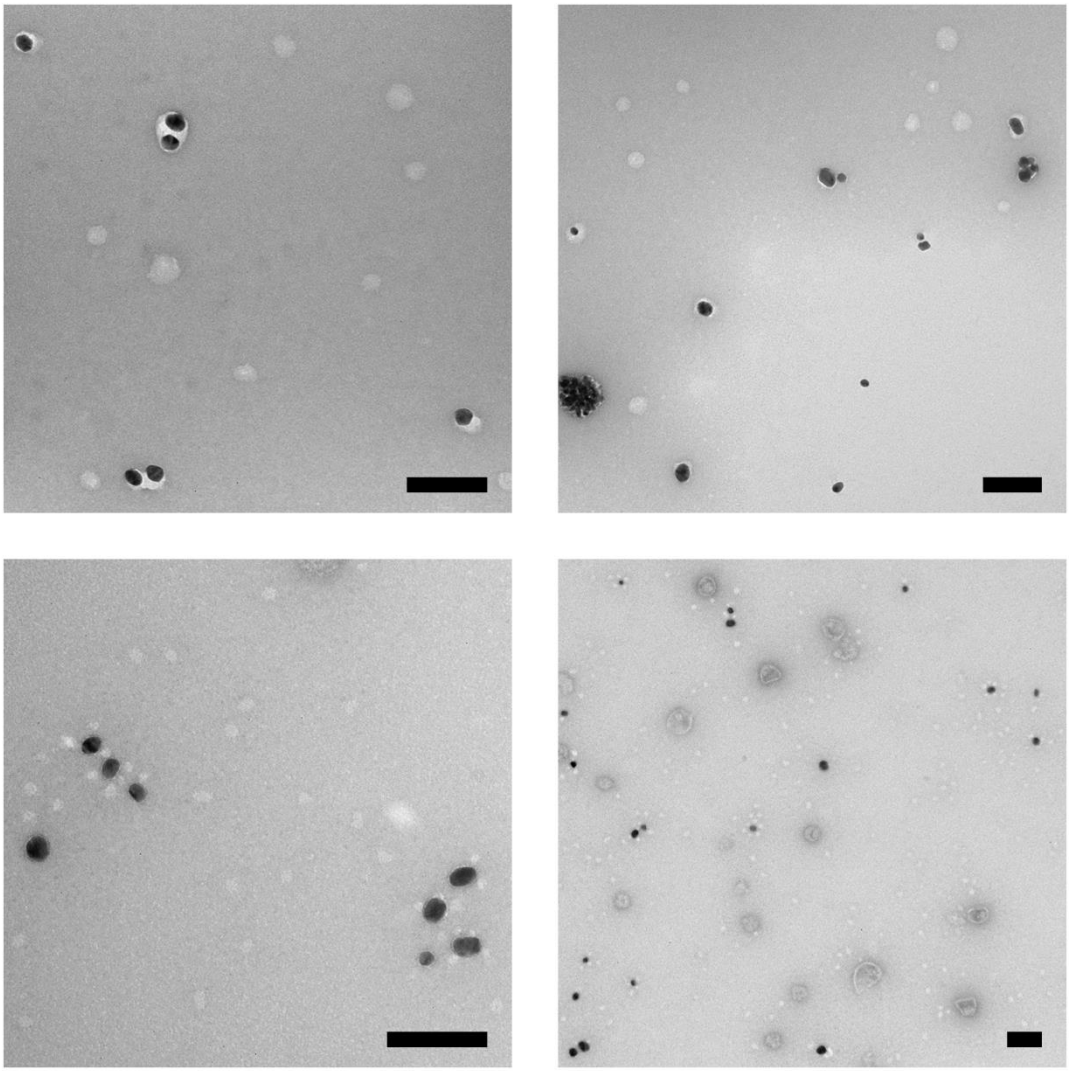

Figure S5. TEM images of the CPLS NPs with 50% PEGylated lipid. Samples were stained with 0.5% uranyl acetate solution. All scale bars 100 nm.

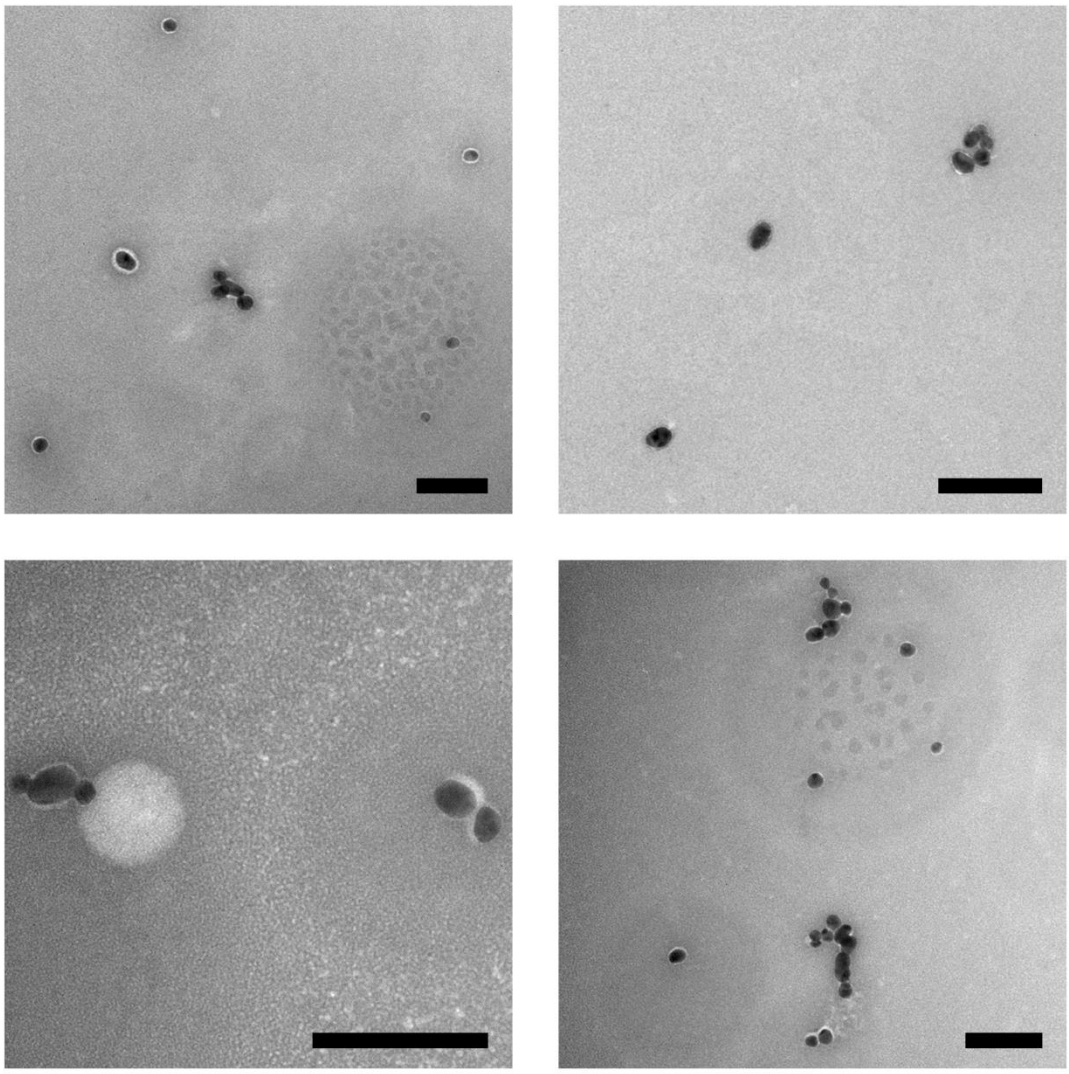

Figure S6. TEM images of the CPLS NPs with 0% PEGylated lipid. Samples were stained with 0.5% uranyl acetate solution. All scale bars 100 nm. Note, uranyl acetate staining of DNA-Au NPs can result in white halo effects due to electrostatic interactions between the stain and the DNA.

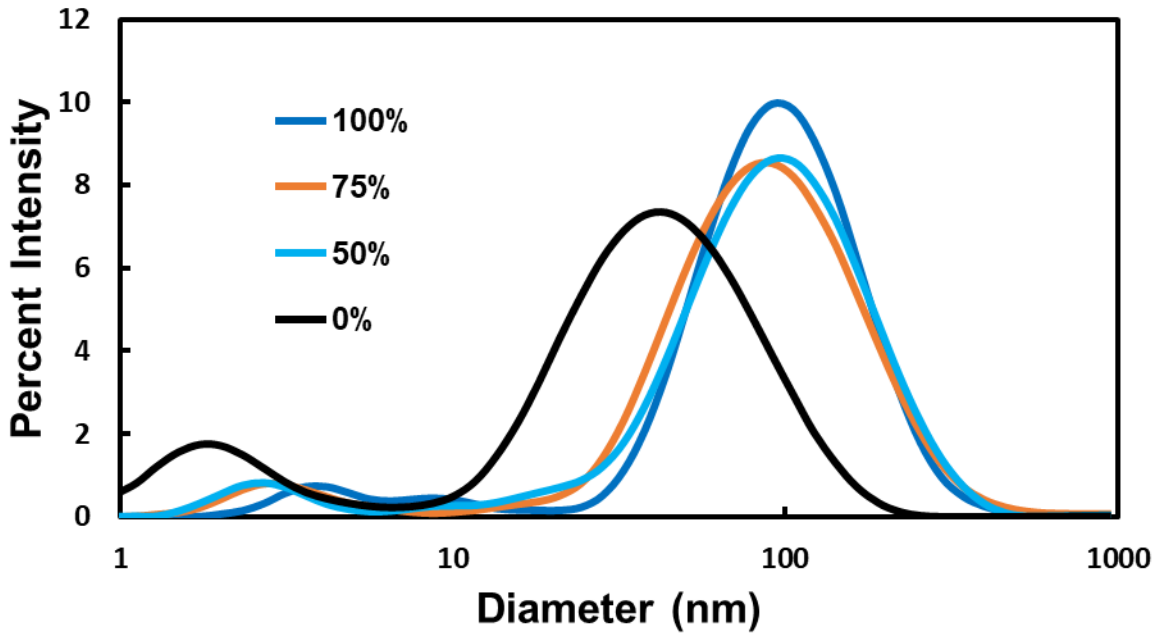

Figure S7. Representative Dynamic Light Scattering (DLS) measurements of the CPLS NPs with variable amounts of the PEGylated lipid with and without addition of the free lipid.

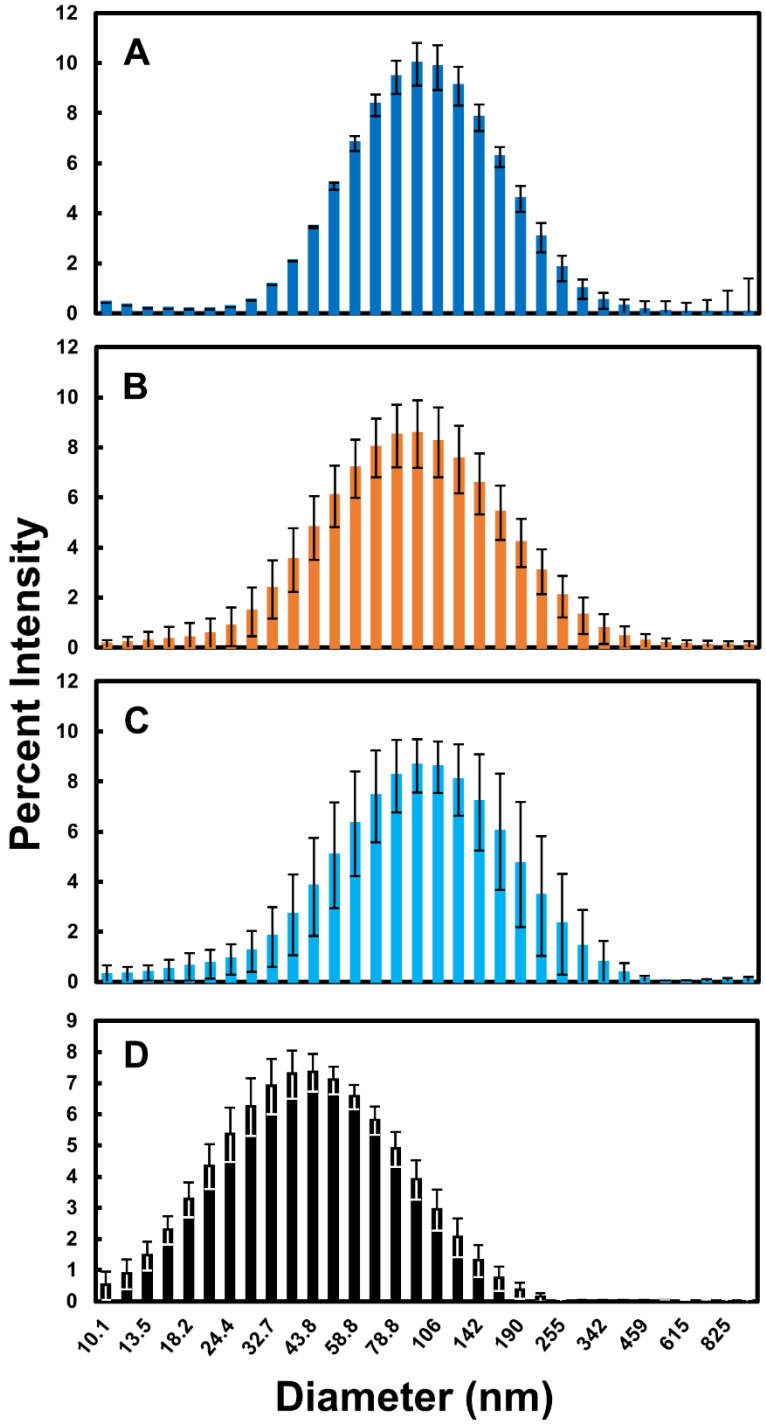

Figure S8. Representative Dynamic Light Scattering (DLS) measurements of the CPLS NPs as a histogram of each individual condition. A. 100% PEG CPLS. B. 75% PEG CPLS. C. 50% PEG CPLS. D. 0% PEG CPLS.

4. Interaction parameters in simulations

The repulsive interaction parameters a_{ij} for all kinds of bead types in the dissipative particle dynamics (DPD) simulations are given in **Table S1**. w, h, t, p and c represent water, lipid head, lipid tail, polymer and inorganic core beads, respectively. The inorganic core beads will experience a large repulsion with all other types of beads to prevent their penetration.

Table S1: Interactive parameters a_{ij}, between beads i and j in the DPD simulation.

$a_{ij}\ (k_{\mathrm{B}}T/r_0)$	**w**	**h**	**t**	**p**	**c**
w	25.0	25.0	100.0	26.3	100.0
h		25.0	100.0	26.3	100.0
t			25.0	100.0	100.0
p				25.0	100.0
c					0.0

5. Estimation of lipid area

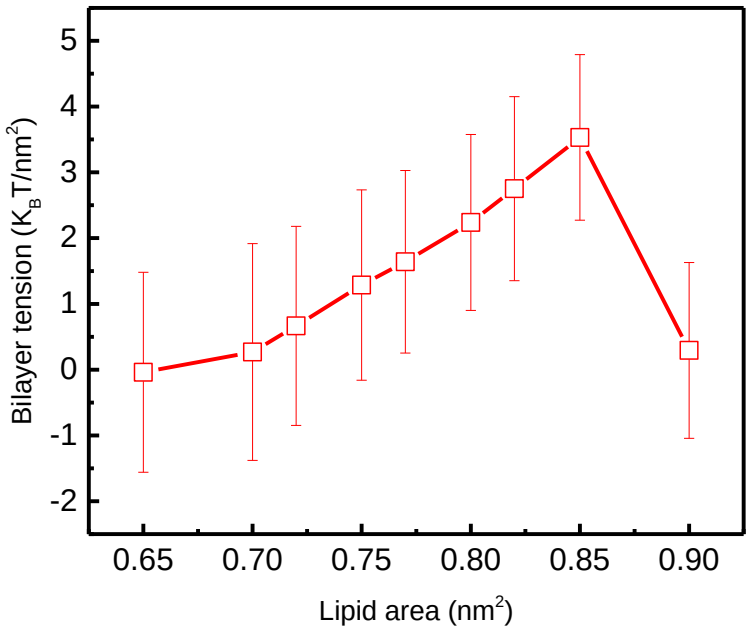

Figure S9. The relationship between lipid area and the lipid bilayer tension. To estimate the lipid area, a function planar bilayer tension against the lipid area is obtained. We assume that the lipid bilayer of the self-assembled template-mediated liposome (TML) is in its relaxed state. Therefore, the lipid area is taken as $a_p = 0.7\ nm^2$ for its zero bilayer tension.

6. Estimation of polymer persistence length

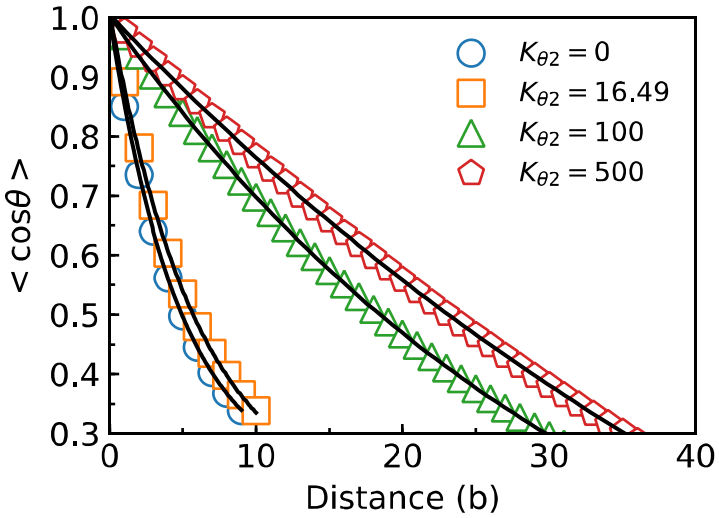

Figure S10. Functions of $< cos\,\theta >$ against the distance along with the polymer chain. The distance here is plot with the unit of bond length *b= 0.4125 nm*

The persistence of a polymer is estimated based on the formula as bellows[1]:

$$< \cos\theta > = \exp(-L/l_p)$$

where θ is defined as the angle between vectors $\overrightarrow{v_0}$ and $\overrightarrow{v_l}$. $\overrightarrow{v_0}$ is the vector that is tangent to the polymer at the position 0. $\overrightarrow{v_l}$ is the vector that is tangent to the polymer at a distance *L* away from position 0. The persistence length l_p can be obtained by fitting the $< \cos\theta >$ according to the formula. To evaluate the l_p of a polymer under certain potential in our simulation, we first relax a single polymer with monomer of 60 in the solvent. Then the relaxed snapshots of the polymer is used to calculate the $< \cos\theta >$ along the polymer length. As shown in Fig S10, the $< \cos\theta >$ values of four different polymers are given along with their corresponding fitting curves based on equation above. The persistence lengths of the four different polymers are 4.93, 6.09, 35.09, and 64.08

with the unit of bond length b=0.4125 *nm*. Their corresponding angular constants are $K_{\theta 2} = 0,\ 16.4946, 100 \text{ and } 500\ k_B T$, respectively. Their bending stiffnesses can be obtained based on the relation between the persistence length and bending stiffness B_s [2]:

$$B_s = P k_B T$$

Therefore, the corresponding bending stiffnesses of the four different polymers in our simulation are 2.034, 2.512, 14.475 and 26.433 $k_B T \cdot nm$, respectively.

7. Self-assembly process of planar polymer tethered lipid bilayer

To find out the critical grafting density σ_{pc} for a planar tethered lipid bilayer membrane, we investigated its self-assembly process. As given in **Figures S11-S14**, polymers are grafted on the planar substrate surface. Similar to our TMLs, the free terminals of the grafted polymers are linked with anchored lipids. The monomer for each polymer is 30. The size of the substrate is $(50 \times 50)\ \mathrm{nm}^2$. The free lipid number added is 7000, which is obtained according to the lipid area and substrate area. We investigated the self-assembly processes at a series of different tethered polymer persistence lengths and grafting densities. Details regarding the self-assembly process are given in **Figures S11-S14**. It is found that the critical grafting density for the planar tethered lipid bilayer is much smaller than the one found for TMLs in the main text. As shown in the figure, the critical grafting density for the case of $\bar{l_p} = 0.17$ is around $\sigma_{pc} = 0.04\ /\ \mathrm{nm}^2$. More importantly, the critical grafting densities for all 3 other cases of $\bar{l_p} = 0.21, 1.21, 2.21$ are the same with the value around $\sigma_{pc} = 0.06\ /\ \mathrm{nm}^2$.

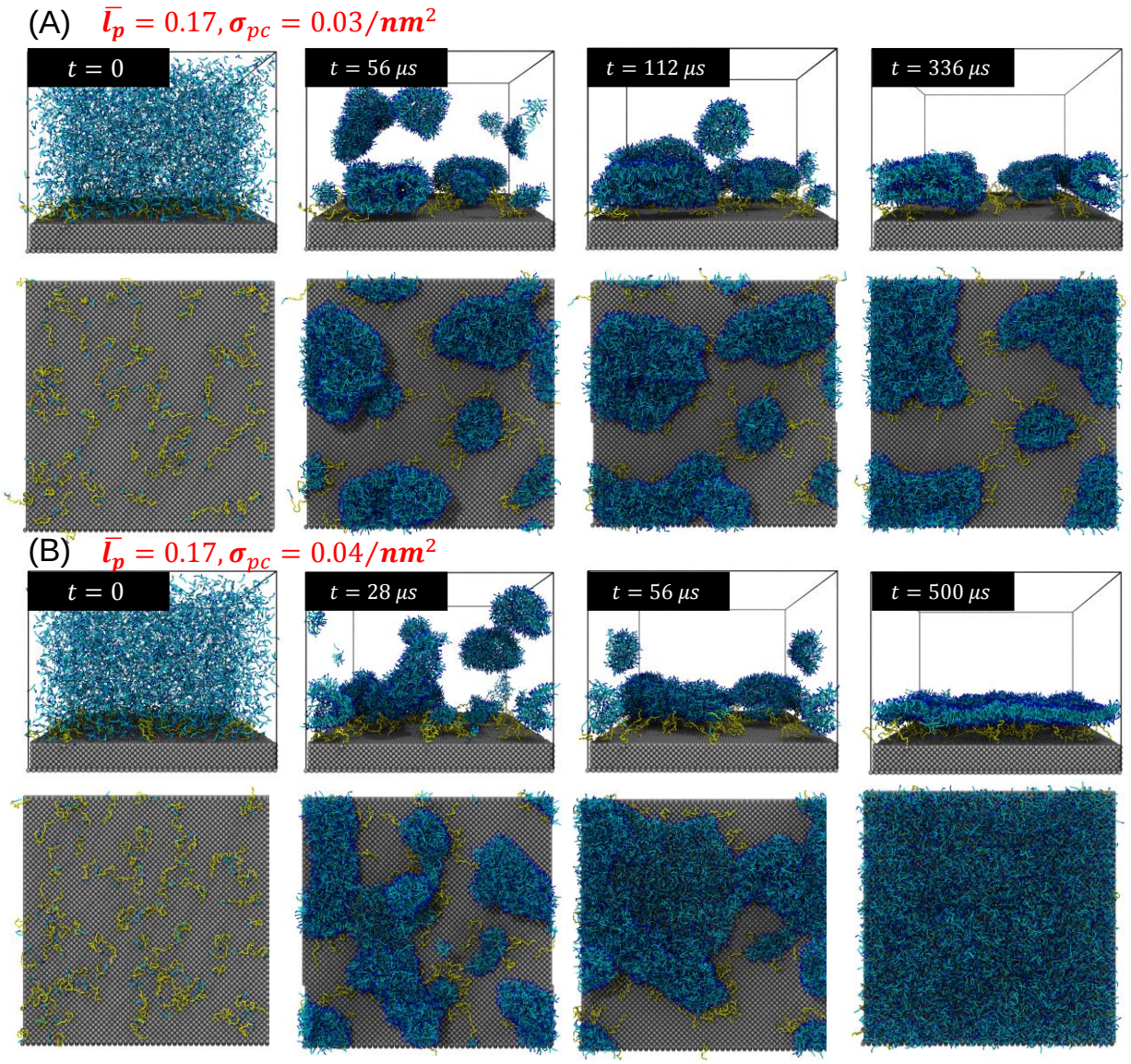

Figure S11. Self-assembly process of planar tethered lipid bilayers with polymer normalized persistence length of $\bar{l}_p = 0.17$. As we can see in Figures (A) and (B), an intact planar lipid bilayer can be assembled at the grafting density $\sigma_{pc} = 0.04\ / nm^2$. However, at $\sigma_{pc} = 0.03\ / nm^2$, an intact bilayer cannot be formed. Therefore, the critical grafting density for $\bar{l}_p = 0.17$ is around $\sigma_{pc} = 0.04\ / nm^2$.

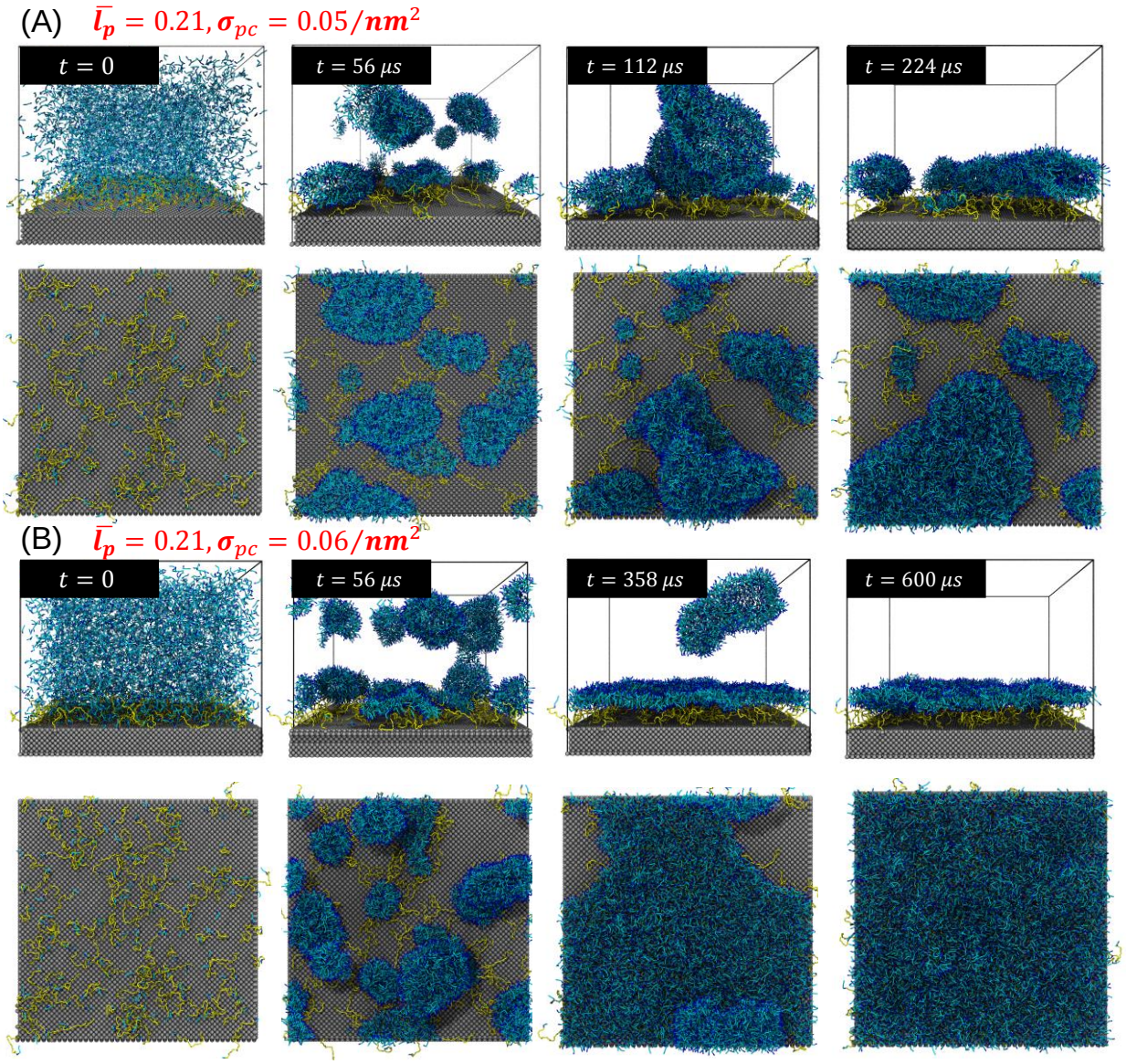

Figure S12. Self-assembly process of planar tethered lipid bilayers with polymer normalized persistence length of $\bar{l}_p = 0.21$. As we can see in Figures (A) and (B), an intact planar lipid bilayer can be assembled at the grafting density $\sigma_{pc} = 0.06\ / nm^2$. However, at $\sigma_{pc} = 0.05\ / nm^2$, an intact bilayer cannot be formed. Therefore, the critical grafting density for $\bar{l}_p = 0.21$, is around $\sigma_{pc} = 0.06\ / nm^2$.

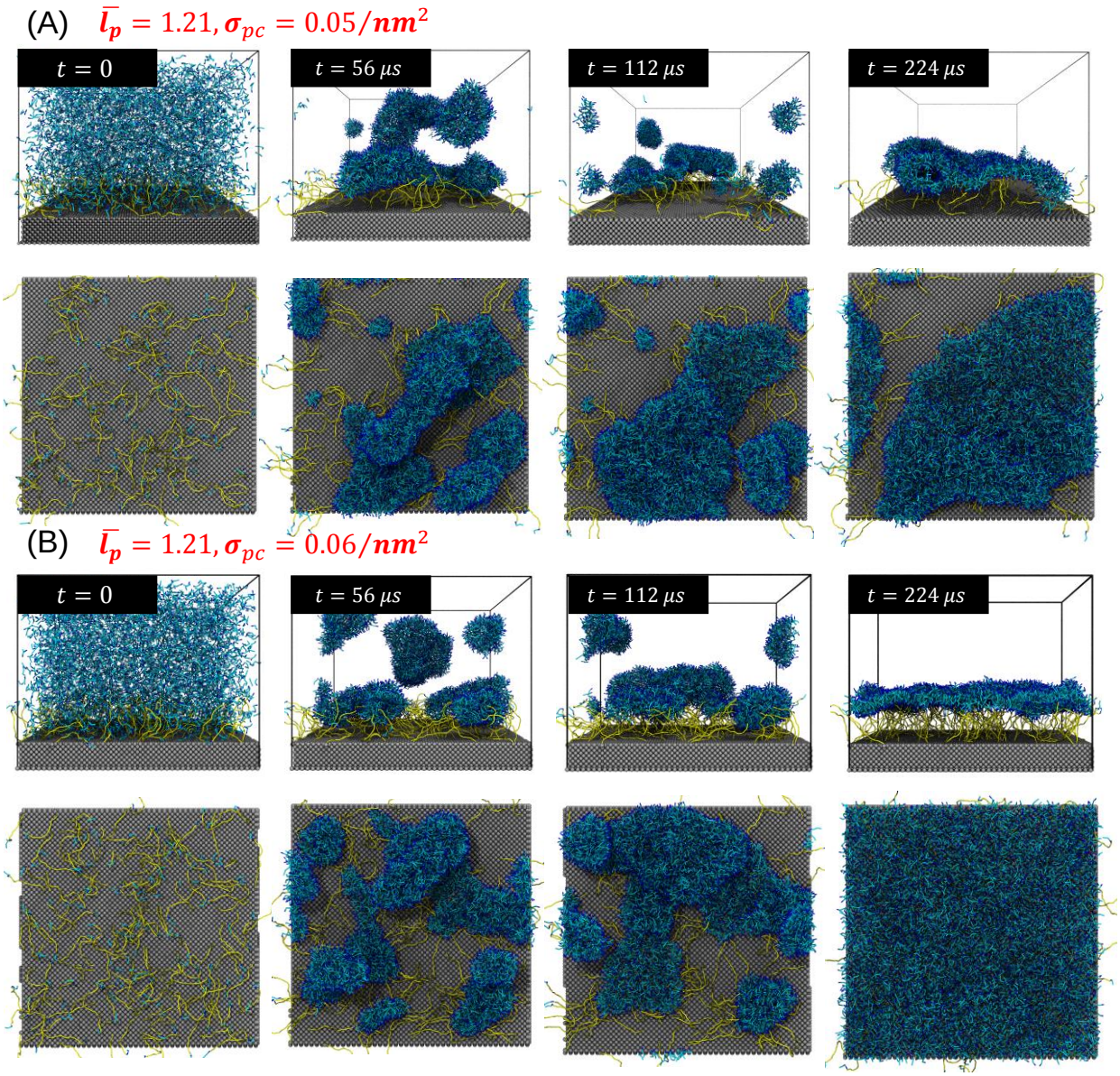

Figure S13. Self-assembly process of planar tethered lipid bilayers with polymer normalized persistence length of $\bar{l}_p = 1.21$. As we can see in Figures (A) and (B), an intact planar lipid bilayer can be assembled at the grafting density $\sigma_{pc} = 0.06\ / nm^2$. However, at $\sigma_{pc} = 0.05\ / nm^2$, an intact bilayer cannot be formed. Therefore, the critical grafting density for $\bar{l}_p = 1.21$, is around $\sigma_{pc} = 0.06\ / nm^2$.

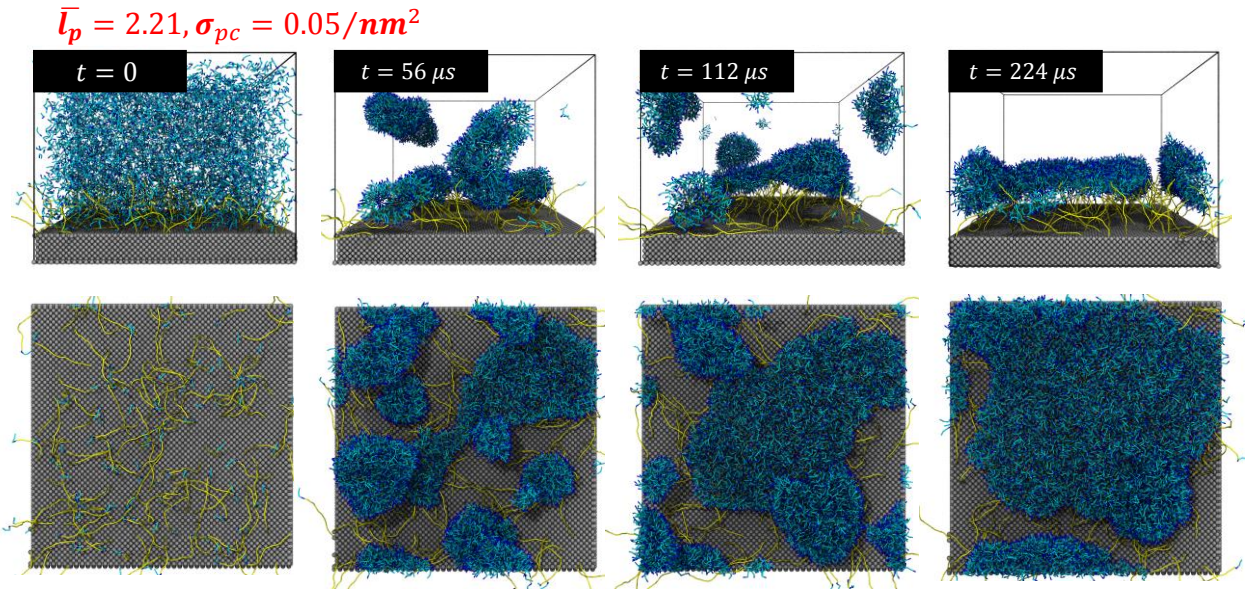

Figure S14. Self-assembly process of a planar tethered lipid bilayer with polymer normalized persistence length of $\bar{l}_p = 2.21$. At $\sigma_{pc} = 0.05\ /\ nm^2$, an intact bilayer cannot be formed. As given in the main text, an intact planar lipid bilayer can be assembled at the grafting density $\sigma_{pc} = 0.06\ /\ nm^2$. Therefore, the critical grafting density for $\bar{l}_p = 2.21$ is around $\sigma_{pc} = 0.06\ /\ nm^2$.

8. References

1. Gittes, F., et al., Flexural rigidity of microtubules and actin filaments measured from thermal fluctuations in shape. The Journal of cell biology, 1993. **120**(4): p. 923-934.
2. Baumann, C.G., et al., Ionic effects on the elasticity of single DNA molecules. Proceedings of the National Academy of Sciences, 1997. **94**(12): p. 6185-6190.