ELECTRONIC SUPPORTING INFORMATION (ESI)

Self-assembled Core-Polyethylene Glycol-Lipid Shell (CPLS) Nanoparticles Yield High Stability in Shear Flow

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1. Model and methodology

1.1. DPD model for lipid bilayer

Table S1: Interaction parameters, a_{ij} , between beads *i* and *j*, in the DPD simulation. S, H, T, E and P represent solvent (water), hydrophilic lipid head, hydrophobic lipid tail, PEG and NP (or substrate) beads, respectively.

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$a_{ij}(k_{\rm B}T/r_0)$	S	Η	Т	E	Р
S	25.0	30.0	75.0	26.3	100.0
Н	30.0	30.0	35.0	26.3	100.0
Т	75.0	35.0	10.0	33.7	100.0
E	26.3	26.3	33.7	25.0	100.0
Р	100.0	100.0	100.0	100.0	0



Figure S1: $H_3(T_4)_2$ model for the lipid molecule (left) and the corresponding planar lipid bilayer in the simulation box (right). The hydrophilic heads and hydrophobic tails of the lipid molecule are colored by blue and cyan respectively. The solvent (water) beads are not shown for clarity.

According to the lipid model developed by Lipowsky et al. [1,2], the lipid molecule is represented by the $H_3(T_4)_2$ model, as shown in Fig. S1. Two lipid tails (with four tail beads each) are connected with two head beads, while the head group contains three head beads. Adjacent beads making the lipid molecules are connected by the harmonic spring potential

Electronic Supporting Information (ESI)

 $U_{s2} = K_{s2}(r_{ij} - r_s)^2$, with spring coefficient $K_{s2} = 64 k_B T/r_0^2$, and equilibrium distance $r_s = 0.5 r_0$. An angular potential $U_{\theta 2} = K_{\theta 2}(1 - \cos \theta)$ with $K_{\theta 2} = 15 k_B T$ is applied to guarantee the stiffness of the lipid tails. Note that bead 2 and 3 are also involved in the angular potentials with beads 4,5 and beads 8,9 respectively. The pair-wise interactions concerning lipids-lipids and lipids-water are taken from the previous studies [1,2], as given in Table. S1.

1.2. DPD model for polyethylene glycol



Figure S2: DPD models for PEG polymer and NP core. (A) DPD model of PEG polymer. The insert in the left shows three connected monomers of PEG polymer. The model of anchored lipid is the same as the lipid in above bilayer. The lipid heads and tails are colored by tan and gray respectively for comparison. (B) The pair radial distribution function of NP core. The inserted figure is the cross-sectional view of the NP core.

Polyethylene glycol (PEG) is a hydrophilic polymer with chemical structure H-(O-CH₂-CH₂)_n-OH, which is also known as the polyethylene oxide (PEO) or polyoxyethylene (POE), depending on its molecule weight. To efficiently model the PEG polymer in our DPD simulations, we adopt the coarse-grained model for PEG developed by Lee *et al* [3]. In this model, each ethylene oxide (O-CH₂-CH₂) group has been coarse-grained into one bead (cf. Fig. S2). The neighboring beads on each PEG chain are connected by a harmonic bond

$$U_{s1} = K_{s1}(r_{ij} - r_s)^2 \tag{1}$$

where K_{s1} is the bond potential constant, r_{ij} and r_s are the instantaneous and equilibrium bond lengths between PEG monomers, respectively. Here $K_{s1} = 2111.3 k_{\rm B}T/r_0^2$ and $r_s = 0.4125 r_0$. The angle potential formed by a triplet is described by

$$U_{\theta 1} = K_{\theta 1} (\cos \theta - \cos \theta_0)^2 \tag{2}$$

where $K_{\theta 1}$ is the angle potential constant, θ and θ_0 are the instantaneous and equilibrium angles formed by two consecutive bonds, respectively. $K_{\theta 1} = 16.4946 k_{\rm B}T$ and $\theta_0 = 130^{\circ}$.

In the previous work done by Lee *et al* [3], the pair interactions are described by the classical Lennard-Jones 6-12 potential. However, in the DPD simulation, the pair interactions are represented by the conservative force \mathbf{F}_{ij}^C with strength of repulsion parameter a_{ij} . According to the previous experimental [4] and computational [5] studies, we set $a_{\text{ES}} = 26.3 \ k_{\text{B}}T/r_0$ and $a_{\text{EE}} = 25 \ k_{\text{B}}T/r_0$. Here the subscripts E and S denote the ethylene oxide and solvent, respectively. The interaction between PEG beads and lipid beads are chosen to reflect the hydrophilicity of PEG polymer, i.e. the a_{ij} of PEG-lipid head is the same as PEG-water. While the a_{ij} of PEG-tail is the same as the one between lipid head and lipid tail.

To validate and verify the PEG model adopted in our DPD simulation, we have studied the radius of gyration (R_g) and end-to-end distance (R_{ee}) of PEG with different chain lengths N. The simulation box of size $(30 \times 30 \times 30) r_0^3$ with periodical boundary conditions applied along x, y and z directions. A single PEG chain with length $N \in [9, 76]$ is inserted into the simulation box. Then, the additional solvent beads are added into the simulation box to satisfy the particle density $3.0 r_0^{-3}$. The system has been firstly equilibrated around 2 million time steps. Then, the coordinates of PEG chain have been saved every 2000 time steps in another 2 million time step simulation. The R_g and R_{ee} predicted by our DPD simulations are in good agreement with the values obtained from all-atom and coarse-grained (CG) simulations, reported by Lee *et al* [3], as given in our previous study [6].

1.3. DPD model for nanoparticle core

The NP core is composed of 1575 beads with a radius $5r_0$. These beads are arranged on a FCC lattice with lattice parameter $0.8r_0$, as shown in the pair radial distribution function in Fig. S2. To get a smooth spherical surface, the core is covered by a layer of spherical shell beads. These shell beads distribute evenly on the surface. All of these produce a tight packing of the core with number density of 3 r_0^{-3} . The whole NP core moves like a rigid body during the simulation [7] to mimic the motion of a hard metal core. Large repulsion between beads of NP core and other beads ($a_{ij} = 100 k_B T/r_0$) is applied to prevent the penetrations of water, polymer and lipid beads. The interaction between NP core beads are turned off since the NP is a rigid body during the simulations.

2. Bilayer tension

The surface tension of bilayer is defined as the integral of difference between normal and lateral component of the pressure tensor [5,8].

$$\tau = \int dz [p_{zz}(z) - 1/2(p_{xx}(z) + p_{yy}(z))]$$

= $A^{-1} \sum_{i < j} (F_{ij,z} z_{ij} - 1/2(F_{ij,x} x_{ij} + F_{ij,y} y_{ij}))$ (3)

where z-axis is the normal direction of the bilayer interface. p_{xx} , p_{yy} or p_{zz} are the pressure components for x, y and z directions, respectively. A is the total area of the planar lipid bi-

layer in the xy-plane. F_{ij} is the total conservative force between beads i and j.

Due to the fact that it is difficult to directly measure the tension of vesicle through simulations [9], here, we try to estimate the bilayer tension by calculating the lipid area. To determine the relationship between bilayer tension and lipid area, planar bilayers and PEG polymers tethered planar bilayers with area of $(50 \times 50) r_0^2$ are built (cf. Figs. S3. A and B). The grafting density of PEG polymers are the same as the one of CPLS NPs in the main test. Afterwards, the simulation box sizes along x and y directions are varied simultaneously to change the bilayer area, the box size along z direction is correspondingly altered to ensure the constant bead density. To capture the feature that the relative position of tethered points on NP core will keep unchanged for CPLSs NP under shear stress, the tethered points on the planer substrate is kept unmoved during simulation. The tension of pure bilayer or PEG polymers tethered bilayer is calculated according to the above equation in equilibrium states, as given in Figs. S3. C and D.



Figure S3: Relationship between bilayer tension and lipid area. (A) Planar bilayer with free lipids only. (B) PEG polymers (N = 60) tethered planar bilayer with grafting density equal to 1.0 chains $/r_0^2$.(C) The relationship between bilayer tension and lipid area for a pure lipid bilayer. (D) The relationship between bilayer tension and lipid area for tethered lipid bilayer with different PEG polymers. N represent PEG polymerization degree. 'free' here denotes the pure lipid bilayer for comparison. Water beads are not shown for clarity in A and B.

3. Stability



Figure S4: Evolution process of pore formation in vesicles with different sizes. (A) The pore formation process in a vesicle with radius $R = 12.17r_0$ under shear rate of $\dot{\gamma} = 0.045\tau^{-1}$. (B) The pore formation process in a vesicle with radius $R = 13.17r_0$ under shear rate of $\dot{\gamma} = 0.04\tau^{-1}$.



Figure S5: Motion of CPLS NPs under shear flow. (A) CPLS NP ($R = 11.43r_0$) under shear rate of $\dot{\gamma} = 0.625\tau^{-1}$ (Same with the Fig. 4A in the main text). (B-C) Snapshots of the NP core, a tethered polymer and marked lipid at different perspectives. For figures in (A-B), the directions of x and z are within the plane of paper. And directions of y is perpendicular to the plane of paper and point to it. For figures in (C), the directions of x and y are within the plane of paper. And directions of z is perpendicular to the plane of paper and point to it.



Figure S6: Evolution process of pore formation in CPLS NPs of different sizes. (A) Snapshots of CPLS NP ($R = 10.28r_0$) with PEG polymers N = 10 under shear rate of $\dot{\gamma} = 0.09\tau^{-1}$. (B) Snapshots of CPLS NP ($R = 12.51r_0$) with PEG polymers N = 30 under shear rate of $\dot{\gamma} = 0.05\tau^{-1}$. (C) Snapshots of CPLS NP ($R = 13.44r_0$) with PEG polymers N = 40 under shear rate of $\dot{\gamma} = 0.045\tau^{-1}$. (D) Snapshots of CPLS NP ($R = 15.03r_0$) with PEG polymers N = 60 under shear rate of $\dot{\gamma} = 0.045\tau^{-1}$.

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