Supporting Information

Encapsulation and Release of Drug Nanoparticles in Functional Polymeric Vesicles

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Simulation Method and Model Additional Information

Similar to MD simulations, DPD captures the time evolution of a many-body system by solving Newton's equation of motion:[1]

$$\frac{\mathrm{d}\vec{r}_i}{\mathrm{d}t} = \vec{v}_i, \quad \frac{\mathrm{d}\vec{v}_i}{\mathrm{d}t} = \frac{\vec{f}_i}{m_i}$$

The non-bonding force acting on the particles is a pair of additional forces, consisting of three parts, $\vec{f}_i = \sum_{j \neq i} \left(\vec{F}^{\mathrm{C}}_{ij} + \vec{F}^{\mathrm{D}}_{ij} + \vec{F}^{\mathrm{R}}_{ij} \right)$, where the sum runs over all particles j within a certain cutoff radius r_{c}. In here, $\vec{v}_i$, m_i, $\vec{f}_i$ represents the velocity, mass, and force acting on the i-th particle, respectively. The non-bonding force acting on the i-th particle is a pair of additional forces $\vec{f}_i$ that contain conservative forces $\vec{F}^{\mathrm{C}}_{ij}$, dissipative forces $\vec{F}^{\mathrm{D}}_{ij}$, and random forces $\vec{F}^{\mathrm{R}}_{ij}$. The sum of the forces acts on all particles within the cut-off radius r_{c}, beyond which the force is ignored. The conservative force $\vec{F}^{\mathrm{C}}_{ij}$ is a soft repulsion taking the form of $\vec{F}^{\mathrm{C}}_{ij} = a_{ij}\ \omega(r_{ij})\hat{r_{ij}}$, where a_{ij} is the repulsive interaction parameter between particle i and j, $\vec{r}_{ij} = \vec{r}_i - \vec{r}_j$, $r_{ij} = |\vec{r}_{ij}|$, $\hat{r_{ij}} = \vec{r}_{ij} / r_{ij}$. The weight function $\omega(r_{ij})$ provides the range of interaction for DPD particles with a b commonly used choice: $\omega(r_{ij}) = 1 - r_{ij} / r_{\mathrm{c}}$ for $r_{ij} \leqslant r_{\mathrm{c}}$ and $\omega(r_{ij}) = 0$ for $r_{ij} > r_{\mathrm{c}}$. The dissipative force is a friction force that acts on the relative velocities of particles, and it is defined by $\vec{F}^{\mathrm{D}}_{ij} = -\gamma\omega^2\ (r_{ij})(\hat{r_{ij}} \times \vec{v}_{ij})\ \hat{r_{ij}}$, where γ is the friction coefficient governing the magnitude of the dissipative force and $\vec{v}_{ij} = \vec{v}_i - \vec{v}_j$. The random force that compensates for the loss of kinetic energy is defined by $\vec{F}^{\mathrm{R}}_{ij} = \sigma\omega(r_{ij})\theta_{ij}\ \hat{r_{ij}}$, where θ_{ij} is a randomly fluctuating variable with Gaussian statistics and $\sigma^2 = 2\gamma k_{\mathrm{B}}T$.

We use a finitely extensible nonlinear elastic (FENE) potential between the consecutive particles: [2] $V_{\mathrm{FENE}}(r_{ij}) = -1/2kR_0^2 \ln[1 - r_{ij}/\ R_0)^2]$ for $r_{ij} < R_0$ and $V_{\mathrm{FENE}}(r_{ij}) = \infty$ for $r_{ij} \geq R_0$. In our simulation, we set $k = 30$ and $R_0 = 1.5r_{\mathrm{c}}$. The value of the FENE spring k is large enough that the bond crossing is not energy efficient. There is no additional angular force between the copolymer arms. Simulations with different initial random configurations and various box sizes have been implemented. Simulation results show that the aggregate morphology in the equilibrium state is independent of the initial conditions. Except for the amount of aggregate in the box after reaching equilibrium, boxes of different sizes will not affect the formation of aggregate.[3] Thus, we simulated in a cube box (30^3) with a numerical density of 3 under periodic boundary conditions. In addition, in this simulation, all of the polymer and solvent beads are of the same mass, $m = 1$. The interaction cutoff radius of the block copolymer and the solvent particles is set to $r_c = 1$ as the unit of length, and the energy scale $k_BT = 1$. Here, k_B is the Boltzmann constant and T is the temperature. The time unit τ is defined as $\tau = (mr_c^2 / k_BT)^{1/2}$. The time integration of the Newton's equation of motion was done using the improved velocity-Verlet algorithm with $\lambda = 0.65$ and $\Delta t = 0.03$.[1] The amplitude of the random noise is set to $\sigma = 3.0$. A typical DPD simulation requires only about 10^5 steps to achieve the balance.[1, 4] In our simulation, we carried out at least 2.0×10^6 steps for each simulation, and the last 2.0×10^5 steps are used for statistics.

Generally speaking, the pair-wise repulsive interaction parameter between the same type of DPD particles is set to $a_{ii} = 25$. The interaction parameter between particles i and j can be estimated by the relationship between the a_{ii} and the Flory–Huggins interaction parameter χ_{ij} at $\rho = 3$ according to the relation:[1] $a_{ij} \approx a_{ii} + 3.27\chi_{ij}$. The interaction parameters can be determined in calculations for dimensionless compatibility. Therefore, the value of $a_{ij} \leq 25$ corresponds to $\chi_{ij} \leq 0$, which indicates that the beads i and j are fairly compatible. As the incompatibility between i and j increases, a_{ij} increases from 25. Therefore, by reasonably changing these parameters, we can achieve the effect of modeling long polymer chains on relatively small DPD chains with different interaction parameters.[1, 5] Here, we set the interaction parameters between the same beads to be 25, i.e., $a_{AA} = a_{BB} = a_{SS} = 25$.

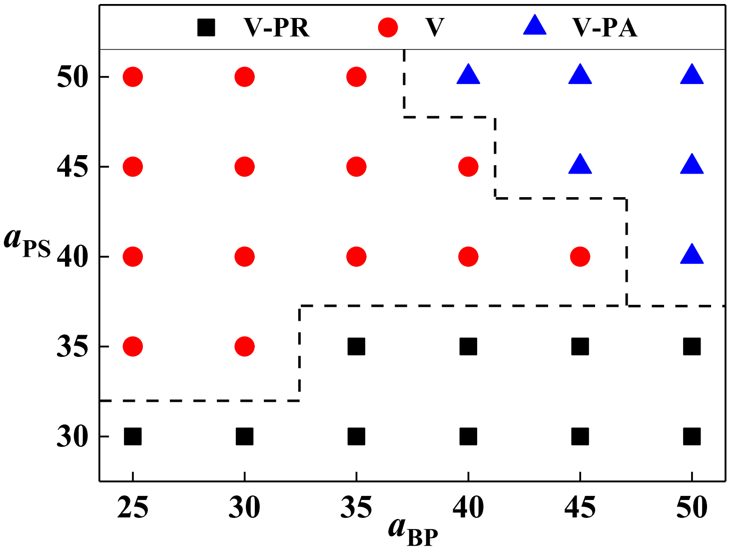

Figure S1. Morphological phase diagram of the self-assembled aggregates formed by R_P =2.00, R_D =1.75 with changing a_{BP} and a_{PS} at φ_P = 0.007, φ_D = 0.010.

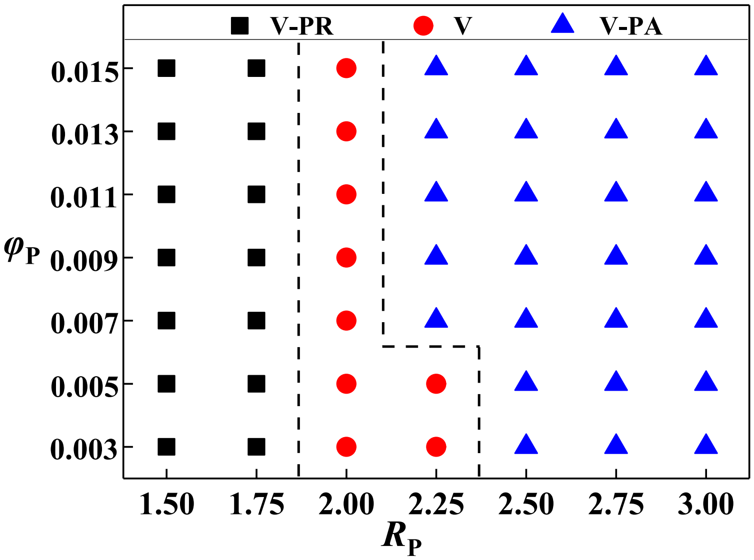

Figure S2. Phase diagram of the self-assembled morphologies by changing the size of nanoparticles R_P and its concentration φ_P, combined with R_D = 1.75, φ_D = 0.030.

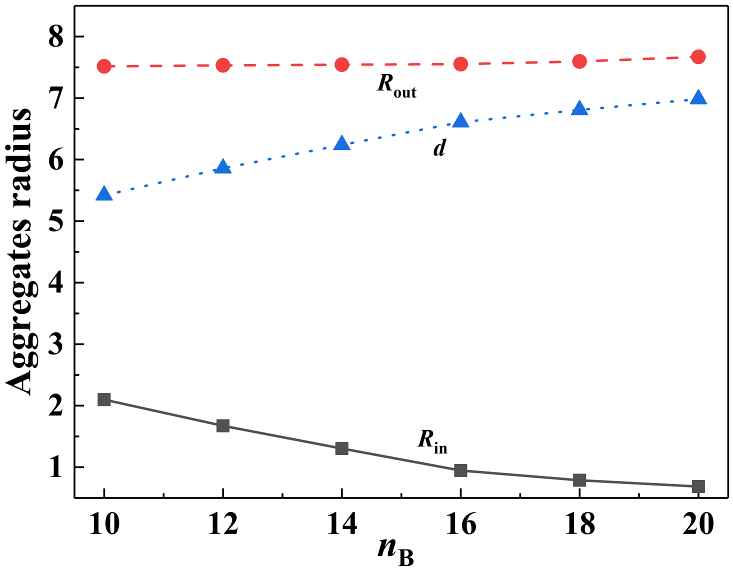

Figure S3. Relationship between the averaged aggregate radius and the length of block B n_B with $R_D = 1.75$, $R_P = 2.00$ at $\varphi_D = 0.010$, $\varphi_P = 0.007$. The outer and inner radii are the average distance from the geometric center of the vesicle to the two layers of hydrophilic beads. The wall thickness is determined by the difference between the outer hydrophobic membrane and the inner hydrophobic membrane.

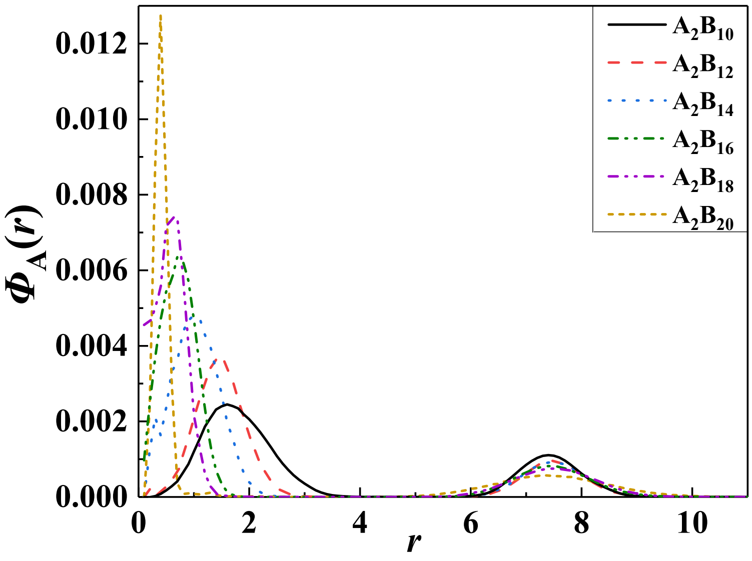

Figure S4. Radial density distributions of the hydrophilic block $\Phi_A(r)$ plotted as a function of the increasing distance r from the geometric center of the aggregates, formed by A_2B_n diblock copolymers with $R_D = 1.75$, $R_P = 2.00$ at $\varphi_D = 0.010$, $\varphi_P = 0.007$. Note that normalizations have been chosen such that $4\pi\int_0^R \Phi_A(r) r^2 \mathrm{d}r = 1$.

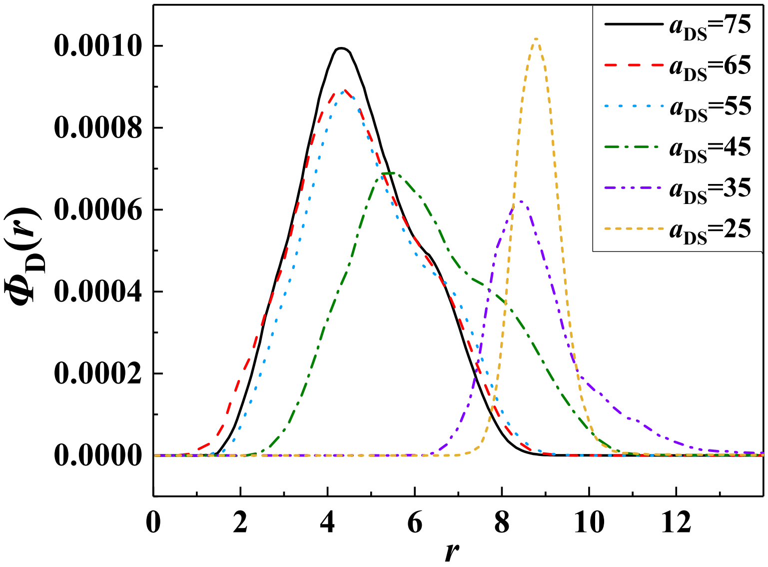

Figure S5. Radial density distributions of the drugs $\Phi_D(r)$ plotted as a function of the distance r from the geometric center of the aggregates, formed by A_2B_{10} diblock copolymers with $R_D = 1.75$, $R_P = 2.00$, $\varphi_P = 0.007$ and $\varphi_D = 0.020$. Note that normalizations have been chosen such that

$$4\pi\int_0^R \Phi_D(r) r^2 \mathrm{d}r = 1$$

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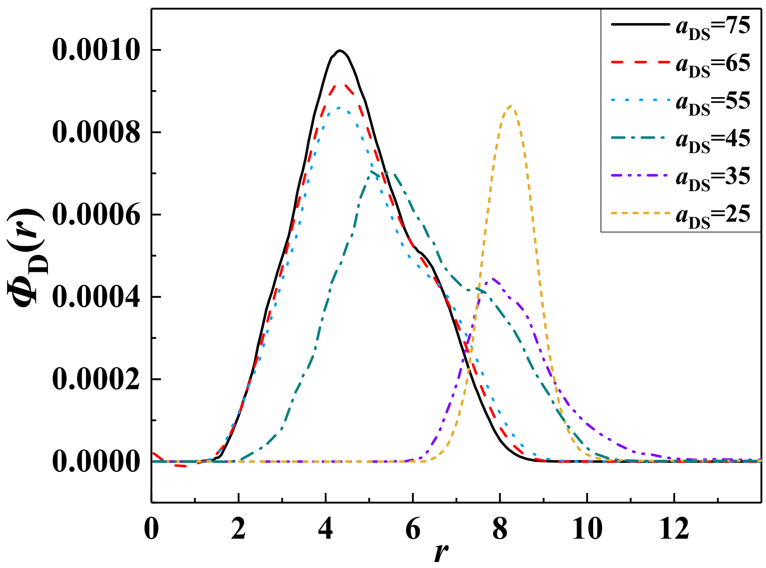

Figure S6. Radial density distributions of the drugs $\Phi_D(r)$ plotted as a function of the distance r from the geometric center of the aggregates, formed by A_2B_{10} diblock copolymers with a_{DS} changed stepwise: 75-65-55-45-35-25 at $R_D = 1.75$, $R_P = 2.00$, $\varphi_P = 0.007$ and $\varphi_D = 0.020$. Note that normalizations have been chosen such that $4\pi\int_0^R \Phi_D(r) r^2 \mathrm{d}r = 1$.

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